THE LIVER WEEK 2025

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THE LIVER WEEK 2025

A Big Welcome to the Liver Festival in Gyeongju, Korea!

May 29 - 31, 2025 | HICO, Gyeongju, Korea

The Korean Association for the Study of the Liver

THE KOREAN ASSOCIATION OF HBP SURGERY

THE KOREAN LIVER CANCER ASSOCIATION

The Korean Liver Transplantation Society

DAY 1 | Thursday, May 29, 2025

ROOM 1

ROOM 3

Basic Research 1 — Beginners' Guide for Basic Research

Basic Research 2 — New Approaches in Translational Science

Young Investigator Meeting

Research Assistant Program

ROOM 6

Ultrasound Trainee Session

ROOM 7

Ultrasound Trainer Session 1

Ultrasound Trainer Session 2

DAY 2 | Friday, May 30, 2025

ROOM 1

KASL Special Interest Group 1. The KASL Steatotic Liver Disease Study Group — Challenges to Overcome in the Era of MASLD

KASL-AASLD Joint Symposium 1 — Randomized Controlled Trials (RCTs) in Hepatology

ROOM 2

ROOM 3

DAY 3 | Saturday, May 31, 2025

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ROOM 2

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Plenary Presentation 1

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Free Paper Presentation

1. Hepato-Biliary and Pancreas Surgery

2. Liver Cancer, Clinical 1

3. MASLD, Clinical

4. HBV Basic and ALD

5. Acute Liver Failure and DILI

6. HBV 1

7. Liver Cancer, Basic

8. Liver Cancer, Clinical 2

9. HBV 2

10. HCV

11. MASLD, LC and Others, Basic

12. Liver Transplantation 1

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Oral Poster Presentation 1

1. Autoimmune Disease

2. MASLD and ALD, Basic

3. MASLD, Clinical 1

4. LC, Clinical and Liver Failure

5. Liver Transplantation 1

6. Liver Cancer, Basic 1

7. Liver Cancer, Clinical 1

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13. Liver Cancer, Clinical 3

14. HBV and LC, Basic

15. Others

16. Liver Cancer, Clinical 4

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18. Liver Cancer, Basic 3

19. Liver Cancer, Clinical 5

20. Biliary and Pancreatic Surgery

Poster Exhibition

1. Acute Liver Failure and Drug-Induced Liver Injury

2. Alcohol-Related Liver Disease, Basic

6. HBV, Basic

7. HBV, Clinical

8. HCV, Basic

9. HCV, Clinical

10. Liver Cancer, Basic

11. Liver Cancer, Clinical

12. Liver Cirrhosis, Portal Hypertension with Cx. Basic

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14. Liver Surgery

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A Big Welcome to the Liver Festival in Gyeongju, Korea

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DAY 1: May 29 (Thu.)

PG Course 1

Viral Hepatitis

Chairs:

So Young Kwon (Konkuk Univ.)
Sang Hoon Park (Hallym Univ.)

Jeong Eun Song

Daegu Catholic University

Self Introduction

Prof. Jeong Eun Song graduated from Daegu Catholic University School of Medicine with her medical degree in 2009 and completed his internship at Seoul Asan Medical Center and residency at the Department of Internal Medicine at Daegu Catholic University Medical Center, receiving her diploma in Internal Medicine in 2015.

She is a Professor of the Department of Internal Medicine, Daegu Catholic University School of Medicine.

Since 2019, she has been active as a committee member in various organizations such as the Korean Association for the Study of the Liver, the Korean Liver Cancer Association, and the Korean Society of Clinical Ultrasound.

Research Interests

Viral Hepatitis, Autoimmune Liver Disease, Hepatocellular Carcinoma

Representative Publications

1. Jeong Eun Song, Min Kyu Kang, Yu Rim Lee, et al. Multicenter analysis of clinical features and prognosis of COVID-19 patients with hepatic impairment. Gut Liver. 2021;15:606-615.
2. Min Kyu Kang, Yu Rim Lee, Se Young Jang, Won Young Tak, Young Oh Kweon, Jeong Eun Song, Rohit Loomba, Soo Young Park, Jung Gil Park. Impact of metabolic factors on risk of cardiovascular disease in nondiabetic metabolic dysfunction-associated fatty liver disease. Hepatol Int. 2023 Jun;17(3):626-635.
3. Ah Young Yang, Kiryeong Kim, Hyun Hee Kwon, Jaechan Leem, Jeong Eun Song. 6-Shogaol Ameliorates Liver Inflammation and Fibrosis in Mice on a Methionine- and Choline-Deficient Diet by Inhibiting Oxidative Stress, Cell Death, and Endoplasmic Reticulum Stress. Molecules. 2024 Jan 15;29(2):419.
4. Min Kyu Kang, Jeong Eun Song, Se Young Jang, et al. The Clinical Significance of Myosteatosis in Survival Outcomes in Patients with Hepatocellular Carcinoma Treated with Sorafenib. Cancers (Basel). 2024 Jan 20;16(2):454.
5. Min Kyu Kang, Jeong Eun Song, Rohit Loomba, Soo Young Park, Won Young Tak, Young Oh Kweon, Yu Rim Lee, Jung Gil Park. Comparative associations of MASLD and MAFLD with the presence and severity of coronary artery calcification. Sci Rep. 2024 Oct 2;14(1):22917

PG Course 1 | DAY 1: May 29 (Thu.) | ROOM 1 [3F]

Optimal Timing Antiviral Therapy for Hepatitis B Virus: When to Start and When to Stop?

Jeong Eun Song *Daegu Catholic University*

Despite substantial progress in the management of chronic hepatitis B (CHB), determining the optimal timing to initiate and discontinue nucleos(t)ide analogue (NUC) therapy remains a critical and evolving challenge. The timing of treatment not only impacts viral suppression and the risk of complications such as cirrhosis and hepatocellular carcinoma (HCC), but also determines the possibility of achieving a functional cure, defined as hepatitis B surface antigen (HBsAg) loss.

Initiation of antiviral therapy has traditionally followed stringent criteria involving HBV DNA levels, alanine aminotransferase (ALT), and fibrosis stage. However, emerging evidence suggests that patients outside current guideline recommendations—particularly those in the gray zone (indeterminate phase)—still face substantial risks of liver-related complications. Expanding treatment indications may prevent disease progression, reduce HCC incidence, and be cost-effective from a population health perspective.[1] Studies such as the TORCH-B[2] and population modeling analyses support simplified or universal treatment strategies, although issues of compliance, cost, and safety must be considered.

Discontinuation of NUCs, particularly in HBeAg-negative, non-cirrhotic patients with sustained viral suppression, has gained interest as a strategy to induce immune reactivation and promote HBsAg clearance. Pivotal studies and large cohort data, including the RETRACT-B study[3] and the Taiwanese cohort study[4], show that post-treatment flares may, in select patients, enhance the chance of HBsAg loss. However, these benefits come with risks. Hepatic flares occurred in over 30% of patients after cessation, with 3–5% experiencing severe flares, and rare cases of hepatic decompensation and death have been reported.

Current evidence supports a highly individualized approach. Initiation of therapy should increasingly consider patients in the gray zone (indeterminate phase), particularly those with significant histologic activity or risk factors for disease progression. Conversely, discontinuation strategies should be confined to carefully selected patients, under close post-cessation monitoring.

This lecture will review current international guidelines, recent pivotal trials, and real-world cohort studies to provide an evidence-based framework for clinicians to determine when to start and when to stop antiviral therapy in patients with chronic hepatitis B. A marker-guided, risk-stratified strategy offers the

best potential to balance therapeutic benefits with safety, while inching closer toward the ultimate goal of HBV functional cure.

References

1. Hui RW, Mak LY, Fung J, Seto WK, Yuen MF. Expanding treatment indications in chronic hepatitis B: Should we treat all patients? Hepatol Int 2025;19:304-314.
2. Hsu YC, Chen CY, Chang IW, Chang CY, Wu CY, Lee TY, Wu MS, et al. Once-daily tenofovir disoproxil fumarate in treatment-naive Taiwanese patients with chronic hepatitis B and minimally raised alanine aminotransferase (TORCH-B): a multicentre, double-blind, placebo-controlled, parallel-group, randomised trial. Lancet Infect Dis 2021;21:823-833.
3. Dongelmans EJ, Hirode G, Hansen BE, Chen CH, Su TH, Seto WK, Furquim d'Almeida A, et al. Predictors of hepatic flares after nucleos(t)ide analogue cessation - Results of a global cohort study (RETRACT-B study). J Hepatol 2025;82:446-455.
4. Jeng WJ, Chen YC, Chien RN, Sheen IS, Liaw YF. Incidence and predictors of hepatitis B surface antigen seroclearance after cessation of nucleos(t)ide analogue therapy in hepatitis B e antigen-negative chronic hepatitis B. Hepatology 2018;68:425-434.

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Jung Hyun Kwon

The Catholic University of Korea

Self Introduction

Prof. Jung Hyun Kwon is a Professor of the Department of Internal Medicine, The Catholic University of Korea and is currently holding a position of Chief of Hepatobiliary Center of Incheon Saint Mary's hospital, simultaneously.

She graduated from The Catholic University of Korea, College of Medicine with his medical degree in 2000 and completed her internship and residency at the Department of Internal medicine, at Seoul Saint Mary's Hospital, The Catholic University of Korea.

Since 2010, she has been taking a number of roles, including treasurer and informatics committee director of the Korean Association of the Study of the Liver (2019-2023) and treasurer director of the Korean Liver cancer study group (2023-2024).

Research Interests

Viral Hepatitis B Natural Course, Viral Hepatitis C Elimination, HCC Risk Factor

Representative Publications

1. Soon Kyu Lee, Soon Woo Nam, Jeong Won Jang and Jung Hyun Kwon*. Long-Term HBsAg Titer Kinetics with Entecavir/Tenofovir: Implications for Predicting Functional Cure and Low Levels. Diagnostics 2024, 14, 495.
2. Soon Kyu Lee, Jung Hyun Kwon*, Sung Won Lee, Hae Lim Lee, Hee Yeon Kim, Chang Wook Kim, Do Seon Song, U Im Chang, Jin Mo Yang, Soon Woo Nam, Seok-Hwan Kim, Myeong Jun Song, Ji Hoon Kim, Ahlim Lee, Hyun Yang, Si Hyun Bae, Ji Won Han, Heechul Nam, Pil Soo Sung, JeongWon Jang, Jong Young Choi, Seung Kew Yoon, Dong Jae Shim, Doyoung Kim and Myungsoo Kim. A Real-World Comparative Analysis of Atezolizumab Plus Bevacizumab and Transarterial Chemoembolization Plus Radiotherapy in Hepatocellular Carcinoma Patients with Portal Vein Tumor Thrombosis. Cancers 2023, 15, 4423.
3. Soon Kyu Lee, Jung Hyun Kwon*. HBeAg-Positive Grey-Zone Patients: Treatment Beyond Guideline? Clin Mol Hepatol . 2023 May 31.
4. Jina Kim 1, Jason Chia-Hsien Cheng 2, Taek-Keun Nam 3, Jin Hee Kim 4, Byoung Kuk Jang 5, Wen-Yen Huang 6, Hiroshi Aikata 7, Myungsoo Kim 8, Jung Hyun Kwon 9, Jinbo Yue 10, Victor Ho Fun Lee 11, Zhaochong Zeng 12, Jinsil Seong 1. Efficacy of Liver-Directed Combined Radiotherapy in Locally Advanced Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis. Cancers (Basel).
5. Lee SK, Kwon JH*, Lee SW, Jang JW, Nam H, Baik KW, Yoo SH, Nam SW, Sung PS, Bae SH, Choi JY, Yoon SK. Sustained Off Therapy Response after Peglyated Interferon Favors Functional Cure and No Disease Progression in Chronic Hepatitis B. Liver Int . 2021 Feb;41(2):288-294
6. Lee SW#, Kwon JH#, Lee HL, Yoo SH, Nam HC, Sung PS, Nam SW, Bae SH, Choi JY, Yoon SK, Han NI, Jang JW. Comparison of tenofovir and entecavir on the risk of hepatocellular carcinoma and mortality in treatment-naïve patients with chronic hepatitis B in Korea: a large-scale, propensity score analysis. Gut. 2020 Jul;69(7):1301-1308.

Challenges and Future Directions for Hepatitis B Virus Cure

Jung Hyun Kwon *The Catholic University of Korea*

Introduction

Chronic hepatitis B virus (HBV) infection remains a major global health burden, affecting nearly 300 million people and causing over 800,000 deaths annually due to complications such as cirrhosis and hepatocellular carcinoma (HCC)[1] Despite decades of therapeutic progress and the widespread adoption of HBV vaccination, a definitive cure remains elusive. Current management relies heavily on long-term nucleos(t)ide analogue (NA) therapy, which suppresses viral replication but rarely achieves durable off-therapy control. A functional cure—defined as sustained HBsAg loss with or without anti-HBs seroconversion—has emerged as a realistic intermediate goal, although it is achieved in only a small subset of patients. This presentation highlights key advances, with a special focus on the 2025 CMH consensus and its implications for future therapeutic strategies.[2,3]

I. Current Barriers to Cure

One of the main challenges in achieving a cure is the persistence of HBV in the form of covalently closed circular DNA (cccDNA) and integrated HBV DNA, both of which continue to express HBsAg despite viral suppression by NAs.[4,5] In HBeAg-negative individuals, integrated HBV DNA is thought to be the primary source of circulating HBsAg. This persistent antigenic burden contributes to T-cell exhaustion, characterized by impaired proliferation and reduced effector function of HBV-specific CD8+ T cells. The expression of inhibitory molecules such as PD-1, along with increased levels of immunoregulatory cytokines, further reinforces immune tolerance. Even after apparent HBsAg loss, residual transcriptionally active cccDNA may lead to reactivation or hepatocarcinogenesis.

II. Direct-Acting Antiviral Agents

The development of novel agents targeting different steps of the HBV life cycle has been a major focus of recent drug discovery. Entry inhibitors like bulevirtide block NTCP-mediated viral entry and are approved for HDV, but their role in HBV monoinfection remains limited.[6] Capsid assembly modulators (CAMs) such as ALG-000184 inhibit encapsidation of pgRNA, reduce cccDNA recycling, and have shown 1.0–1.5 log IU/mL reductions in HBsAg in some trials.[7,8] RNA interference (RNAi) therapies, including

antisense oligonucleotides (ASOs) like bepirovirsen [9,10] and siRNAs such as JNJ-3989 and VIR-2218[11-13] degrade HBV transcripts from both cccDNA and integrated DNA. The B-Clear study showed that 9–10% of patients on bepirovirsen achieved undetectable HBsAg by 24 weeks, particularly among those with baseline HBsAg levels <3 log IU/Ml.[9] Further, FXR agonists like vonafexor act as transcriptional repressors, though their effect on HBsAg levels remains modest (typically ~0.1 log IU/mL).[14]

III. Immune Modulatory Approaches

Immunologic restoration is a key pillar of HBV cure strategies. Approaches include the reversal of T-cell exhaustion, activation of innate immunity, and enhancement of virus-specific adaptive responses. Checkpoint inhibitors such as nivolumab and envafolimab have shown up to 0.5 log IU/mL reductions in HBsAg in selected patients, though immune-mediated hepatic inflammation remains a concern.[15] Toll-like receptor (TLR) agonists—selgantolimod (TLR8) and ruzotolimod (TLR7)—stimulate innate immune pathways and have achieved modest HBsAg declines (0.07–0.15 log IU/mL) in virally suppressed individuals.[16-18] Therapeutic vaccines aim to reinduce HBV-specific T cell responses and include candidates like VTP-300 and BRII-179.[19,20] VTP-300, based on ChAdOx and MVA viral vectors targeting polymerase, core, and surface proteins, induced ≥0.5 log IU/mL HBsAg decline in approximately 40% of participants, particularly when combined with low-dose pegylated interferon. Emerging monoclonal antibodies such as tobevibart and lenvervimab are being developed to neutralize circulating HBsAg and reduce antigen burden.[21] Although still in early development, these may play a role in future combination regimens.

IV. Combination Strategies and Future Concepts

Monotherapy with new agents has delivered limited success in achieving functional cure, prompting a shift toward rational combinations.[2] For instance, the REEF-1 and REEF-2 trials explored combinations of siRNAs (e.g., daplusiran or tomligisiran) with capsid assembly modulators (e.g., bersacapavir). Other regimens pair viral silencers (e.g., siRNA, CAM) with immune activators, such as checkpoint inhibitors, peg-IFN, or therapeutic vaccines. BRII-179, with or without IFN-α, has also been evaluated. Future trial designs are expected to incorporate patient-specific factors—such as baseline HBsAg level, prior treatment response, and immune status—to guide personalized combination regimens and optimize cure strategies.

V. Biomarker Development and Personalized Medicine

The use of predictive biomarkers has become central to patient stratification, response monitoring, and treatment personalization.[3] [22] HBV RNA, derived from pregenomic RNA, reflects ongoing transcription from cccDNA and serves as a marker of replication competence. Hepatitis B core-related antigen (HBcrAg) is particularly informative in HBeAg-negative individuals and correlates with cccDNA activity and relapse risk. Although intrahepatic cccDNA quantification is the gold standard, it is currently limited to research applications. The integration of these biomarkers into clinical protocols will help optimize treatment duration, identify appropriate candidates for treatment discontinuation, and inform adaptive therapy in real-time.

VI. Unmet Needs and Remaining Challenges

Despite progress, significant hurdles remain. Functional cure remains rare in patients with high baseline HBsAg levels, cirrhosis, or treatment-resistant HBV. Even after HBsAg clearance, residual cccDNA and integrated DNA may allow relapse or HCC progression. Safety concerns surrounding immune modulators and checkpoint inhibitors, particularly in vulnerable populations, must be balanced against potential benefits. Optimal sequencing and duration of combination therapy remain undefined. Access to novel agents is limited by cost and availability, especially in low-resource settings. Ultimately, the global elimination of HBV will require not only therapeutic innovation but also equitable access and healthcare infrastructure development.

Conclusion

In summary, the field of HBV therapeutics has entered a transformative phase. The shift toward finite-duration regimens, antigen-lowering strategies, immune restoration, and biomarker-guided therapy holds promise for achieving functional cure. While commercialized cure regimens remain elusive, multiple agents are progressing through phase II/III development, and combination trials have demonstrated encouraging efficacy. Continued investment in translational research, global collaboration, and access frameworks will be essential to realize the vision of HBV elimination.

References

1. Guidelines for the Prevention, Diagnosis, Care and Treatment for People with Chronic Hepatitis B Infection (Text Extract): Executive Summary. Infect Dis Immun 2024;4:103-105.
2. Hui RW, Mak LY, Fung J, Seto WK, Yuen MF. Prospect of emerging treatments for hepatitis B virus functional cure. Clin Mol Hepatol 2025;31:S165-181.
3. Yardeni D, Chang KM, Ghany MG. Current Best Practice in Hepatitis B Management and Understanding Long-term Prospects for Cure. Gastroenterology 2023;164:42-60.e46.
4. Yeo YH, Ho HJ, Yang HI, Tseng TC, Hosaka T, Trinh HN, et al. Factors Associated With Rates of HBsAg Seroclearance in Adults With Chronic HBV Infection: A Systematic Review and Meta-analysis. Gastroenterology 2019;156:635-646.e639.
5. Chevaliez S, Hézode C, Bahrami S, Grare M, Pawlotsky JM. Long-term hepatitis B surface antigen (HBsAg) kinetics during nucleoside/nucleotide analogue therapy: finite treatment duration unlikely. J Hepatol 2013;58:676-683.
6. Wedemeyer H, Aleman S, Brunetto MR, Blank A, Andreone P, Bogomolov P, et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. N Engl J Med 2023;389:22-32.
7. Hui R, Mak L-YL, Seto W-K, Yuen M-F. Role of Core/Capsid Inhibitors in Functional Cure Strategies for Chronic Hepatitis B. Current Hepatology Reports 2020;19:1-9.
8. Yuen M-F, Gane E, Agarwal K, Niu J, Ren H, Ding Y, et al. WED-365 Extended treatment of HBeAg+ CHB subjects

with the Capsid assembly modulator ALG-000184 with or without Entecavir is associated with reductions in viral markers and favorable anti-HBeAb trends. Journal of Hepatology 2024;80:S807-S808.
9. Yuen MF, Lim SG, Plesniak R, Tsuji K, Janssen HLA, Pojoga C, et al. Efficacy and Safety of Bepirovirsen in Chronic Hepatitis B Infection. N Engl J Med 2022;387:1957-1968.
10. Gadano A, Arbune M, Atsukawa M, Fujiyama S, Gankina N, John B, et al. Evidence of durable response to bepirovirsen in B-Clear responders: B-Sure first annual report. Journal of Hepatology 2023;78:S110-S112.
11. Yuen MF, Locarnini S, Lim TH, Strasser SI, Sievert W, Cheng W, et al. Combination treatments including the small-interfering RNA JNJ-3989 induce rapid and sometimes prolonged viral responses in patients with CHB. J Hepatol 2022;77:1287-1298.
12. Gane E, Lim YS, Kim JB, Jadhav V, Shen L, Bakardjiev AI, et al. Evaluation of RNAi therapeutics VIR-2218 and ALN-HBV for chronic hepatitis B: Results from randomized clinical trials. J Hepatol 2023;79:924-932.
13. Mak LY, Wooddell CI, Lenz O, Schluep T, Hamilton J, Davis HL, et al. Long-term hepatitis B surface antigen response after finite treatment of ARC-520 or JNJ-3989. Gut 2025;74:440-450.
14. Erken R, Andre P, Roy E, Kootstra N, Barzic N, Girma H, et al. Farnesoid X receptor agonist for the treatment of chronic hepatitis B: A safety study. J Viral Hepat 2021;28:1690-1698.
15. Qian J, Xie Y, Mao Q, Xie Q, Gu Y, Chen X, et al. A randomized phase 2b study of subcutaneous PD-L1 antibody ASC22 in virally-suppressed, HBeAg negative chronic hepatitis B patients. Hepatology (Baltimore, Md) 2024;81.
16. Janssen HL, Lim YS, Kim HJ, Sowah L, Tseng CH, Coffin CS, et al. Safety, pharmacodynamics, and antiviral activity of selgantolimod in viremic patients with chronic hepatitis B virus infection. JHEP Rep 2024;6:100975.
17. Yuen MF, Balabanska R, Cottreel E, Chen E, Duan D, Jiang Q, et al. TLR7 agonist RO7020531 versus placebo in healthy volunteers and patients with chronic hepatitis B virus infection: a randomised, observer-blind, placebo-controlled, phase 1 trial. Lancet Infect Dis 2023;23:496-507.
18. Gane EJ, Dunbar PR, Brooks AE, Zhang F, Chen D, Wallin JJ, et al. Safety and efficacy of the oral TLR8 agonist selgantolimod in individuals with chronic hepatitis B under viral suppression. J Hepatol 2023;78:513-523.
19. Tak WY, Chuang WL, Chen CY, Tseng KC, Lim YS, Lo GH, et al. Phase Ib/IIa randomized study of heterologous ChAdOx1-HBV/MVA-HBV therapeutic vaccination (VTP-300) as monotherapy and combined with low-dose nivolumab in virally-suppressed patients with CHB. J Hepatol 2024;81:949-959.
20. Ma H, Lim TH, Leerapun A, Weltman M, Jia J, Lim YS, et al. Therapeutic vaccine BRII-179 restores HBV-specific immune responses in patients with chronic HBV in a phase Ib/IIa study. JHEP Rep 2021;3:100361.
21. Lee HW, Park JY, Hong T, Park MS, Ahn SH. Efficacy of Lenvervimab, a Recombinant Human Immunoglobulin, in Treatment of Chronic Hepatitis B Virus Infection. Clin Gastroenterol Hepatol 2020;18:3043-3045.e3041.
22. van Campenhout MJH, van Bömmel F, Pfefferkorn M, Fischer J, Deichsel D, Boonstra A, et al. Serum hepatitis B virus RNA predicts response to peginterferon treatment in HBeAg-positive chronic hepatitis B. J Viral Hepat 2020;27:610-619.

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Seong Kyun Na

Inje University

Self Introduction

Prof. Seong Kyun Na is a Professor of the Department of Internal Medicine, Inje University Sanggye Paik Hospital. He completed his residency at the Department of Internal Medicine at Hallym University Hospital, and received his doctoral degree from Jeju National University. Since 2024, he is serving as a member of the Academic Committee of the Korean Association for the Study of the Liver.

Research Interests

Viral Hepatitis, Cirrhosis, Hepatocellular Carcinoma

Representative Publications

1. ALBI versus Child-Pugh grading systems for liver function in patients with hepatocellular carcinoma. Na SK, Yim SY, Suh SJ et al. J Surg Oncol 2018;117:912-921.
2. The effectiveness of transarterial chemoembolization in recurrent hepatocellular-cholangiocarcinoma after resection. Na SK, Choi GH, Lee HC et al. PLoS ONE 13(6): e0198138.
3. Aspartate Aminotransferase-to-Platelet Ratio or Fibros-4 Index Predicts the Development of Hepatocellular Carcinoma in Chronic Hepatitis C Patients with Sustained Virologic Response to Interferon Therapy. Na SK, Lee SJ, Cho YK, et al. J Interferon Cytokine Res 2019;39:703-710.
4. Prognosis Following Sustained Virologic Response in Korean Chronic Hepatitis C Patients Treated with Sofosbuvir-Based Treatment: Data from a Multicenter Prospective Observational Study up to 7 Years. Park Y, Na SK, Yoon JH, Kim SE, Park JW, Kim GA, Lee HY, Lee YS, Kim JH. Medicina (Kaunas). 2024 Jul 14;60(7):1132.

Emerging Viral Hepatitis: New Insights into Hepatitis D and E Infections

Seong Kyun Na *Inje University*

The Hepatitis D virus (HDV) is a defective hepatotropic pathogen that depends on the hepatitis B surface antigen (HBsAg) for its assembly and spread. Its genome consists of a circular, single-stranded RNA comprising approximately 1700 nucleotides. Over the last quarter-century, the incidence of hepatitis D has shifted, largely due to the global adoption of HBV vaccination initiatives that have helped control HBV infection.[1] The presence of antibodies to the hepatitis D antigen (anti-HDV antibodies) is a key indicator of HDV exposure, detectable in all immunocompetent individuals with the infection. Individuals who test positive for anti-HDV antibodies should undergo serum HDV RNA testing to confirm the presence of an active infection. HDV infection can occur in two ways: either as a coinfection with HBV in individuals who have not been previously exposed to HBV, or as a superinfection in those who already have a chronic HBV infection.[2] The most critical factor for disease progression is the continuous and intense presence of HDV in the bloodstream.[3] Pegylated interferon alfa has been administered following established guidelines, though its effectiveness is limited. A recent phase 2b study showed that combination therapy with pegylated interferon alfa and bulevirtide showed better therapeutic effects.[4]

Hepatitis E virus (HEV) is a small non-enveloped virus primarily transmitted via the fecal-oral route. HEV infection is usually asymptomatic. Symptomatic cases present as self-limited, acute icteric hepatitis. Pregnant women and immunocompromised patients are at higher risk for severe complications and chronic infection.[5] While acute HEV infection typically does not necessitate antiviral therapy, it should be considered for patients at high risk or those with a chronic infection. Ribavirin has demonstrated effectiveness across various studies and stands as the most widely used treatment option.

References

1. Rizzetto M, Hamid S, Negro F. The changing context of hepatitis D. J Hepatol 2021;74(5):1200-1211. (In eng). DOI: 10.1016/j.jhep.2021.01.014.
2. Farci P, Niro GA. Clinical features of hepatitis D. Semin Liver Dis 2012;32(3):228-36. (In eng). DOI: 10.1055/s-0032-1323628.
3. Kamal H, Westman G, Falconer K, et al. Long-Term Study of Hepatitis Delta Virus Infection at Secondary Care Centers: The Impact of Viremia on Liver-Related Outcomes. Hepatology 2020;72(4):1177-1190. (In eng). DOI: 10.1002/hep.31214.
4. Asselah T, Chulanov V, Lampertico P, et al. Bulevirtide Combined with Pegylated Interferon for Chronic Hepatitis D. New England Journal of Medicine 2024;391(2):133-143. DOI: 10.1056/nejmoa2314134.
5. Humzah I, Aalam S, Marina R, Bilal Fazal M. Hepatitis E infection: A review. World Journal of Virology 2023. DOI: 10.5501/wjv.v12.i5.262.

Young Kul Jung

Korea University

Self Introduction

Educational

1999.2 Bachelor, Korea University, College of Medicine Seoul, Korea
2004.2 Master, Korea University, Graduate School of Medicine Seoul, Korea
2012.2 PhD, Korea University, Graduate School of Medicine Seoul, Korea

Professional Experience

1999-2004 Intern/Resident, Korea University Medical Center, Seoul, Korea
2004-2007 Public Health Service Ganghwa Public Health Center, Incheon
2007-2009 Fellowship, Guro Hospital Korea University Medical Center, Seoul, Korea
2009-2014 Assistant Professor, Gachon University of Medicine and Science Gil Medical Center
2014-2019 Associate Professor, Ansan Hospital Korea University Medical Center
2018-2019 Visiting Professor, Kyoto University iPS Cell Research Center
2019-Present Professor, Ansan Hospital Korea University Medical Center

Other Experience and Professional Memberships

Director of the Guideline Committee in Korean Association for the Study of the Liver (KASL)
Member of the Education Committee in Korean Association for Internal Medcine (KAIM)
Member in The Korean Society of Gastroenterology
Member in The Korean Liver Cancer Association

Research Interests

Cirrhosis, Viral Hepatitis, Alcoholic Hepatitis, ACLF, HCC, iPS Cell, Regeneration Medicine

Representative Publications

1. Yim HJ, Kim TH, Suh SJ, Yim SY, Jung YK, Seo YS, Kang SH, Kim MY, Baik SK, Kim HS, Kim YS, Park SY, Kim BI, Park JY, Heo J, Sohn JH, Heo NY, Han KH, Um SH. Response-Guided Therapy With Cefotaxime, Ceftriaxone, or Ciprofloxacin for Spontaneous Bacterial Peritonitis: A Randomized Trial: A Validation Study of 2021 AASLD Practice Guidance for SBP. Am J Gastroenterol. 2023 Apr 1;118(4):654-663.
2. Liu C, Cao Z, Yan H, Wong YJ, Xie Q, Hirooka M, Enomoto H, Kim TH, Hanafy AS, Liu Y, Huang Y, Li X, Kang N, Koizumi Y, Hiasa Y, Nishimura T, Iijima H, Jung YK, Yim HJ, Guo Y, Zhang L, Ma J, Kumar M, Jindal A, Teh KB, Sarin SK, Qi X. Correction to: A Novel SAVE Score to Stratify Decompensation Risk in Compensated Advanced Chronic Liver Disease (CHESS2102): An International Multicenter Cohort Study. Am J Gastroenterol. 2023 Jul 20.
3. Kim TH, Yim HJ, Jung YK, Song DS, Yoon EL, Kim HY, Kang SH, Chang Y, Yoo JJ, Jun BG, Lee SW, Park JG, Park JW, Kim SE, Kim TY, Jeong SW, Suk KT, Kim MY, Kim SG, Kim W, Jang JY, Yang JM, Kim DJ; Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group. New prognostic model for hospitalized patients with alcoholic cirrhosis and Maddrey's discriminant function <32. Hepatol Int. 2024 Apr;18(2):500-508.
4. Shin SK, Oh S, Chun SK, Ahn MJ, Lee SM, Kim K, Kang H, Lee J, Shin SP, Lee J, Jung YK. Immune signature and therapeutic approach of natural killer cell in chronic liver disease and hepatocellular carcinoma. J Gastroenterol Hepatol. 2024 May 27.
5. Kim TH, Jung YK, Yim HJ. Correspondence on Letter regarding "Impacts of muscle mass dynamics on prognosis of outpatients with cirrhosis". Clin Mol Hepatol. 2023 Jan;29(1):173-175.

New KASL Guideline 2025
Updated KASL Guidelines on Chronic Hepatitis C

Young Kul Jung *Korea University*

Following the 2017 revision, the hepatitis C treatment landscape experienced revolutionary changes due to the development of pan-genotypic direct-acting antivirals (DAAs). These pan-genotypic DAA-based treatments have significantly fewer side effects, shorter treatment durations, and have increased sustained virological response (SVR) rates to over 95%, minimizing differences in SVR rates across different HCV genotypes. These advancements have simplified the hepatitis C treatment paradigm, enabling more patients to receive adequate treatment.

Recently, the World Health Organization (WHO) proposed a global strategy aimed at eliminating hepatitis C by 2030, prompting nations worldwide to strengthen policies aimed at improving early diagnosis and treatment accessibility. Similarly, South Korea is actively working to enhance its national hepatitis C management framework and reduce disease burden through proactive treatment approaches. Consequently, KASL has initiated this revision to align with WHO objectives and to provide updated guidelines tailored to the local medical environment.

This 2025 revision comprehensively reviewed recent domestic and international research findings and incorporated evidence-based treatment strategies. It emphasizes simplified treatment strategies, primarily recommending pan-genotypic DAAs irrespective of genotype classification. Moreover, it provides more explicit guidance on retreatment strategies for patients who previously experienced treatment failure, as well as treatment protocols for patients with cirrhosis, comorbidities, and other special conditions, such as chronic kidney disease and transplant recipients.

Furthermore, the updated guidelines strengthen early screening and treatment recommendations to enhance access to hepatitis C diagnosis and care. They propose a screening-integrated treatment strategy aligned with recent changes in domestic health policies and insurance coverage, aiming to deliver practical treatment guidelines beneficial to patients and healthcare providers.

The 2025 KASL hepatitis C guidelines have been developed based on the latest clinical evidence to provide practical support for medical practice. KASL remains committed to continuously updating guidelines and conducting research in alignment with global hepatitis C elimination goals, thereby offering optimal clinical guidance.

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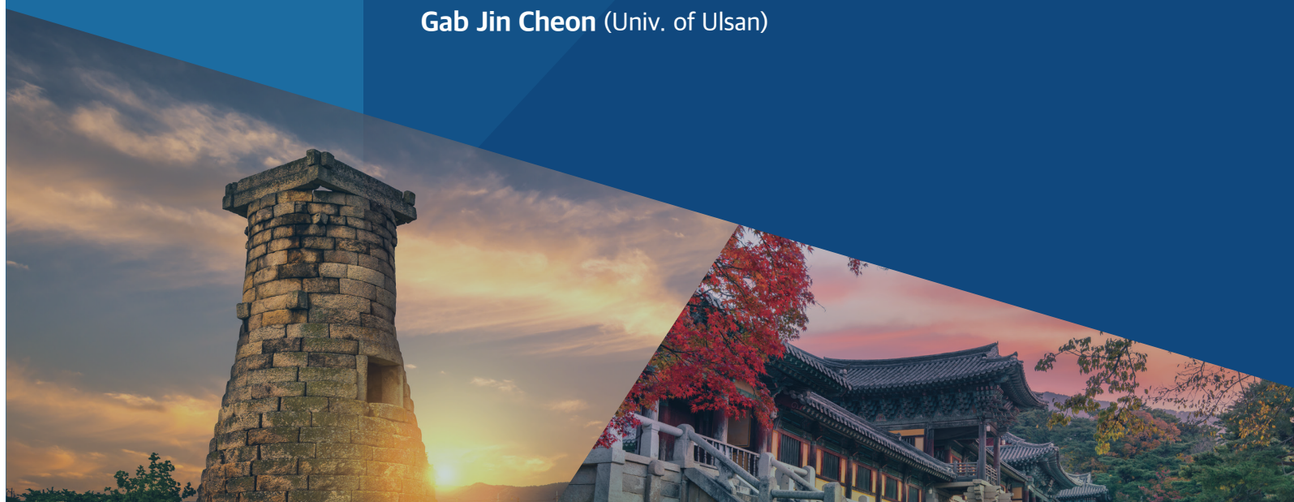
DAY 1: May 29 (Thu.)

PG Course 2

Steatotic Liver Disease and Liver Fibrosis

Chairs:

Joo Hyun Sohn (Hanyang Univ.)
Gab Jin Cheon (Univ. of Ulsan)



Won Sohn

Sungkyunkwan University

Self Introduction

Educational

1995.3-2002.2 M.D., Hanyang University, Seoul, Korea
2004.3-2006.2 M.Sc., Hanyang University, Seoul, Korea
2011.3-2013.2 Ph.D., Hanyang University, Seoul, Korea

Professional Experience

2002.3-2003.2 Internship, Hanyang University Hospital
2003.3-2007.2 Residentship, Department internal medicine, Hanyang University Hospital
2007.3-2010.4 Attending Physician, Department of internal medicine, In-kok Jae Hospital.
2010.5-2012.2 Clinical Fellowship, Division of Gastroenterology, Hanyang University Hospital
2012.3-2013.2 Attending Physician, Division of Gastroenterology, Hanyang University Hospital
2013.3-2015.2 Research Fellowship, Division of Gastroenterology, Samsung Medical Center
2015.3-2017.2 Attending Physician, Liver Center and Internal Medicine, Bundang Jesaeng Hospital
2017.3-2019.2 Assistant Professor, Division of Gastroenterology, Wonkwang University Sanbon Hospital
2019.3-Present Associate Professor, Division of Gastroenterology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine

Research Interests

Liver Fibrosis, Steatotic Liver Disease, Hepatocellular Carcinoma

Representative Publications

1. Sohn W, Park SY, Lee TH, et al. Effect of direct-acting antivirals on disease burden of hepatitis C virus infection in South Korea in 2007–2021: a nationwide, multicentre, retrospective cohort study. eClinicalMedicine. 2024;7:102671
2. Sohn W, Chang Y, Cho YK, et al. Isolated Hepatitis B core antibody positivity and long-term liver-related mortality in Korea: A cohort study. Am J Gastroenterol. 2023;118(1):95-104.
3. Sohn W, Kang D, Kang M, et al. Impact of nationwide hepatocellular carcinoma surveillance on the prognosis in patients with chronic liver disease. Clin Mol Hepatol. 2022;28(4):851-863.
4. Sohn W, Kwon HJ, Chang Y, et al. Liver fibrosis in Asians with metabolic dysfunction-associated fatty liver disease. Clin Gastroenterol Hepatol. 2022 May;20(5):e1135-e1148
5. Sohn W, Cho JY, Kim JH, et al. Risk score model for the development of hepatocellular carcinoma in treatment-naïve patients receiving oral antiviral treatment for chronic hepatitis B. Clin Mol Hepatol.2017;23(2):170-178.

From Chronic Inflammation to Fibrogenesis

Won Sohn *Sungkyunkwan University*

Steatotic liver disease (also known as fatty liver disease) is the overarching term for conditions characterized by abnormal lipid accumulation in the liver. Steatotic liver disease includes metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-related liver disease (ALD) and MetALD, the new classification for the overlap between MASLD and ALD, and rare causes of liver steatosis. Steatotic liver disease affects around 30% of the global population and is mainly driven by obesity, type 2 diabetes, insulin resistance, and alcohol intake. However, only a small proportion of patients with steatotic liver disease progress to advanced fibrosis or cirrhosis. Steatohepatitis is a condition of chronic inflammation in the hepatocytes with fat accumulation. The diagnosis of steatohepatitis is based on three histological features: steatosis (lipid droplets within hepatocytes), inflammation (infiltration of inflammatory cells in the liver lobules), and hepatocyte ballooning.

Mechanisms of chronic inflammation and fibrogenesis

Liver resident and recruited immune cells, stressed hepatocytes and liver sinusoidal endothelial cells (LSECs) contribute to development of the chronic inflammation associated with SLD. Metabolic injury is influenced by various factors resulting in pathogenic cascades including ER stress, oxidative stress and mitochondrial dysfunction in hepatocytes. Lipotoxicity, as a consequence of free fatty acid (FFA) overload and increased de novo lipogenesis, leads to release of stress signals and induction of cell death mechanisms of the metabolically stressed hepatocyte, which in turn activate immune responses. Inflammatory mediators reaching the liver are key contributors of disease progression as they influence hepatic cell functions. The hepatocytes, the most abundant liver cells, achieve the detoxifying and metabolic needs of the body. The remaining liver cells comprise the non-parenchymal cells, counting liver stellate cells (HSCs), LSECs, and a variety of immune cells. Inflammatory process develops in steatohepatitis by the roles of these liver cells. Hepatocytes sense PAMPs DAMPs, metabolite molecules (saturated FFA), and release inflammatory mediators (TNF-a, IL-1b). Also, hepatocyte death (apoptosis) leads to DAMPs induced inflammation and immune reaction. LSECs orchestrate release of proinflammatory mediators and enhance liver inflammation, injury, and fibrosis. Macrophages sense PAMPs DAMPs and metabolites (saturated FFA) and contribute to the recruitment and activation of other hepatic immune cells via inflammatory chemokines and cytokines. NK cells have a role of production of IFN/TNF-a and late macrophage polarization towards a pro-inflammatory phenotype.

Inflammatory processes modulate fibrogenesis in steatohepatiutis. During progression of chronic liver

inflammation, pro-fibrogenic mediators and cell-cell interactions lead to activation and trans-differentiation of quiescent HSCs to extracellular matrix-producing myofibroblasts. Upon cessation of metabolic injury, pro-resolving factors and anti-inflammatory reprogrammed immune cells revert myofibroblasts to a quiescent-like HSC phenotype or support elimination of activated HSCs, initiating tissue repair and regeneration. During metabolic liver injury, toxic lipids can promote HSC activation via direct and indirect mechanisms. Accumulation of cholesterol and fatty acids leads to the release of hedgehog ligands and extracellular vesicles from hepatocytes resulting in HSC proliferation and ECM production. In addition, cholesterol-laden hepatocytes are engulfed by liver-resident and infiltrating macrophages, causing inflammasome activation, production of pro-inflammatory cytokines and TGF β, which further perpetuates liver inflammation, HSC activation and fibrogenesis.

Clinical impact of chronic inflammation and fibrogenesis

Chronic inflammation (MASH) and fibrosis are associated with disease severity and poor prognosis of patients with MASLD. Patients with steatohepatitis have more cardiometabolic factors (obesity, T2DM, dyslipidemia, hypertension, and metabolic syndrome) in those with simple steatosis. Prevalence of liver fibrosis is higher in patients with MASH than in those with metabolic dysfunction-associated with steatotic liver (MASL). Significant fibrosis was observed in 4.4%, and 32.8% in simple steatosis, and steatohepatitis, respectively. A meta-analysis reported that among overweight individuals with NAFLD, the prevalence of liver fibrosis (F1–4) was 46.6% (95% CI 26.6–67.7), that of advanced fibrosis (F3–4) was 6.7% (95% CI 4.4–10.0), and that of cirrhosis (F4) was 2.5% (95% CI 1.6–3.7). In overweight individuals with NASH, the prevalence was even higher, with the prevalence of liver fibrosis at 72.6% (95% CI 49.4–87.8), that of advanced fibrosis (F3–4) at 19.4% (95% CI 7.6–41.1), and that of cirrhosis (F4) at 1.7% (95% CI 0.4–6.6). Chronic inflammation leads to fibrosis progression in patients with MASLD. While average progression of 1 fibrosis stage is 14.3 years in patients with simple steatosis, that is 7.1 years in those with steatohepatitis. In a Swedish study involving biopsy-proven patients with MASLD followed for 13 years, all-cause mortality and cause-specific mortality is higher in patients with steatohepatitis and fibrosis, followed by steatohepatitis without fibrosis, and simple steatosis. T2DM is an independent risk factor for fibrosis progression in patients with MASLD. In 447 patients with biopsy-proven MASLD, fibrosis progression with ≥1-stage increase in participants with T2DM compared to participants without T2DM (adjusted HR, 1.69, 95% CI 1.17–2.43). A cohort study diagnosing MASLD using transient elastography showed that the severity of liver fibrosis worsened as the number of cardiometabolic risk factors increased. A meta-analysis reveals that participants with T2DM had a significantly higher risk of hepatic decompensation and HCC development in MASLD.

Therapeutic implications for chronic inflammation and fibrogenesis

Metabolic injury to the liver causes inflammatory processes that drive progression of NASH and liver fibrosis, supporting the concept of "anti-inflammatory" and "antifibrotic" therapeutic strategies. Pharmacologic strategies target the metabolic dysregulation and injury of hepatocytes as well as extrahepatic inflammatory signals. Anti-inflammatory strategies target the activation of immune sentinels, the subsequent recruitment of immune cells as well as the complex intercellular crosstalk of parenchymal and non-parenchymal cells. Extrahepatic mediators, e.g. from the gut, adipose tissue or the because they can impact inflammation and fibrosis as well. Several pharmacological agents have been developed for targeting key metabolic pathways, including lipogenesis (e.g., aramchol, inhibitors of acetyl-CoA carboxylase or fatty acid synthase), energy availability (e.g., glucagon-like peptide 1 [GLP-1] receptor and/or glucagon agonists) or lipid handling (e.g., fatty acid b-oxidation via nuclear receptors, such as THR mimetics like resmetirom). Long-chain omega-3 fatty acids are known to beneficially regulate inflammatory pathways in the course of MASH, but therapeutic efficacy is highly limited by peroxidation and subsequent degradation. Structurally engineered fatty acids, such as icosabutate, improve resistance to peroxidative processes, and thus represent a promising approach to maintaining the beneficial metabolic effects of long-chain omega-3 fatty acids.

The end point of new drug for MASH treatment is a resolution of steatohepatitis with no worsening of fibrosis and an improvement of at least one fibrosis stage with no worsening of steatohepatitis. The US FDA approved resmetirom for the first time as a drug treatment for NASH in 2024. This drug was developed to target a selective THR-β agonist. It selectively acts on intrahepatic THR-β to induce conversion of T4 to T3 in the liver, improves damaged mitochondrial function, lowers intrahepatic lipid accumulation, and induces improvement of intrahepatic inflammation and liver fibrosis. A phase III clinical trial was conducted on patients with NASH with F2/F3 liver fibrosis without cirrhosis. The relative liver-specific expression of selective THR-β agonists lowers blood cholesterol and triglyceride levels, increases intrahepatic bile acid synthesis, and plays an important role in intrahepatic fatty acid oxidation. The relative liver-specific expression of selective THR-β agonists lowers blood cholesterol and triglyceride levels, increases intrahepatic bile acid synthesis, and plays an important role in intrahepatic fatty acid oxidation. In a multicenter, randomized, double-blind, placebo-controlled study (MAESTRO-NASH) involving 1,759 patients with NASH with histologically diagnosed F2/F3 liver fibrosis, resmetirom, a selective THR-β agonist, showed significant improvement in steatohepatitis in 25.9% of the 80-mg group and 29.9% of the 100-mg group without worsening of liver fibrosis compared to placebo (9.7%) ($p<0.001$). Improvement in liver fibrosis of one or more stages was observed in 24% of the 80-mg group and 26% of the 100-mg group, which was statistically significant compared to 14% of the placebo group ($p<0.001$).

References

1. Luci C, Bouriet M, Leclere PS. et al. Chronic Inflammation in Non-Alcoholic Steatohepatitis: Molecular Mechanisms and Therapeutic Strategies. Front Endocrinol. 2020 Dec 14:11:597648.
2. Tacke F, Puengel T, Loomba R. et al. An integrated view of anti-inflammatory and antifibrotic targets for the treatment of NASH. J Hepatol. 2023;79(2):552-566.
3. Mortality in biopsy-confirmed nonalcoholic fatty liver disease: results from a nationwide cohort. Simon TG, Roelstraete B, Khalili H. et al. Gut. 2021;70(7):1375-1382.
4. Fibrosis progression in nonalcoholic fatty liver vs nonalcoholic steatohepatitis: a systematic review and meta-analysis of paired-biopsy studies. Singh S, Allen AM, Wang Z. et al. Clinical Gastroenterology and Hepatology 2015;13:643–654.
5. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. Harrison SA, Bedossa P, Guy CD. N Engl J Med. 2024;390(6):497-509.
6. KASL clinical practice guidelines for the management of metabolic dysfunction-associated steatotic liver disease 2025. Clin Mol Hepatol. 2025 Feb;31(Suppl):S1-S31.

Ji-Won Park

Hallym University

Self Introduction

Prof. Jiwon Park is an associated professor of the department of Internal Medicine, Hallym University Sacred Heart Hospital. She graduated from Hallym University College of Medicine with her medical degree in 2003 and completed her internship and residency at the Department of Internal Medicine at Hallym University Kangdong Sacred Heart Hospital, receiving her diploma in Internal Medicine in 2009.
She has served as a member of the Research Planning Committee of the Korean Association for the Study of the Liver (2018-2019), a member of the Informatics Committee of the Korean Association for the Study of the Liver (2020-20023), and a member of the Insurance Committee of the Korean Liver Cancer Association (2020-2023).

Research Interests

MASLD, Alcohol Related Liver Disease, Liver Cirrhosis, Hepatocellular Carcinoma

Representative Publications

1. Clinicopathologic Significance of Quaking Expression in Hepatocellular Carcinoma. Sung-Eun Kim, Cheol Keun Park, Ji-Won Park, Jung Woo Lee, Ji-Young Choe and Yoon Ah Cho. in vivo. 2024;38: 2064-2073.
2. Serum S100B Levels in Patients with Liver Cirrhosis and Hepatic Encephalopathy. Mo-Jong Kim, Jung-Hee Kim, Jang-Han Jung, Sung-Eun Kim, Hyoung-Su Kim, Myoung-Kuk Jang, Sang-Hoon Park, Myung-Seok Lee, Ki Tae Suk, Dong Joon Kim, Eun-Kyoung Choi and Ji-Won Park. Diagnostics. 2023; 13(3):333.
3. A Multicenter Retrospective Study on Clinical Characteristics and Outcome of Pyogenic Liver Abscess Focusing Multidrug-Resistant Organisms. Ji-Won Park, Jung-Hee Kim, Jang-Han Jung, Sung-Eun Kim, Hyoung-Su Kim, Haemin Jeong, Ki Tae Suk, Myoung-Kuk Jang, Dong-Joon Kim, Myung-Seok Lee and Sang-Hoon Park. J Clin Med. 2022; 11 (4):1114.
4. Role of Microbiota-Derived Metabolites in Alcoholic and Non-Alcoholic Fatty Liver Diseases. Ji-Won Park, Sung-Eun Kim, Na Young Lee, Jung-Hee Kim, Jang-Han Jung, Myoung-Kuk Jang, Sang-Hoon Park, Myung-Seok Lee, Dong-Joon Kim, Hyoung-Su Kim, and Ki Tae Suk, Int J Mol Sci. 2021; 23(1): 426.
5. Primary Biliary Cholangitis and Primary Sclerosing Cholangitis: Current Knowledge of Pathogenesis and Therapeutics. Ji-Won Park, Jung-Hee Kim, Sung-Eun Kim, Jang Han Jung , Myoung-Kuk Jang, Sang-Hoon Park, Myung-Seok Lee, Hyoung-Su Kim, Ki Tae Suk and Dong Joon Kim, Biomedicines. 2022; 10(6): 1288.

Impact of Genetic and Environmental Risk Factors on Liver Fibrosis

Ji-Won Park *Hallym University*

The natural history of metabolic dysfunction-associated steatotic liver disease (MASLD) is complex and lengthy. A small percentage of patients develop inflammation, which can lead to progressive fibrosis and potentially result in cirrhosis. Progression to cirrhosis occurs in 3-5% of patients and typically takes more than 20 years. However, the rate of progression of MASLD varies due to several factors, including genetics, metabolic risk factors, and environmental influences. Genome-wide association studies (GWAS) have identified robust and consistent associations related to the progression of MASLD. Notably, single nucleotide polymorphisms in PNPLA3 (patatin-like phospholipase domain-containing 3), TM6SF2 (transmembrane 6 superfamily member 2), GCKR (glucokinase regulator), MBOAT7 (membrane-bound O-acyltransferase domain-containing 7), and HSD17B13 (hydroxysteroid 17-beta dehydrogenase 13) have been shown to be strongly associated with the development and progression of MASLD. These genetic variants play crucial roles in lipid droplet remodeling, the secretion of hepatic very low-density lipoprotein, and lipogenesis. Furthermore, environmental risk factors can accelerate the progression of fibrosis. These factors include cigarette smoking, exposure to environmental toxins, poor dietary habits, sedentary lifestyles, and irregular sleep patterns. Smoking contributes to liver fibrosis through a series of sequential events, including lipotoxicity, oxidative stress, endoplasmic reticulum (ER) stress, inflammation, and apoptosis in hepatocytes. This process activates hepatic regeneration and fibrogenesis, leads to the deposition of the extracellular matrix (ECM), and promotes hepatic fibrosis in MASLD. The effects of endocrine-disrupting chemicals (EDCs) in MASLD occur through the activation of transcription factors that disrupt the balance between lipid influx and efflux in the liver, promote mitochondrial dysfunction, and enhance major inflammatory responses during the progression of metabolic dysfunction-associated steatotic hepatitis (MASH). In terms of diets, the consumption of red and processed meats, as well as increased fructose intake, has been reported to be associated with MASLD and liver fibrosis. Identifying modifiable risk factors for disease progression and implementing preventive measures are essential for alleviating the burden on public health. By extension, in the era of precision medicine, the development of targeted therapies that can selectively silence genetic variants implicated in the promotion and progression of MASLD will be a promising approach to treating MASLD.

Byoung Kuk Jang

Keimyung University

Self Introduction

Prof. Byoung Kuk Jang is a Professor of the Department of Internal medicine, Keimyung University College of Medicine. He graduated from Keimyung University College of Medicine with his medical degree in 1995 and completed his internship and residency at the Department of Internal medicine at Keimyung University Dongsan Hospital, receiving his diploma in Internal medicine in 2000.

He has been taking a number of roles, including Chairman of the KASL steatotic liver disease study group (2024-).

Research Interests

MASLD, Liver Fibrosis, HCC

Representative Publications

1. Clusterin Deficiency Exacerbates Cholestatic Liver Disease Through ER Stress and NLRP3 Inflammasome Activation. Cell Biosci. 2025 Mar 15;15(1):36.
2. Clusterin Inhibits Lipopolysaccharide Induced Liver Injury. Sci Rep. 2025 Feb 18;15(1):5975.
3. Lobeglitazone Inhibits LPS-induced NLRP3 Inflammasome Activation and Inflammation in the Liver. PLoS One. 2023 Aug 24;18(8):e0290532.
4. High Sodium Intake, as Assessed by Urinary Sodium Excretion, Is Associated with Nonalcoholic Fatty Liver Disease or Sarcopenia. Gut Liver. 2023 May 15;17(3):456-465.
5. Evogliptin Directly Inhibits Inflammatory and Fibrotic Signaling in Isolated Liver Cells. Int J Mol Sci. 2022 Oct 1;23(19):11636.
6. Increased Levels of Phosphorylated ERK Induce CTGF Expression in Autophagy-Deficient Mouse Hepatocytes. Cells. 2022 Aug 30;11(17):2704.

PG Course 2 | DAY 1: May 29 (Thu.) | ROOM 1 [3F]

New KASL Guideline 2024

Updated KASL Guidelines on Metabolic Dysfunction-Associated Steatotic Liver Disease

Byoung Kuk Jang *Keimyung University*

Recently, the concept of metabolic dysfunction-associated steatotic liver disease (MASLD) has been introduced to replace the existing non-alcoholic fatty liver disease (NAFLD). Unlike the existing term 'non-alcoholic', which had the disadvantage of being an exclusive diagnosis, it has now been established that it is closely related to "metabolic dysfunction" such as obesity, insulin resistance, diabetes, hypertension, and dyslipidemia. Therefore, the recent introduction and introduction of MASLD as a fatty liver disease accompanied by at least one metabolic abnormality in the West has led to a paradigm shift in the perception of the disease. This change signifies a paradigm shift in the understanding of fatty liver disease, and it emphasizes comprehensive management of the root cause of patients with fatty liver disease. Accordingly, the Korean Association for the Study of the Liver has also raised the need to establish a new Korean term for MASLD and to organize the similarities and differences with NAFLD, which has been traditionally used. In addition, resmetirom, an oral thyroid hormone receptor-beta (THR-β) agonist, a new treatment drug for metabolic dysfunction-associated steatohepatitis (MASH), was approved by the Food and Drug Administration (FDA) for the first time in March 2024 through successful phase 3 clinical trials. Therefore, KASL has partially revised the KASL Non-alcoholic Fatty Liver Disease Treatment Guidelines established in 2021 to keep up with these changing times. In the revised guidelines, the guidelines have adopted a partial revision method to revise and supplement the treatment recommendations for 11 major clinical topics that require reflection of the latest knowledge. This revision covers the Korean name, definition, diagnosis, clinical features, and prognosis of metabolic fatty liver disease, a new concept of fatty liver disease, and updates on drug treatment for steatohepatitis. The pediatric and adolescent section also focuses on defining and diagnosing metabolic fatty liver disease. This revision of the guideline is intended to allow the achievements of the development of modern medicine, which is rapidly developing, to be applied to clinical settings.

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DAY 1: May 29 (Thu.)

Special Lecture

Chair:

Han Chu Lee (Univ. of Ulsan)

Dong-Charn Cho

Korea Science Journalists Association

Self Introduction

Education

1994.03-2000.02 M.D. Hanyang University College of Medicine, Seoul, South Korea (Medicine)
2001.08-2003.09 M.S. Hanyang University Graduate School, Seoul, South Korea (Neurosurgery)
2007.03-2010.09 Ph.D. Hanyang University Graduate School, Seoul, South Korea (Neurosurgery)

Professional Certifications

2000 Medical License, Republic of Korea
2005 Board Certification in Neurosurgery

Professional Experience

2008.09-2025-01 Medical Science Reporter, SBS News Bureau, Seoul, Korea
2008.04-2008.09 Neurosurgery Fellow, Department of Neurosurgery, Hanyang University Hospital, Seoul, Korea
2006.02-2008.04 Chief of Neurosurgery, Seoul Military Hospital, Seoul, Korea
2001.03-2005.02 Neurosurgical Resident, Department of Neurosurgery, Hanyang University Hospital, Seoul, Korea
2000.03-2001.02 Intern, Hanyang University Hospital, Seoul, Korea
2017.12-2018.12 Visiting Research Fellow, Albert Einstein College of Medicine, New York, USA

Professional Memberships

2008–Present Korean Science Journalists Association
2008–Present Korean Broadcasters Association
2008–Present Korea Press Association
2008–Present Korea Broadcasting Journalists Club
2008–Present Korean Brain Tumor Society
2001–Present Korean Neurosurgical Society
2000–Present Korean Medical Association

Representative Publications

1. Are You Sleeping Well?, An SBS Medical Reporter's Guide to the Science of Sleep. Pampas, 2018.
2. Humanities for Growing Minds, vol. 24: Medicine, What Is Healthcare for All? Eulpaso, 2023.
3. All About Suicide Prevention: Theory and Policy, Chapter 24: The Role of Mass Media in Suicide Prevention. Hakjisa, 2023.

How Do Medical Policies and Media Work in an Aging Era?

Dong-Charn Cho *Korea Science Journalists Association*

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PG Course 3

Alcohol-Associated Liver Disease and Cirrhosis

Chairs:

Hong Soo Kim (Soonchunhyang Univ.)
Oh Sang Kwon (Gachon Univ.)

Ha Il Kim

Hanyang University

Self Introduction

Professor Ha Il Kim is a Professor in the Department of Gastroenterology and Hepatology at Hanyang University College of Medicine and currently serves as a practicing hepatologist at Hanyang University Guri Hospital.
He obtained his M.D. from Hanyang University College of Medicine in 2013, followed by internship, residency, and fellowship training in gastroenterology at Asan Medical Center. In 2020, he was awarded a Ph.D. in Internal Medicine from the University of Ulsan College of Medicine.
His clinical and research interests include steatotic liver disease, hepatocellular carcinoma, and big data-driven analysis in hepatology.

Research Interests

Steatotic Liver Disease, Hepatocellular Carcinoma, Big Data-Driven Analysis

Representative Publications

1. Association of comorbidity duration with the occurrence and prognosis of steatotic liver disease, Digestive Diseases and Sciences, 2025.
2. Impact of metabolic risk factors on the hepatic and cardiac outcomes in patients with alcohol- and non-alcohol-related fatty liver disease, 2023, JHEP Reports
3. Loco-regional therapies competing with radiofrequency ablation in potential indications for hepatocellular carcinoma: a network meta-analysis, 2023, Clin Mole Hepatol
4. Postresection Period-Specific Hazard of Recurrence as a Framework for Surveillance Strategy in Patients with Hepatocellular Carcinoma: A Multicenter Outcome Study, Liver Cancer, 2022
5. Incidence and management patterns of alcohol-related liver disease in Korea: A nationwide standard cohort study, Scientific Report, 2021

Identification of High-Risk Groups in Alcohol-Associated Liver Disease

Ha Il Kim *Hanyang University*

Alcohol-associated liver disease (ALD) is a major global health concern, ranking among the leading causes of cirrhosis and hepatocellular carcinoma. In South Korea, recent data indicate an increasing trend in alcohol-related liver complications, driven by high per capita alcohol consumption, changing drinking patterns, and limited public awareness. Despite its prevalence, ALD often remains undiagnosed until late stages due to its asymptomatic progression and lack of standardized early screening strategies.

This presentation focuses on the clinical identification of individuals at high risk of developing ALD. Understanding the interplay between alcohol intake, metabolic comorbidities, genetic predisposition, and socioeconomic factors is crucial for early detection and prevention. Heavy alcohol consumption, typically defined as >40g/day for men and >20g/day for women, especially over prolonged periods, remains the primary risk factor. However, not all heavy drinkers develop ALD, suggesting that additional host-related factors contribute significantly to disease susceptibility.

Coexisting conditions such as obesity, type 2 diabetes mellitus, and metabolic syndrome significantly amplify the risk of liver injury, indicating a synergistic effect between metabolic dysfunction and alcohol toxicity. Genetic variants, particularly the I148M polymorphism in PNPLA3, have been associated with increased hepatic fat accumulation, inflammation, and fibrosis in ALD, as shown in genome-wide association studies. Other variants like TM6SF2 and MBOAT7 also contribute to individual susceptibility.

In clinical practice, early recognition of high-risk individuals requires a combination of thorough alcohol history-taking and objective assessments. Validated tools such as the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) questionnaire offer a practical means to identify problematic drinking patterns. Non-invasive fibrosis scoring systems, including the FIB-4 index and AST-to-ALT ratio, are accessible and cost-effective methods to stratify liver disease severity without imaging or biopsy. Where available, transient elastography (FibroScan) can add value by assessing liver fibrosis in a non-invasive-manner.

Case-based approaches will be discussed to illustrate how these tools can be applied in real-world clinical scenarios, particularly in primary and secondary care settings. Furthermore, emerging evidence suggests that machine learning and integrative omics approaches may offer refined models for individ-

ualized risk prediction in the near future.

In conclusion, ALD represents a preventable yet frequently overlooked liver disease. Identifying high-risk individuals through a structured, multifactorial approach—combining clinical judgment with practical screening tools—is essential to enable timely intervention. This lecture aims to equip clinicians with a framework for proactive risk assessment, patient education, and referral strategies, ultimately contributing to improved outcomesinALD.

References

1. Arab JP, et al., Alcohol-Associated Liver Disease: Integrated Management with Alcohol Use Disorder. Clin Gastroenterol Hepatol. 2023 Jul;21(8):2124-2134
2. Stickel F et al., The genetics of alcohol dependence and alcohol-related liver disease. J Hepatol. 2017 Jan;66(1):195-211.
3. Israelsen, et al., Non-invasive tests for alcohol-associated liver disease. Hepatology 80(6) 1390-1407, December 2024.
4. Burton et al., Prevention of Alcohol-associated Liver disease. The American Journal of Gastroenterology:10.14309/ajg.0000000000003427, March 26, 2025.
5. Torp, N., Israelsen, M. & Krag, A. The steatotic liver disease burden paradox: unravelling the key role of alcohol. Nat Rev Gastroenterol Hepatol 22, 281–292 (2025)

Jeong-Ju Yoo

Soonchunhyang University

Self Introduction

Prof. Jeong-Ju Yoo, currently an Associate Professor in the Department of Hepatology, Internal Medicine, at Soonchunhyang University College of Medicine, Soonchunhyang University Bucheon Hospital, Korea.

She completed her medical education at Seoul National University College of Medicine, earning my M.D. degree in 2009, followed by a Master's (2015) and Ph.D. (2019) in Internal Medicine from the same institution.

Her professional career includes medical internship (2009-2010) and residency in Internal Medicine (2010-2014) at Seoul National University Hospital. She was also a Research Fellow at the Department of Internal Medicine and Liver Research Institute at Seoul National University College of Medicine (2014-2015). In 2016, she joined Soonchunhyang University Bucheon Hospital as an Assistant Professor, and she has been serving as an Associate Professor since 2024.

Her clinical and research interests primarily focus on hepatology, particularly viral hepatitis, liver cirrhosis, hepatocellular carcinoma, liver fibrosis, and metabolic liver diseases. She has published numerous peer-reviewed articles and has received multiple awards for excellence in research and presentations, including Best Presentation Awards at major academic conferences.

Currently, she actively participates in several academic societies, serving on various committees, including the Korean Association for the Study of the Liver, Korean Liver Cancer Association, and Korean Society of Gastroenterology.

Research Interests

- Hepatocellular Carcinoma (HCC): Pathogenesis, Therapeutic Strategies, and Prognostic Factors
- Metabolic Liver Diseases: Non-Alcoholic Fatty Liver Disease (NAFLD) and Metabolic-Associated Fatty Liver Disease (MAFLD)
- Liver Fibrosis and Portal Hypertension: Non-Invasive Diagnostic Methods and Clinical Management
- Clinical Applications of Ultrasound and Elastography in Liver Disease
- Prognostic Modeling and Biomarkers for Chronic Liver Diseases
- Viral Hepatitis Management and Antiviral Therapies
- Microbiome Studies in Liver Cirrhosis and Related Complications

Representative Publications

1. Estimation of renal function in patients with liver cirrhosis: Impact of muscle mass and sex. Jeong-Ju Yoo et al. Journal of Hepatology, 2019;70:847-854.
2. Validation of the Texas Hepatocellular Carcinoma Risk Index Predictive Model for Hepatocellular Carcinoma in Asian Cohort. Jeong-Ju Yoo et al. Clinical Gastroenterology and Hepatology, 2024 Mar 13; S1542-3565(24)00255-6.
3. Risk of dyslipidemia in chronic hepatitis B patients taking tenofovir alafenamide: a systematic review and meta-analysis. Jeong-Ju Yoo et al. Hepatology International, 2023 Apr 26.
4. Efficacy of antiviral prophylaxis in HBsAg-negative, anti-HBc positive patients undergoing hematopoietic stem cell transplantation. Jeong-Ju Yoo et al. Liver International, 2015 Dec;35(12):2530-2536.
5. Long-term prognosis and the need for histologic assessment of chronic hepatitis B in the serological immune-tolerant phase. Jeong-Ju Yoo et al. Clinical and Molecular Hepatology, 2023 Apr;29(2):482-495.

Therapeutic Strategies for Alcohol-Use Disorder and Alcoholic Hepatitis

Jeong-Ju Yoo *Soonchunhyang University*

Alcohol-associated liver disease encompasses a wide spectrum of conditions, from simple hepatic steatosis to cirrhosis and hepatocellular carcinoma. Among these, alcohol use disorder and alcoholic hepatitis represent two clinically important and therapeutically actionable stages that significantly influence long-term outcomes. This lecture will provide a comprehensive overview of current therapeutic strategies for both alcohol use disorder and alcoholic hepatitis, with an emphasis on evidence-based approaches and integration into clinical practice.

1. Management of Alcohol Use Disorder:

Alcohol use disorder is a chronic, relapsing condition with neurobiological, behavioral, and social dimensions. The foundation of treatment includes psychosocial interventions such as motivational interviewing, cognitive behavioral therapy, and structured group therapy. Pharmacological options are also available, including naltrexone and acamprosate, which help reduce cravings and support abstinence, and disulfiram, which provides aversive conditioning. In patients with impaired liver function, baclofen may be preferred due to its renal clearance and relatively favorable safety profile. A multidisciplinary care model, involving hepatologists, psychiatrists, addiction specialists, and social workers, is essential for sustained recovery and relapse prevention.

2. Treatment of Alcoholic Hepatitis:

Alcoholic hepatitis is a severe inflammatory liver condition characterized by jaundice and liver dysfunction, often with high short-term mortality. Clinical scoring systems such as the Maddrey's Discriminant Function, the Model for End-stage Liver Disease (MELD) score, and the Lille model are useful in assessing disease severity and guiding therapeutic decisions. In moderate to severe cases, corticosteroid therapy (typically prednisolone) is considered, unless contraindications such as active infection are present. Treatment response is evaluated after 7 days using the Lille score to determine continuation or discontinuation of steroids. Nutritional support, including protein-calorie repletion and vitamin supplementation (especially thiamine), forms a critical component of care. Although pentoxifylline was once considered as an alternative, recent data have not supported its efficacy. Novel therapies, including immunomodulatory agents and regenerative strategies, are under investigation.

3. Integrated Care Model:

Addressing alcoholic hepatitis without treating the underlying alcohol use disorder is insufficient. The management of these conditions should not be compartmentalized but rather approached through a unified strategy that combines detoxification, medical stabilization, psychosocial support, and long-term behavioral therapy. This integrated model is key to preventing relapse, reducing readmissions, and improving survival. The lecture will present clinical decision pathways that incorporate both immediate inpatient management and coordinated outpatient follow-up.

Conclusion

The effective treatment of patients with alcohol-associated liver disease requires clinicians to simultaneously manage both the liver injury and the underlying addiction. This presentation will provide practical, up-to-date guidance on therapeutic strategies for alcohol use disorder and alcoholic hepatitis, highlighting the importance of a multidisciplinary and longitudinal approach. Participants will gain tools to apply in real-world clinical settings, ultimately improving patient outcomes in this high-risk population.

Ki Tae Yoon

Pusan National University

Self Introduction

Educational

1994.03-2000.02 B.S., Yonsei University College of Medicine, Seoul, Korea
2004.09-2006.08 M.S., Graduate School, Yonsei University College of Medicine, Seoul, Korea
2009.03-2015.02 Ph.D., Pusan National University School of Medicine, Yangsan, Korea

Postgraduate Career

2000.03-2001.02 Internship, Yonsei University Severance Hospital
2003.03-2006.02 Residency, Department of Internal Medicine, Yonsei University Severance Hospital
2007.03-2008.02 Fellow, Division of Gastroenterology and Hepatology, Yonsei University Severance Hospital
2008.03-2014.03 Clinical assistant Professor, Division of Gastroenterology and Hepatology, Pusan National University Yangsan Hospital
2014.04-2021.08 Assistant Professor, Division of Gastroenterology and Hepatology, Pusan National University Yangsan Hospital
2021.09-2025.03 Associate Professor, Division of Gastroenterology and Hepatology, Pusan National University Yangsan Hospital
2025.03-Present Associate Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Pusan National University and Liver center, Pusan National University Yangsan Hospital
2017.08-2019.01 Visiting researcher, Division of Gastroenterology and Hepatology, Foothill Medical Centre, Cumming School of Medicine, University of Calgary

Academic Activities

2024.7-Present KLCA (Korean Liver Cancer Association) Financial Director
2023.12-Present KASL (Korean Association for the Study of the Liver) Publication Committee Member
2023.12-Present KASL Medical Policy Committee Member

Research Interests

Clinical Study for Hepatocellular Carcinoma, Chronic Hepatitis B, Chronic Hepatitis C

PG Course 3 | DAY 1: May 29 (Thu.) | ROOM 1 [3F]

Medical and Interventional Treatments in Portal Hypertension

Ki Tae Yoon *Pusan National University*

Introduction

Portal hypertension (PH), defined as an increased pressure gradient between the portal vein and hepatic veins, is a critical pathophysiological hallmark of cirrhosis and its complications. Clinically significant portal hypertension (CSPH), usually defined as a hepatic venous pressure gradient (HVPG) ≥10 mmHg, is associated with the development of gastroesophageal varices, ascites, spontaneous bacterial peritonitis, and hepatic encephalopathy. This presentation outlines the current strategies in medical and interventional management of PH, guided by stage-specific risk and patient phenotype.

Medical Therapies

Medical treatment remains foundational, particularly in the prophylaxis and management of variceal hemorrhage. Non-selective beta-blockers (NSBBs) such as propranolol and nadolol reduce cardiac output and induce splanchnic vasoconstriction, thereby decreasing portal venous inflow. Carvedilol, a third-generation NSBB with additional alpha-1 adrenergic blockade, offers a greater reduction in HVPG (~20%) and is often preferred in primary prophylaxis settings. However, carvedilol should be used cautiously in patients with low mean arterial pressure or refractory ascites.

In the context of acute variceal bleeding, vasoactive agents such as terlipressin, somatostatin, and octreotide are initiated immediately to control bleeding while arranging for endoscopic variceal ligation (EVL). Antibiotic prophylaxis with ceftriaxone or quinolones is also a cornerstone in reducing infection-related mortality in cirrhotic patients.

In patients with ascites, long-term use of NSBBs requires careful evaluation. Emerging evidence suggests that in patients with severe or refractory ascites, NSBBs may worsen outcomes, possibly due to impaired circulatory reserve. Thus, treatment must be individualized.

Endoscopic and Radiological Interventions

Endoscopic variceal ligation remains the standard of care for both primary and secondary prophylaxis of esophageal varices. Combined with NSBBs, EVL significantly reduces the risk of rebleeding and improves survival. In gastric varices, especially GOV2 and IGV1 types, cyanoacrylate injection is the pre-

ferred modality.

For patients with recurrent variceal bleeding or refractory ascites, transjugular intrahepatic portosystemic shunt (TIPS) represents the most effective interventional treatment. TIPS effectively decompresses the portal system by creating a low-resistance channel between the portal and hepatic veins. Covered stents (ePTFE) have improved patency and reduced complications compared to bare-metal stents.

The concept of early or preemptive TIPS—within 72 hours of acute variceal bleeding—has been shown to improve survival in selected high-risk patients (Child-Pugh class C <14 or B with active bleeding at endoscopy). However, patient selection remains crucial, as TIPS is associated with a higher incidence of hepatic encephalopathy (HE), particularly in elderly patients or those with sarcopenia.

Recent advancements include pressure-guided TIPS placement and the exploration of balloon-occluded retrograde transvenous obliteration (BRTO) or PARTO techniques, particularly for gastric varices or patients with hepatic encephalopathy where diversion of portosystemic flow needs to be modulated.

Emerging Concepts and Future Directions

The role of HVPG-guided therapy is expanding. HVPG remains the gold standard for assessing the severity of PH and therapeutic response. A reduction of ≥10% from baseline or to <12 mmHg is predictive of reduced risk of variceal bleeding. Newer non-invasive surrogates, such as spleen stiffness measurement by elastography and dynamic MRI perfusion studies, are under evaluation.

Combination strategies using NSBBs and statins have also shown promise. Statins, particularly simvastatin, may improve endothelial function and hepatic perfusion, potentially reducing portal pressure and improving survival in cirrhosis.

Additionally, modulation of the gut-liver axis through antibiotics (e.g., rifaximin) and probiotics is an area of interest, especially in reducing systemic inflammation and portal pressure.

Conclusions

Managing portal hypertension requires a dynamic, patient-centered approach that balances hemodynamic goals with liver functional reserve and comorbidities. Integration of medical therapy, endoscopic management, and interventional radiology must be tailored based on disease stage and individual risk profile. Continued research into non-invasive monitoring, pharmacologic targets, and optimal timing for intervention will further refine the paradigm of care.

References

1. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal Hypertension and Variceal Bleeding in Cirrhosis: A Position Paper by the Baveno VII Consensus. J Hepatol. 2022;76(3):959-974.
2. Tripathi D, Stanley AJ, Hayes PC, et al. UK Guidelines on the Management of Variceal Haemorrhage in Cirrhotic Patients. Gut. 2015;64(11):1680-1704.

3. Bureau C, Thabut D, Oberti F, et al. Early TIPS with Covered Stents Increases Survival in High-Risk Variceal Bleeding. Gastroenterology. 2017;152(3):541-549.
4. Sauerbruch T, et al. Effect of Nonselective Beta-Blockers on Survival in Patients with Cirrhosis and Ascites. N Engl J Med. 2013;368:234-243.
5. Bosch J, Gracia-Sancho J. The Role of the Hepatic Microcirculation in the Pathogenesis of Cirrhosis and Portal Hypertension. Hepatology. 2013;53(5):1652-1659.

Jong-In Chang

Chung-Ang University

Self Introduction

Education

2019-2023 Graduated from School of Medicine, Sungkyunkwan University, PhD
2011-2015 Graduated from School of Medicine, Kyung Hee University, Medical Doctor, Master of Medicine
2002-2009 Graduated from College of Korean (Oriental) Medicine, Gachon University (Formerly Kyungwon University), Korean (Oriental) Medical Doctor

Professional Experiences

2023-Present Assistant Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chung-Ang University Gwangmyeong Hospital
2022-2023 Clinical Assistant Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chung-Ang University Gwangmyeong Hospital
2020-2022 Fellow, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Samsung Medical Center
2016-2020 Resident, Internal Medicine, Samsung Medical Center
2015-2016 Intern, Samsung Medical Center

Research Interests

Viral Hepatitis, Steatotic Liver Disease, Hepatocellular Carcinoma

Representative Publications

1. Chang JI, Kim JH, Sinn DH, Cho JY, Kim KM, Oh JH, Park Y, Sohn W, Goh MJ, Kang W, Gwak GY, Paik YH, Choi MS, Lee JH, Koh KC, Paik SW. Clinical Outcomes and Validation of Ursodeoxycholic Acid Response Scores in Patients with Korean Primary Biliary Cholangitis: A Multicenter Cohort Study. Gut Liver. 2023 Mar 31. doi: 10.5009/gnl220420. PMID: 36999383.
2. Chang JI, Sinn DH, Jeong WK, Hwang JA, Won HY, Kim K, Kang W, Gwak GY, Paik YH, Choi MS, Lee JH, Koh KC, Paik SW. Imaging features of hepatobiliary MRI and the risk of hepatocellular carcinoma development. Scand J Gastroenterol. 2022 Dec;57(12):1470-1477. doi: 10.1080/00365521.2022.2093124. PMID: 35786290.
3. Chang JI, Sinn DH, Cho H, Kim S, Kang W, Gwak GY, Paik YH, Choi MS, Lee JH, Koh KC, Paik SW. Clinical Outcomes of Hepatitis B Virus-Related Hepatocellular Carcinoma Patients with Undetectable Serum HBV DNA Levels. Dig Dis Sci. 2022 Sep;67(9):4565-4573. doi: 10.1007/s10620-021-07312-8. PMID: 34800218.

Recent Advances in the Management of Acute-on-Chronic Liver Failure

Jong-In Chang *Chung-Ang University*

Acute-on-chronic liver failure (ACLF) is a distinct clinical syndrome characterized by rapid deterioration of liver function in patients with chronic liver diseases, typically cirrhosis, associated with organ failure and high short-term mortality. International societies including the North American Consortium for the Study of End-Stage Liver Disease (NACSELD), the European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) consortium, and the Asian Pacific Association for the Study of the Liver (APASL) have established distinct criteria and management strategies for ACLF.

The NACSELD defines ACLF by acute deterioration of liver function accompanied by two or more extrahepatic organ failures (renal, neurologic, circulatory, or respiratory) in patients with CLD, including non-cirrhotic CLD, incorporating the presence of infection and sepsis as important clinical factors.[1] The EASL-CLIF consortium defines ACLF as a syndrome in cirrhotic patients characterized by acute decompensation (ascites, hepatic encephalopathy, gastrointestinal hemorrhage, bacterial infections) and organ failure, evaluated by the CLIF-consortium organ failure score.[2] APASL guidelines uniquely emphasize acute hepatic insults characterized by jaundice (bilirubin $\geq$ 5 mg/dL) and coagulopathy (INR $\geq$ 1.5), complicated within four weeks by ascites or hepatic encephalopathy, explicitly excluding prior hepatic decompensation and extrahepatic organ failure from initial diagnostic criteria.[3]

Management principles are generally shared between the guidelines. First, early diagnosis and risk stratification using NACSELD or CLIF-C scoring systems are recommended. Second, identification and treatment of precipitating factors, especially bacterial infections, gastrointestinal bleeding, or severe alcoholic hepatitis, is paramount. Third, organ support following standard critical care should be individualized. Vasopressors, renal replacement therapy, and ventilatory support are frequently required. Both American Association for the Study of Liver Diseases (AASLD) and EASL guidelines recommend early liver transplantation (LT) evaluation, acknowledging that timely LT is often the only curative option.

Treatment strategies consistently involve early identification and management of precipitating events, supportive care, organ-specific interventions, and early liver transplantation evaluation. Emerging extracorporeal liver support therapies (e.g., plasma exchange, hemoperfusion) show promise as bridging therapies, although clinical evidence varies.[4-6] LT remains the definitive curative intervention for advanced ACLF, especially in grade 3 patients, significantly improving survival and quality of life. Recent

data suggest favorable long-term outcomes post-transplantation, comparable to patients without ACLF.[6] Key prognostic indicators include frailty, sarcopenia, MELD-Na, and CLIF-C ACLF scores, emphasizing the importance of personalized assessments to optimize patient selection and transplantation timing.[7]

In conclusion, ACLF is a heterogeneous syndrome defined differently across guidelines but consistently associated with poor prognosis. Early diagnosis, individualized organ support, and timely LT are key to improving outcomes. Integration of the pragmatic recommendations from the EASL and AASLD guidelines may optimize patient-focused management. Future research should aim to harmonize global diagnostic criteria and validate early predictive biomarkers, while also advancing therapeutic strategies that target systemic inflammation and immune-metabolic dysregulation. There remains an urgent need to develop effective interventions that go beyond supportive care and LT to improve outcomes in ACLF.

Keywords: Acute-on-chronic liver failure; Organ failure; Liver transplantation

References

1. Karvellas CJ, Bajaj JS, Kamath PS, Napolitano L, O'Leary JG, Sola E, et al. AASLD Practice Guidance on Acute-on-chronic liver failure and the management of critically ill patients with cirrhosis. Hepatology 2024;79:1463-1502.
2. European Association for the Study of the L. EASL Clinical Practice Guidelines on acute-on-chronic liver failure. J Hepatol 2023;79:461-491.
3. Sarin SK, Choudhury A, Sharma MK, Maiwall R, Al Mahtab M, Rahman S, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update. Hepatol Int 2019;13:353-390.
4. Piano S, Mahmud N, Caraceni P, Tonon M, Mookerjee RP. Mechanisms and treatment approaches for ACLF. Liver Int 2025;45:e15733.
5. Yadav M, Maiwal R, Kumar Br V, Tripathi G, Sharma N, Sharma N, et al. Comparative metabolome analysis reveals higher potential of haemoperfusion adsorption in providing favourable outcome in ACLF patients. Liver Int 2024;44:1189-1201.
6. Artru F, Sacleux SC, Ursic-Bedoya J, Ntandja Wandji LC, Lutu A, L'Hermite S, et al. Long-term outcome following liver transplantation of patients with ACLF grade 3. J Hepatol 2025;82:62-71.
7. Perdiguero GG, Spina JC, Martinez J, Savluk L, Saidman J, Bonifacio M, et al. Enhancing ACLF prediction by integrating sarcopenia assessment and frailty in liver transplant candidates on the waiting list. JHEP Rep 2024;6:100985.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 1: May 29 (Thu.)

PG Course 4

Hepatic Tumors

Chairs:

Chang Hyeong Lee (Daegu Catholic Univ.)
Byung Seok Lee (Chungnam National Univ.)

Tae Hyung Kim

Korea University

Self Introduction

Prof. Tae Hyung Kim is a Professor of the Department of Gastroenterology and Hepatology, Korea University Anam Hospital.

He graduated from Korea University College of Medicine with his medical degree in 2006 and completed his internship and residency at the Department of Internal Medicine at Korea University Hospital, receiving his diploma in Internal Medicine in 2011.

Since 2022, he has been taking a number of roles, including board members of the Korean Association of the Study of the Liver (2022-2023), Korean Liver Cancer Association (2022-2024), and Korean association of Gastroenterology (2023-2024).

Research Interests

Viral Hepatitis, Liver Cirrhosis, MASLD, Liver Cancer

Representative Publications

1. Kim TH, Kim JH, Yim HJ, et al. Noninferiority Outcomes of Besifovir Compared to Tenofovir Alafenamide in Treatment-Naïve Patients with Chronic Hepatitis B. Gut and Liver. 2024;18(2):305-315.
2. Kim TH, Yim HJ, Jung YK,et al. Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group. New prognostic model for hospitalized patients with alcoholic cirrhosis and Maddrey's discriminant function <32. Hepatol Int. 2024;18(2):500-508.
3. Yim HJ, Kim TH, Suh SJ, et al. Response-Guided Therapy with Cefotaxime, Ceftriaxone, or Ciprofloxacin for Spontaneous Bacterial Peritonitis: A Randomized Trial: A Validation Study of 2021 AASLD Practice Guidance for SBP. Am J Gastroenterol. 2023;118(4):654-663.
4. Kim TH, Jung YK, Yim HJ,et al. Impacts of muscle mass dynamics on prognosis of outpatients with cirrhosis. Clin Mol Hepatol. 2022;28(4):876-889.

Surveillance Programs for Hepatocellular Carcinoma according to Risk Factors

Tae Hyung Kim *Korea University*

1. Introduction

Hepatocellular carcinoma (HCC) represents a significant global health concern, ranking as the sixth most common malignancy and the third leading cause of cancer-related mortality worldwide.[1] While therapeutic modalities and survival rates for other cancers have substantially improved over the past decades, the prognosis for HCC remains unfavorable.

The early stages of HCC are frequently asymptomatic, underscoring the critical role of the surveillance. Early detection significantly enhances the potential for curative treatments, such as resection, transplantation, or ablation, leading to substantially higher 5-year survival rates (exceeding 50-70%) compared to advanced stages.[2] Surveillance programs aim to shift diagnoses to earlier Barcelona Clinic Liver Cancer (BCLC) stages, thereby increasing the applicability of curative options. The disparity in survival rates between early and late HCC stages strongly supports the implementation of effective surveillance programs in high-risk populations.

2. Risk Factors for HCC Development

2.1 Chronic Viral Hepatitis B and C (CHB and CHC)

Globally, CHB and CHC represents the most prevalent risk factor for HCC. These viral infections induce chronic hepatic injury, inflammation, and fibrosis, thereby elevating the risk of malignant transformation. HBV, a DNA virus, can integrate into the host genome, acting as a mutagen and inducing genomic instability. Notably, HBV can lead to HCC in the absence of overt cirrhosis, albeit typically with underlying fibrosis. Specific HBV factors, such as viral load, genotype (C and F), and particular mutations (preS, BCP, HBx), are associated with increased risk.[3] Conversely, HCV, an RNA virus, does not integrate into the host genome but promotes HCC through indirect mechanisms, including chronic inflammation, fibrosis, and activation of oncogenic pathways. In HCV patients, HCC almost invariably arises in the setting of cirrhosis. Co-infection with both HBV and HCV increases the risk of HCC compared to mono-infection.

2.2 Cirrhosis (LC)

The annual risk of HCC in patients with cirrhosis varies from 1% to 8%, depending on the etiology and

severity. Common causes of cirrhosis include chronic viral hepatitis, excessive alcohol consumption, steatotic liver disease (SLD), autoimmune liver diseases, and hereditary metabolic disorders. The cirrhotic liver is more susceptible to the accumulation of DNA mutations that can lead to HCC. Cirrhosis serves as the final common pathway for various forms of hepatic injury, increasing the likelihood of progression to HCC, thus emphasizing the importance of surveillance in all cirrhotic patients irrespective of the initial cause.

2.3 Alcohol Consumption

Prolonged and excessive alcohol consumption can lead to irreversible liver damage and cirrhosis, significantly increasing the risk of HCC. Chronic ingestion of specific daily amounts of alcohol is strongly associated with HCC.[4] Alcohol-related liver disease is a leading cause of HCC in Western countries. The role of alcohol in HCC development is primarily mediated through the induction of cirrhosis, highlighting the need for risk assessment based on the level and duration of alcohol intake.

2.4 Metabolic-Dysfunction Associated Steatotic Liver Disease (MASLD) and Type2 Diabetes

MASLD, characterized by hepatic fat accumulation, is increasingly prevalent, particularly in overweight individuals and those with metabolic syndrome. Especially, Type 2 diabetes mellitus is associated with an increased risk of HCC, particularly when coexisting with other risk factors such as obesity and viral hepatitis. The strong association between metabolic disorders and HCC underlines the necessity of considering these factors in risk stratification and surveillance strategies.

3. Surveillance Programs

3.1 Current Surveillance Process

Major hepatology societies, including the AASLD, EASL, APASL, and NCCN, recommend surveillance for patients at high risk, especially LC, for HCC development. Some guidelines do not recommend surveillance for CHC patients without LC after SVR. Most of guidelines supported the abdominal ultrasonography (US) every 6 months, with or without alpha-fetoprotein (AFP) testing.[5,6]

3.2 Image Modalities

US has limitations including highly operator dependent and worse performance in patients with obesity or ascites. There are emerging data for CT and MRI-based surveillance, but cost effectiveness and harm of the tests were problematic. Recently, it has been proposed the abbreviated MRI as an alternative for US, but needed more validations.

3.3 Risk Stratification

Advanced fibrosis (stage F3) is a significant risk factor, and some guidelines recommend surveillance in these patients even without LC. HCC development in patients with alcohol-associated liver disease or

MASLD, regardless of the presence of LC, has been increasing, but markedly low in patients without LC compared those with LC. Thus, the risk stratification will be required for patients without LC, and even those with LC.

For patients with CHB, many predictive models for HCC development have been established including REACH-B, PAGE-B, mPAGE-B, CU-HCC, GAG-HCC, LSM-HCC, and PLAN-B models.[7] Using other biomarkers, including AFP-L3 and des-gamma carboxy-prothrombin (DCP), many new models such as ASAP, male-ABCD, HES or GALAD have been developed and validated.[5] They showed good performance of 60-80% sensitivities for early HCC detection. Recently, circulating tumor DNA (ctDNA), microRNAs, long non-coding RNAs, and extracellular vesicles were also studied for the surveillance of HCC. In addition, AI will show promising results in improving HCC detection and classification even using traditional markers and modalities.

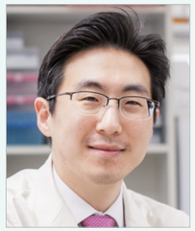
4. Summary

Risk factor-based HCC surveillance is crucial for early detection and improved survival. LC remains a primary indication for surveillance across various etiologies. Specific risk factors and prediction models guide surveillance in non-cirrhotic CHB patients. While HCV eradication reduces risk, surveillance remains important in advanced liver disease. MASLD presents unique challenges due to non-cirrhotic HCC, necessitating refined risk stratification. In addition, personalized and risk-stratified surveillance programs are essential for optimizing outcomes and resource utilization.

Advancing the field of HCC surveillance requires ongoing research into novel biomarkers and advanced imaging techniques, validation and implementation of AI-based tools, development of risk stratification models for all high-risk groups, and further studies to evaluate the cost-effectiveness of various surveillance strategies.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74(3):229-263.
2. An J, Chang Y, Choi GH, et al. Hepatocellular Carcinoma in Korea: An Analysis of the 2016-2018 Korean Nationwide Cancer Registry. J Liver Cancer 2025.
3. Shen C, Jiang X, Li M, Luo Y. Hepatitis Virus and Hepatocellular Carcinoma: Recent Advances. Cancers (Basel) 2023;15(2).
4. Ganne-Carrié N, Nahon P. Differences between hepatocellular carcinoma caused by alcohol and other aetiologies. J Hepatol 2024.
5. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol 2025;82(2):315-374.
6. Singal AG, Llovet JM, Yarchoan M, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology 2023;78(6):1922-1965.
7. Yu JH, Cho SG, Jin YJ, Lee JW. The best predictive model for hepatocellular carcinoma in patients with chronic hepatitis B infection. Clin Mol Hepatol 2022;28(3):351-361.



Wonseok Kang

Sungkyunkwan University

Self Introduction

Prof. Wonseok Kang is an Associate Professor of Medicine at Sungkyunkwan University School of Medicine, and the Chief of Digestive Disease Center at Samsung Medical Center, Seoul, Korea.

He graduated from Yonsei University with his medical degree in 2004 and completed his residency at the Department of Internal Medicine in Severance Hospital in 2009. After completing his clinical training, he pursued a Ph.D. in Medical Science and Engineering at Korea Advanced Institute of Science and Technology (KAIST) in 2013.

Recently, he spent a year as a Visiting Research Scholar at The Jackson Laboratory for Genomic Medicine and Yale School of Medicine in Connecticut, USA. After returning from his sabbatical, he is currently focusing on translational research in the field of hepatology in relation to his clinical practice.

Research Interests

- Hepatocellular Carcinoma, Immunotherapy, Biomarkers
- Viral Hepatitis, Autoimmune Liver Disease

Representative Publications

1. Molecular landscape of tumor-associated tissue-resident memory T cells in tumor microenvironment of hepatocellular carcinoma. Cell Commun Signal 2025
2. Unraveling the immune-activated tumor microenvironment correlated with clinical response to atezolizumab plus bevacizumab in advanced HCC. JHEP Rep. 2024
3. Hepatocellular carcinoma patients with high circulating cytotoxic T cells and intra-tumoral immune signature benefit from pembrolizumab: results from a single-arm phase 2 trial. Genome Med 2022

PG Course 4 | DAY 1: May 29 (Thu.) | ROOM 1 [3F]

Neoadjuvant and Adjuvant Therapies for Hepatocellular Carcinoma

Wonseok Kang *Sungkyunkwan University*

Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality worldwide. Although resection, ablation, and transplantation offer curative options for early-stage disease, high recurrence rates underscore the need for effective perioperative systemic therapies. Neoadjuvant and adjuvant therapies are being actively investigated to improve outcomes for HCC patients.

After years of limited progress with systemic treatments, immune checkpoint inhibitors (ICIs) targeting PD-1, PD-L1, and CTLA-4 have shown promise, reflecting the immunogenic nature of HCC. Recent advances include the Phase III IMBrave050 trial, which demonstrated a significant reduction in recurrence risk with adjuvant atezolizumab plus bevacizumab in high-risk patients following resection or ablation. Nonetheless, no neoadjuvant or adjuvant therapy is currently FDA-approved for HCC, and post-treatment surveillance remains standard. Multiple ongoing Phase III trials are evaluating additional immunotherapeutic strategies in the perioperative setting.

Neoadjuvant approaches are increasingly explored for their potential to downstage tumors, treat micrometastases early, and facilitate resection or transplantation in previously inoperable cases. Early-phase studies combining ICIs with tyrosine kinase inhibitors or other agents have shown encouraging pathologic response rates and feasibility. However, a major challenge is the lack of validated surrogate endpoints; measures such as pathologic complete response (pCR) and major pathologic response (MPR) require further validation in the context of immunotherapy for HCC.

Systemic therapies are also being investigated as bridging or downstaging strategies for liver transplantation candidates, with the goal of improving outcomes beyond those achieved with traditional locoregional therapies such as TACE or TARE. However, the use of immunotherapy after transplantation remains limited due to the risk of graft rejection.

This rapidly evolving landscape highlights the need for multidisciplinary collaboration and personalized treatment planning. Future research should focus on identifying predictive biomarkers, such as circulating tumor DNA (ctDNA), optimizing therapeutic combinations and timing, and establishing reliable endpoints. Well-designed clinical trials will be essential to develop effective perioperative protocols and improve long-term outcomes for patients with HCC.

References

1. Llovet JM, et al. Hepatocellular carcinoma. Nat Rev Dis Primers. 2021;7:6.
2. Finn RS, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med. 2020;382:1894-1905.
3. Zhu AX, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. Lancet Oncol. 2018;19:940-952.
4. Yau T, et al. Nivolumab plus Ipilimumab in Advanced Hepatocellular Carcinoma: CheckMate 040 Study. J Clin Oncol. 2022;40:1-10.
5. Kaseb AO, et al. Neoadjuvant and adjuvant immunotherapy in hepatocellular carcinoma: current status and future directions. J Hepatocell Carcinoma. 2022;9:1-15.
6. Sangro B, et al. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol. 2025;82:315-374.
7. Marron TU, Finn RS. Neoadjuvant and adjuvant immunotherapy for hepatocellular carcinoma: current status and future directions. Hepatology. 2023;77:15-27.
8. Rimassa L, et al. Tolerability and efficacy of systemic therapies in hepatocellular carcinoma: a review. Liver Int. 2021;41:1247-1260.
9. Imamura H, et al. Risk factors contributing to early and late phase intrahepatic recurrence of hepatocellular carcinoma after hepatectomy. J Hepatol. 2003;38:200-207.
10. Lee JH, et al. Adjuvant immunotherapy with autologous cytokine-induced killer cells for hepatocellular carcinoma. Gastroenterology. 2015;148:1383-1391.
11. Bruix J, et al. Adjuvant sorafenib for hepatocellular carcinoma after resection or ablation (STORM): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Oncol. 2015;16:1344-1354.
12. Vogel A, et al. Adjuvant and neoadjuvant therapies for hepatocellular carcinoma. Hepatology. 2024 [article in press].
13. D'Alessio A, et al. Pathological response following neoadjuvant immune checkpoint inhibitors in patients with hepatocellular carcinoma: a cross-trial, patient-level analysis. Lancet Oncol. 2024;25:1465-1475.
14. Wang K, et al. Adjuvant sintilimab in resected high-risk hepatocellular carcinoma: a randomized, controlled, phase 2 trial. Nat Med. 2024;30:708-715.
15. Berardi G, et al. Recurrence and tumor-related death after resection of hepatocellular carcinoma in patients with metabolic syndrome. JHEP Reports. 2024;6:1-9.
16. Llovet JM, et al. Adjuvant and neoadjuvant immunotherapies in hepatocellular carcinoma. Nat Rev Clin Oncol. 2024;21:294-311.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

So Yeon Kim

University of Ulsan

Self Introduction

Prof. So Yeon Kim is a Professor in the Abdominal Imaging Section, Department of Radiology, University of Ulsan College of Medicine, Asan Medical Center (AMC), Seoul, Korea. After earning her M.D. from the University of Ulsan College of Medicine in 1999, Prof. Kim completed a radiology residency and an Abdominal Imaging fellowship at AMC. From 2008 to 2011 he served as Clinical Instructor and Assistant Professor of Radiology at Seoul National University Bundang Hospital. Since 2011 she has been a full-time faculty member in the Department of Radiology at AMC.

Research Interests

Prof. Kim's clinical and academic focus centers on abdominal imaging of the liver, pancreas, and biliary system, with particular expertise in liver tumors including hepatic adenomas. Over the past decade she has led a prolific research program aimed at improving the detection, imaging characterization, and image-guided thermal ablation of malignant hepatic lesions. Her group's recent work involves identifying advanced MRI and CT biomarkers that differentiate hepatocellular adenoma subtypes, enabling precise risk stratification for hemorrhage or malignant transformation and guiding patient-specific decisions.

To date, Prof. Kim has authored more than 200 peer-reviewed articles and has contributed seven book chapters on abdominal imaging. She remains actively involved in performing ultrasound- and CT-guided tumor ablation for hepatic neoplasms, translating his research findings directly into patient care.

Representative Publications

1. Heo S, Kim B, Kim SY, et al. A Multicenter Study on Hepatocellular Adenomas in Korea: Clinicopathological and Imaging Features with an Emphasis on β Catenin Mutated Subtype. Liver International 2025;45:e16155.
2. Heo S, Song IH, Reizine E, et al. Insights into hepatocellular adenomas in Asia: molecular subtypes, clinical characteristics, imaging features, and hepatocellular carcinoma risk. J Liver Cancer 2025;25;67-78.
3. Heo S, Kim SY, Lee SJ, et al. LI-RADS Ultrasound Surveillance Version 2024: comparison with Version 2017 for hepatocellular carcinoma detection and risk factors for Visualization Score C. AJR Am J Roentgenol 2025;Epub ahead of print:1-10.
4. Park HJ, Kang HJ, Kim SY, et al. Effects of hepatic fibrosis on the quantification of hepatic steatosis using the controlled attenuation parameter in patients with chronic hepatitis B. Ultrasonography 2025;44:83-91.
5. Kim HY, Hong S, Heo S, et al. Comparison of clinical and MRI features of hepatic angiosarcoma and epithelioid hemangioendothelioma. Abdom Radiol (NY) 2025;50:619-632.

Rising Tide: Hepatocellular Adenomas in Korea

So Yeon Kim *University of Ulsan*

Hepatocellular adenomas (HCAs) are a heterogeneous group of benign monoclonal liver tumors with distinct molecular subtypes, each associated with specific risk factors, imaging features, and potential complications, including malignant transformation.[1] The molecular classification of HCAs — as outlined in the World Health Organization (WHO) 2019 guidelines[2]— has been well-established and categorizes HCAs into distinct subtypes: HNF1α-mutated HCA (HHCA), inflammatory HCA (IHCA), β-catenin mutated HCA (βHCA), including β-catenin mutated inflammatory HCA (βIHCA), sonic hedgehog HCA, and unclassified HCA (UHCA). However, the majority of HCA studies were predominantly conducted in Western populations, emerging data from Asia, including Korea, reveal important epidemiologic differences that necessitate region-specific diagnostic and management strategies.

In this lecture, I will present recent findings from a multicenter study of HCAs in Korea, which demonstrate a rising incidence of these tumors over the past decade.[3] So far HCAs have been considered rare tumors in Asian countries; however, this trend appears to be changing, likely driven by the increasing use of cross-sectional imaging and a growing prevalence of obesity. Notably, the clinicopathologic characteristics of HCAs in Korea differ significantly from those in the West, with a higher prevalence among male patients, low rates of oral contraceptive use, and a predominance of inflammatory subtypes — patterns that align with reports from other East Asian countries.[4-6]

Advances in genomic characterization have identified βHCAs, particularly those involving exon 3 mutations, as high-risk subtypes due to their strong association with hepatocellular carcinoma (HCC) development. Identifying these high-risk subtypes is a critical component of clinical management.[7] In settings where DNA/RNA sequencing is not readily available, additional immunohistochemical markers, such as glutamine synthetase (GS) or nuclear β-catenin staining, may aid in diagnosis. Furthermore, high signal intensity on the hepatobiliary phase of gadoxetic acid-enhanced MRI has emerged as a promising imaging biomarker for βHCAexon3 and βIHCAexon3.[8-10]

Our Korean multicenter study developed and validated an imaging-based scoring system to differentiate βHCAs using tumor heterogeneity and hepatobiliary phase signal intensity on MRI, demonstrating excellent diagnostic performance.[3] These findings are consistent with those reported in previous studies from Western countries.[8-10]

Differential diagnosis remains challenging, particularly when distinguishing HCA from other hepatocellular tumors such as focal nodular hyperplasia and hepatocellular carcinoma which can exhibit similar imaging features. This challenge is further complicated in Korean populations by the high prevalence of hepatitis, which increases the risk of HCC.

This lecture will review the updated molecular classification of HCAs, highlight the distinctive features of HCAs in Korea, and discuss the critical role of imaging in non-invasive subtype classification and risk stratification. Finally, I will address the future direction for HCA research in Asia, emphasizing the need for region-specific data, further validation of imaging-based models, and the integration of genomic tools to optimize patient outcomes and guide precision management strategies.[11]

References

1. Bioulac-Sage P, Gouw ASH, Balabaud C, Sempoux C. Hepatocellular adenoma: what we know, what we do not know, and why it matters. Histopathology 2022;80:878-897
2. Bioulac-Sage P KS, Nault JC. . Hepatocellular adenoma. In WHO Classification of Tumours Editorial Board ed. World Health Organization classification of tumours, 5th edn. Digestive system tumours. , 5th ed. Lyon: IARC Press
3. Heo S, Kim B, Kim SY, Kang HJ, Song IH, Lee SH, et al. A Multicenter Study on Hepatocellular Adenomas in Korea: Clinicopathological and Imaging Features With an Emphasis on β-Catenin Mutated Subtype. Liver Int 2025;45:e16155
4. Lin H, van den Esschert J, Liu C, van Gulik TM. Systematic review of hepatocellular adenoma in China and other regions. J Gastroenterol Hepatol 2011;26:28-35
5. Sasaki M, Nakanuma Y. Overview of Hepatocellular Adenoma in Japan. International Journal of Hepatology 2012;2012:648131
6. Huang WC, Liau JY, Jeng YM, Liu KL, Lin CN, Song HL, et al. Hepatocellular adenoma in Taiwan: Distinct ensemble of male predominance, overweight/obesity, and inflammatory subtype. J Gastroenterol Hepatol 2020;35:680-688
7. Nault JC, Couchy G, Balabaud C, Morcrette G, Caruso S, Blanc JF, et al. Molecular Classification of Hepatocellular Adenoma Associates With Risk Factors, Bleeding, and Malignant Transformation. Gastroenterology 2017;152:880-894 e886
8. Tse JR, Felker ER, Naini BV, Shen L, Shen J, Lu DSK, et al. Hepatocellular Adenomas: Molecular Basis and Multimodality Imaging Update. Radiographics 2023;43:e220134
9. Reizine E, Ronot M, Ghosn M, Calderaro J, Frulio N, Bioulac-Sage P, et al. Hepatospecific MR contrast agent uptake on hepatobiliary phase can be used as a biomarker of marked β-catenin activation in hepatocellular adenoma. Eur Radiol 2021;31:3417-3426
10. Tse JR, Felker ER, Cao JJ, Naini BV, Liang T, Lu DSK, et al. Hepatocellular Adenoma Subtypes Based on 2017 Classification System: Exploratory Study of Gadoxetate Disodium-Enhanced MRI Features With Proposal of a Diagnostic Algorithm. AJR Am J Roentgenol 2023;220:539-550
11. Heo S, Song IH, Reizine E, Ronot M, Nault JC, Kim HY, et al. Insights into hepatocellular adenomas in Asia: molecular subtypes, clinical characteristics, imaging features, and hepatocellular carcinoma risks. J Liver Cancer 2025;25:67-78

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LIVER WEEK 2025
May 29 - 31, 2025 | HICO, Gyeongju, Korea

Pil Soo Sung

The Catholic University of Korea

Self Introduction

Education and Training

2007.02 M.D. Medicine College of Medicine, The Catholic University of Korea, Seoul, Korea
2011.08 M.S. Internal Medicine (Hepatology), The Catholic University of Korea, Seoul, Korea
2016.02 Ph.D. Immunology, Graduate School of Medical Science & Engineering, KAIST, Daejeon, Korea

Positions and Honors

2007-2008 Rotating Internship, Catholic Medical Center, The Catholic University of Korea, Seoul, Korea
2008-2012 Residency, Department of Internal Medicine, Seoul St. Mary's hospital, The Catholic University of Korea, Seoul, Korea
2012-2016 Researcher and teaching assistant, Graduate School of Medical Science & Engineering, KAIST, Daejeon, Korea
2016-2018 Clinical Fellowship, Department of Internal Medicine, Seoul St. Mary's hospital, The Catholic University of Korea, Seoul, Korea
2018-2020 Clinical Assistant Professor, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea
2020-2022 Assistant Professor, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea
2022-2025 Associate Professor, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea
2025-Present Professor, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea

Professional Memberships

2007-Present The Korean Association of Medicine
2012-Present The Korean Association of Internal Medicine, The Korean Association for the Study of the Liver
2013-Present The Korean Association of Immunologists
2014-Present The Korean Society of Biochemistry and Molecular Biology

Research Interests

Hepatocellular Carcinoma, Liver Diseases, Liver Biopsy

Representative Publications

1. Dynamic Peripheral T-Cell Analysis Identifies On-Treatment Prognostic Biomarkers of Atezolizumab plus Bevacizumab in Hepatocellular Carcinoma. Han JW, Kang MW, Lee SK, Yang H, Kim JH, Yoo JS, Cho HS, Jang EJ, Seo DH, Kwon JH, Nam SW, Bae SH, Jang JW, Choi JY, Yoon SK, Sung PS. Liver Cancer. 2024 Sep 2;14(1):104-116. doi: 10.1159/000541181. eCollection 2025 Mar.
2. Intrahepatic IgA complex induces polarization of cancer-associated fibroblasts to matrix phenotypes in the tumor microenvironment of HCC. Park JG, Roh PR, Kang MW, Cho SW, Hwangbo S, Jung HD, Kim HU, Kim JH, Yoo JS, Han JW, Jang JW, Choi JY, Yoon SK, You YK, Choi HJ, Ryu JY, Sung PS. Hepatology. 2024 Nov 1;80(5):1074-1086. doi: 10.1097/HEP.0000000000000772. Epub 2024 Feb 15.
3. Intrahepatic inflammatory IgA+PD-L1high monocytes in hepatocellular carcinoma development and immunotherapy. Sung PS, Park DJ, Roh PR, Mun KD, Cho SW, Lee GW, Jung ES, Lee SH, Jang JW, Bae SH, Choi JY, Choi J, Ahn J, Yoon SK. J Immunother Cancer. 2022 May;10(5):e003618. doi: 10.1136/jitc-2021-003618.
4. Crosstalk between tumor-associated macrophages and neighboring cells in hepatocellular carcinoma. Sung PS. Clin Mol Hepatol. 2021 Oct 19. doi: 10.3350/cmh.2021.0308. Online ahead of print.
5. EpCAM-high liver cancer stem cells resist natural killer cell-mediated cytotoxicity by upregulating CEACAM1. Park DJ, Sung PS, Kim JH, Lee GW, Jang JW, Jung ES, Bae SH, Choi JY, Yoon SK. J Immunother Cancer. 2020 Mar;8(1):e000301. doi: 10.1136/jitc-2019-000301.

Diagnosis and Treatment of Combined Hepatocellular Carcinoma-Cholangiocarcinoma

Pil Soo Sung *The Catholic University of Korea*

1. Definition and Classification

Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a rare primary liver cancer, accounting for approximately 1–5% of all primary liver cancers. It features both hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (iCCA) components within the same tumor.

According to the 5th WHO Classification (2019):

Classical type: Tumor contains intermixed areas of HCC and iCCA.

Intermediate cell carcinoma: Tumor composed of biphenotypic cells expressing both hepatocytic (e.g., HepPar1) and cholangiocytic (e.g., CK19) markers.

Earlier subclassifications (e.g., Allen and Goodman) are no longer used.

2. Histogenesis and Cellular Origin

The cell of origin for cHCC-CCA remains debated. Multiple hypotheses exist

Transformation from mature hepatocytes, particularly under oncogenic stimulation and biliary transdifferentiation (e.g., via NOTCH signaling).

Derivation from hepatic progenitor cells capable of bipotential differentiation.

Less likely, transformation of cholangiocytes with acquisition of hepatocellular markers.

Lineage-tracing studies in mouse models and recent human hepatocyte reprogramming experiments have shown that hepatocytes can give rise to cHCC-CCA under certain genetic conditions.

3. Clinical Features

Epidemiology: prevalence varies by cohort (typically ~1%).

Risk Factors: Similar to HCC—HBV, HCV, alcohol, metabolic dysfunction-associated steatotic liver disease.

Serum Markers: May show elevation of both HCC markers (AFP, PIVKA-II) and iCCA markers (CEA, CA19-

9), but patterns are inconsistent.

4. Diagnosis

Imaging: May mimic either HCC or iCCA. Typical findings include mixed arterial enhancement and delayed washout, but imaging alone is unreliable.

Biopsy: Critical for accurate diagnosis, especially when tumor markers and imaging are discordant. Immunohistochemistry shows co-expression of hepatocytic and biliary markers.

5. Treatment Strategy

Surgery: First-line option if resectable. Prognosis is poorer than HCC but variable compared to iCCA.

Liver Transplantation: Performed in selected cases, but criteria are not standardized.

Locoregional Therapies: TACE or RFA may be used, usually following HCC protocols.

Systemic Therapy: No established standard. Historically treated as either HCC (e.g., sorafenib, atezo/bev) or iCCA (e.g., gemcitabine/cisplatin). Recent studies suggest immunotherapy (ICIs) has potential efficacy in cHCC-CCA, with response rates up to 20–33%.

6. Future Directions

Ongoing trials (e.g., jRCTs031220099, NCT05211323) are exploring the efficacy of ICI combinations in cHCC-CCA. Genomic profiling and refined subclassification may lead to personalized therapy and improved outcomes. Greater recognition and pathological confirmation are needed to establish cHCC-CCA as a distinct clinical entity.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

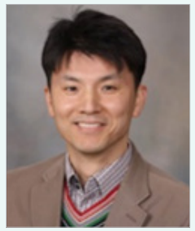
DAY 1: May 29 (Thu.)

Basic Research 1

Beginners' Guide for Basic Research

Chairs:

Jung-Hwan Yoon (Seoul National Univ.)
Won-Il Jeong (KAIST)



Jeong Won Jang

The Catholic University of Korea

Self Introduction

Prof. Jang is a Professor of Internal Medicine at The Catholic University of Korea. He received his medical degree from The Catholic University of Korea, and completed his Internal Medicine Residency and Hepatology/Gastroenterology Fellowship at Seoul St. Mary's Hospital in Seoul. He has been a faculty member of The Catholic University of Korea since 2005, and has been working at affiliated hospitals, Incheon St. Mary's Hospital (2005-2012) and Seoul St. Mary's Hospital (2013 ~ present). Between 2014 and 2015, he has worked as a Visiting Scientist at Center for Basic Research in Digestive Diseases, Mayo Clinic, Minnesota, USA.

He is currently a board member of The Korean Liver Cancer Study Group and has served as a board member of the Korean Association for the Study of Liver Diseases. He has authored and co-authored over 150 articles and two books, and is the editorial board member of four international liver journals.

Research Interests

- HBV Direct Oncogenic Potential and Integration into the Host Genome
- The Reactivation and Immunology of Hepatitis B
- Genomic Alterations and Biomarker Discovery in Liver Diseases and Hepatocarcinogenesis

Representative Publications

1. Han JW, .. Jang JW. A Machine Learning Algorithm Facilitates Prognosis Prediction and Treatment Selection for Barcelona Clinic Liver Cancer Stage C Hepatocellular Carcinoma. Clin Cancer Res 2024;30:2812-2821.
2. Nam H, Kim DY, .. Jang JW. Development and Validation of a Risk Prediction Model for Patients with Hepatocellular Carcinoma Receiving Atezolizumab-Bevacizumab. Hepatology 2025 [In press]
3. Kim JS, Kim HS, .., Jang JW. Male preference for TERT alterations and HBV integration in young-age HBV-related HCC: implications for sex disparity. Clin Mol Hepatol 2025;31:509-524.
4. Nam H, Lee J, .. Jang JW. Analysis of Immune-Related Adverse Events of Atezolizumab and Bevacizumab in Patients with Hepatocellular Carcinoma: A Multicenter Cohort Study. Liver Cancer 2023;13:413-425.
5. Yang H, Bae SH, .. Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol 2022;77:632-641.

Why Hepatologists Should Engage in Basic and Translational Research

Jeong Won Jang *The Catholic University of Korea*

As the burden of liver disease continues to rise globally, hepatologists are uniquely positioned to bridge the gap between clinical care and scientific discovery. This presentation explores the critical role of hepatologists in driving basic and translational research and argues that their active participation is essential to advancing the field of hepatology.

Basic research provides the foundational knowledge necessary to understand the complex pathophysiology of liver diseases, many of which involve multifactorial mechanisms rather than single causal agents. By uncovering molecular pathways, cellular mechanisms, and genetic factors, basic science lays the groundwork for the development of novel therapies and diagnostic tools. Translational research, in turn, transforms these discoveries into real-world applications—targeted treatments, biomarkers, and strategies for early detection and intervention.

Clinical hepatologists, positioned at the frontline of patient care, are uniquely equipped to identify unmet clinical needs, recognize patterns, and raise critical questions that can drive laboratory investigations. Their insights are invaluable in shaping research that is both scientifically rigorous and clinically relevant. The concept of "bench-to-bedside and bedside-to-bench" underscores the bidirectional nature of translational research, where clinical challenges inspire scientific exploration, and scientific breakthroughs inform clinical practice.

Several pressing issues in hepatology—such as the global rise in MASLD (metabolic dysfunction-associated steatotic liver disease), the lack of effective biomarkers for treatment of hepatocellular carcinoma, and the complexities of liver transplantation—require multidisciplinary, research-driven solutions. In this context, clinician-researchers are essential collaborators, contributing both practical insight and ensuring that research outcomes remain patient-centered and applicable to real-world care.

A notable example from the field is Dr. Harvey J. Alter, a distinguished clinician-scientist and co-recipient of the 2020 Nobel Prize in Physiology or Medicine for the discovery of the hepatitis C virus (HCV). As both a practicing physician and researcher, Dr. Alter played a pivotal role in leading a groundbreaking initiative at the NIH Clinical Center to uncover the causes of and reduce the risk of transfusion-associated hepatitis. Through this work, he successfully discovered and isolated HCV. His contributions directly enabled the development of novel diagnostics and antiviral therapies. These advances significantly

reduced transfusion-transmitted hepatitis and ultimately laid the foundation for a cure for HCV infection. Dr. Alter's career exemplifies how clinician-scientists can shape clinical practice and public health through evidence-based innovation.

Moreover, involving hepatologists in research fosters the development of the next generation of physician-scientists, who are poised to lead both in clinical practice and in the lab. This dual capability helps address workforce shortages while strengthening the discipline's future capacity to meet evolving challenges.

In summary, for hepatology to continue evolving and effectively address future demands, it is imperative that clinicians engage in research. Hepatologists are not only caregivers—they are essential drivers of discovery, innovation, and the implementation of improved medical solutions. Through sustained collaboration between laboratory researchers and clinicians, we can advance toward more effective, personalized, and preventive liver care.

Core Messages

- Liver diseases are multifactorial, requiring more than symptom-based care.
- Clinical care alone cannot ensure long-term patient outcomes without research support.
- Hepatologists can identify unmet needs and raise critical research questions.
- Basic research underpins evidence-based medicine.
- Translational research connects bench and bedside in both directions.
- Clinician–scientist collaboration drives impactful innovation.
- Research-active hepatologists strengthen the field's future.

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Young-Sun Lee

Korea University

Self Introduction

Academic Qualifications

2000.03-2006.02 M.D., in Korea University Medical College
2008.09-2010.08 M.S., Department of Medicine in Korea University Medical College
2011.02-2015.02 Ph.D., Graduate School of Medical Science & Engineering, KAIST, Korea

Professional Experience

2018.09-2021.02 Assistant Professor in Department of Internal Medicine, Division of Gastroenterology and Hepatology, Guro Hospital, Korea University College of Medicine
2021.03-Present Associate Professor in Department of Internal Medicine, Division of Gastroenterology and Hepatology, Guro Hospital, Korea University College of Medicine

Research Interests

NAFLD, HCC, Immunity

Representative Publications

1. Lee YS, Seki E. In Vivo and in Vitro Models to Study Liver Fibrosis: Mechanisms and Limitations. Cell Mol Gastroenterol Hepatol 2023.
2. Lee YS, Lee JE, Yi HS, et al. MRE-based NASH score for diagnosis of nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease. Hepatol Int 2022;16:316-24.
3. Kim TH, Lee Y, Lee YS, et al. Circulating miRNA is a useful diagnostic biomarker for nonalcoholic steatohepatitis in nonalcoholic fatty liver disease. Sci Rep 2021;11:14639.
4. Lee YS, Jung YK, Kim JH, et al. Effect of urea cream on sorafenib-associated hand-foot skin reaction in patients with hepatocellular carcinoma: A multicenter, randomised, double-blind controlled study. Eur J Cancer 2020;140:19-27.
5. Hyun MH, Lee YS, Kim JH, et al. Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies. Hepatology 2018;68:977-93.

Essential Steps to Setting up a Hepatology Research Lab

Young-Sun Lee *Korea University*

Establishing a hepatology research lab as a hepatology can be a transformative step toward contributing meaningfully to liver disease research. This lecture offers a practical roadmap for early-career clinicians aiming to build a productive and sustainable research foundation in hepatology.

The first essential step is to define a focused research interest, such as metabolic dysfunction-associated steatotic liver disease (MASLD), hepatocellular carcinoma (HCC), or viral hepatitis. Physicians should begin by identifying clinically relevant problems they encounter in practice and refining these into feasible and novel research questions. A thorough literature review helps uncover knowledge gaps and establish a unique research direction.

Building the infrastructure for a research lab requires thoughtful planning. Clinicians must secure ethical approval for human or animal studies, set up appropriate sample collection and biobanking systems, and identify necessary lab equipment. Collaboration with institutional core facilities—such as pathology, genomics, or biostatistics—can provide technical support and reduce startup costs.

Equally important is assembling the right team. Choosing experienced mentors and interdisciplinary collaborators enhances research quality. Recruiting motivated students, lab technicians, or research coordinators and providing proper training are key to building a cohesive team. Time management strategies are essential to balance clinical responsibilities with research activities.

Securing funding is another pillar of successful research. Early-career physicians should explore institutional grants, national funding agencies, and professional societies for starter grants. Writing competitive grant proposals involves clearly articulating research aims, methods, budgets, and anticipated outcomes. A solid understanding of research ethics and budgeting is also vital for project sustainability.

As research progresses, attention shifts to data analysis and dissemination. Proper data management, statistical planning, and collaboration with experts are necessary to ensure scientific rigor. Writing and publishing scientific manuscripts in reputable journals, responding constructively to peer reviewers, and presenting at academic meetings are essential for research visibility and career development.

In summary, setting up a hepatology research lab involves several domainss: defining your focus, building infrastructure, assembling a team, securing funding, ensuring ethical and logistical oversight, and translating results into publications. With strategic planning, mentorship, and perseverance, physician-researchers can make meaningful contributions to the field of hepatology and improve patient care through science.

Sejoon Lee

Seoul National University

Self Introduction

Prof. Sejoon Lee is an Associate Professor of the Precision Medicine Center and the Department of Genomic Medicine at Seoul National University Bundang Hospital. He also serves as a Visiting Professor in the Department of Healthcare Convergence at Seoul National University. (2018~Current)

He earned his Ph.D. in Bio and Brain Engineering from KAIST, where he specialized in biomedical data mining and machine learning. He has held research positions at the Samsung Genome Institute and SD Genomics, and has extensive experience in next-generation sequencing (NGS), population genetics, and the development of clinical bioinformatics tools.

Research Interests

With a strong background in cancer genomics, clinical bioinformatics, and biomedical data science, his research focuses on applying genomic technologies to precision medicine and translational research.

Representative Publications

1. Jin-Wook Choi, Jin-Ok Lee, Sejoon Lee* (2024) "Detecting microsatellite instability by length comparison of microsatellites in the 3□ untranslated region with RNA-seq" Briefings in Bioinformatics (*Corresponding Author)
2. Kyung-Ah Kim1, Sejoon Lee1, Hye Jung Park, Eun Sun Jang, Youn Jae Lee, Sung Bum Cho, Young Suk Kim, In Hee Kim, Byung Seok Lee, Woo Jin Chung, Sang Hoon Ahn, Seungtaek Kim, Sook Hyang Jeong (2023) "Analysis of Hepatitis C Virus Resistance-Associated Substitutions in Direct-Acting Antiviral Failure in South Korea Using Next-Generation Sequencing." Clinical and Molecular Hepatology (1First Author)
3. Jae Won Yun1, Sejoon Lee1, Sejong Chun, Kwangwoo Lee, Hongsook Kim (2021) "Comprehensive analysis of oncogenic signatures and consequent repurposed drugs in TMPRSS2: ERG fusion - positive prostate cancer" Clinical and Translational Medicine (1First Author)
4. Isidro Cortes-Ciriano1, Sejoon Lee1, Woong-Yang Park, Tae-Min Kim and Peter J. Park (2017) "A molecular portrait of microsatellite instability across multiple cancers" Nature Communications (1First Author)
5. Sejoon Lee1, Soohyun Lee1, Scott Ouellette, Woong-Yang Park, Eunjung Lee and Peter J. Park (2017) "NGSCheckMate: Software for ensuring sample identity in next-generation sequencing studies within and across data types" Nucleic Acids Research (1First Author)

How to Interpret Basic Research Data in Hepatology

Sejoon Lee *Seoul National University*

The integration of basic science and clinical hepatology is essential for advancing our understanding of liver diseases and developing novel therapeutic strategies. However, many clinicians and early-career researchers face challenges in interpreting complex basic research data, especially those derived from rapidly evolving genomic technologies. This educational session aims to bridge this gap by offering a practical and clinically relevant guide to interpreting fundamental research data in hepatology.

The presentation will cover key categories of basic experimental data, including gene expression profiling (e.g., RNA-seq), genomic variant analysis (e.g., WES/WGS), epigenetic data (e.g., DNA methylation), and functional studies using cell and animal models. Special focus will be given to understanding how genomic data are generated, processed, and interpreted—from raw data acquisition to downstream analyses such as differential expression, pathway enrichment, and biomarker discovery.

Common pitfalls in data interpretation, such as overfitting, batch effects, lack of reproducibility, and misinterpretation of statistical versus biological significance, will be discussed. Real-world case examples from hepatology research will illustrate the process of interpreting basic data in the context of liver diseases such as NAFLD, liver fibrosis, viral hepatitis, and hepatocellular carcinoma.

Through this session, attendees will develop skills to critically evaluate basic research papers, utilize publicly available datasets, and assess the clinical relevance of genomic findings. Ultimately, this understanding will foster more effective interdisciplinary collaboration and lead to advancements in the treatment of patients with liver diseases.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 1: May 29 (Thu.)

Basic Research 2

New Approaches in Translational Science

Chair:

Kyun-Hwan Kim (Sungkyunkwan Univ.)

Jong-Eun Park

KAIST

Self Introduction

Prof. Park research is focused on understanding how the information stored in genome can be interpreted and expressed to coordinate diverse biological phenomenon. During his PhD training, he studied non-coding RNAs and the mechanism post-transcriptional regulations, including miRNA biogenesis, poly(A) tail mediated translational regulation during cell cycle and ncRNA processing by nuclear deadenylases. As he joined the Dr. Sarah Teichmann's lab in Sanger Institute, he actively participated in the Human Cell Atlas from its beginning. He developed batch correction method which can applied onto large scale single-cell dataset. He also led the Human thymus atlas project, reconstructing the development and aging of human organ at single-cell resolution. Since 2020, he became independent researcher at the Graduate School of Medical Science and Engineering, KAIST, where he is applying single-cell omics to understand complex phenomenon such as aging, cancer, and autoimmune disorders, especially focusing on the large-scale data integration and interpretation.

Research Interests

Aging, Liver Fibrosis, Cancer, Systems Immunology, Bioinformatics, Single-Cell and Spatial Omics

Representative Publications

1. Tak, K. Y.*, Kim, J.*, Park, M.*, …, Kim, C.#, Park, J.-E.# (2025). Quasi-spatial single-cell transcriptome based on physical properties defines early aging associated niche in liver tissue. Nature Aging.
2. Kim, S.*, Jeon, J. H., …, Park J.-E.#, Yeo J.# (2024). Innate responses against the mRNA component of mRNA vaccine promote cellular immunity through IFN-β at the injection site. Nature Communications, 15:7226.
3. Kang, J.*, Lee, J.-H.*, …, Lee, S.-H.#, Choi, J. K.#, Park J.-E# (2024). Systematic dissection of tumor-normal single-cell ecosystems across a thousand tumors of 30 cancer types. Nature Communications, 15:4067.
4. Kim, S.*, Leem, G.*, ..., Kang C. M.#, Bang. S.#, Park J.-E# (2024). Integrative analysis of spatial and single-cell transcriptome data from human pancreatic cancer reveals an intermediate cancer cell population associated with poor prognosis. Genome Medicine, 16:20.
5. Kwon, J.*, Kang, J.*, ..., An H. J.#, Lee H.-O.#, Park J.-E#, Choi, J. K.# (2023). Single-cell mapping of combinatorial target antigens for CAR switches using logic gates. Nature Biotechnology, 1-13.

Basic Research 2 | DAY 1: May 29 (Thu.) | ROOM 3 [2F]

Advances in Spatial Omics and Data Analysis

Jong-Eun Park *KAIST*

Using an automatic public data search process, we unbiasedly collected over 20 million single-cell transcriptomic profiles from more than 500 independent studies, which contain more than 2,000 single-cell transcriptome datasets from diverse human organs and disease states. We invented a single-cell data remapping pipeline for the efficient re-analysis of the whole dataset from the raw sequence files at its highest genome coverage while excluding the biases from computational data processing steps. Metadata information has been curated and classified to provide harmonized terminology for the entire dataset. The integration of remapped single-cell transcriptome dataset minimizes the batch effect, allowing for the robust identification of cell types and the organ-specific, disease-specific, and sex-specific gene signatures for each cell type. Using this reference atlas of human cell types, we provide a universal reference for the deconvolution and interpretation of multi-organ spatial transcriptomics data collection. Finally, we have applied large language model to replicate the manual curation process, which could reach up to ~90% accuracy. In conclusion, we represent a fully curated, annotated, and harmonized cell network which augments spatial transcriptomics data analysis.

Junil Kim

Soongsil University

Self Introduction

Prof. Junil Kim is a Professor of the Department of Bioinformatics, Soongsil University College of Natural Science and is currently holding a position of Director of the Institute for Biological Systems.

He graduated from Interdisciplinary Graduate Program in Bioinformatics at Seoul National University with his master's degree in 2008 and received his Ph.D. degree in systems biology from Korea Advanced Institute of Science and Technology (KAIST) in 2014.

Since 2022, he has been taking a number of roles, including committee member of the Korean Society of Bioinformatics (2022-Present), the Korean Society of Molecular and Cellular Biology (2022-Present), Korea Genome Organization (2023-Present), and the Korean Society for Biochemistry and Molecular Biology (2024-Present).

Research Interests

- Piecing Together Jigsaw Puzzle and Single Cell Dynamics in Time-Space Continuum Using AI
- Evolutionary Design Principle of Biomolecular Regulatory Networks
- Predicting Phenotypes of the Bio-Organisms from Genomic Information and Their Interactions

Representative Publications

1. Rakbin Sung*, Hyeonkyu Kim*, Junil Kim**, and Daewon Lee**, "FastTENET: a Python framework for manycore computing acceleration of TENET", Bioinformatics, Vol. 40, Issue 12, btae699, 1 Dec 2024
2. Junil Kim*, Michaela Mrugala Rothová*, Esha Madan*, et al., "Neighbor-specific gene expression revealed from physically interacting cells during mouse embryonic development", PNAS (IF: 12.777), Vol. 120, Issue 2, e2205371120, 3 Jan. 2023 (*co-fist author)
3. Dongha Kim*, Junil Kim*, Young Suk Yu, Yong Ryoul Kim, Sung-hee Baek, Kyoung-Jae Won, "Systemic approaches using single cell transcriptome reveal that C/EBP γ regulates autophagy under amino acid starved condition", Nucleic Acids Research (IF: 19.160), Vol. 50, Issue 13, 7298-7309, 22 July 2022 (*co-fist author)
4. Guangzheng Weng, Junil Kim**, and Kyoung Jae Won**, "VeTra: a tool for trajectory inference based on RNA velocity", Bioinformatics (IF: 6.931), Vol. 37, Issue 20, p3509-3513, 15 Oct. 2021. (**co-corresponding author)
5. Junil Kim, Simon T. Jakobsen, Kedar N. Natarajan, Kyoung Jae Won, "TENET: Gene network reconstruction using transfer entropy reveals key regulatory factors from single cell transcriptomic data", Nucleic Acids Research (IF: 19.160), Vol. 49, Issue 1, e1-e1, 11 Jan. 2021.

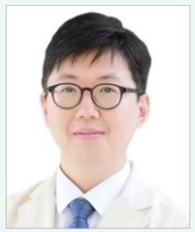
Heterogeneity in Hepatocellular Carcinoma Diagnosis and Treatment via Spatial Gene Profiling

Junil Kim *Soongsil University*

Many clinical researchers have developed targeted therapy and immunotherapy for the case of advanced stage of hepatocellular carcinoma (HCC). However, the molecular mechanisms of HCC development still need to be investigated to improve the response rate of those therapies. In this talk, I will present two of my recent studies.

First, I will present a single nucleus RNA sequencing analysis obtained from HCC patients. The snRNA-seq data were generated from biopsy samples of six patients with Barcelona Clinic Liver Cancer (BCLC) advanced C stage. I first found that the gene expression heterogeneity in hepatocytes were mainly dissected by vascular invasion. To identify the key regulators of malignant progression of hepatocytes, I applied TENET, a gene regulatory network (GRN) inference tool based on pseudotime-ordered single cell expression. TENET predicts that two novel transcription factors, which regulates many targets and regulates each other. This finding was comprehensively validated by overexpression and knockdown of those two regulators in various HCC cell lines. This study suggested that GRN analysis with single cell transcriptomics may provide new therapeutic targets for HCC.

My second presentation topic is Pan-cancer spatial transcriptomics analysis obtained from publicly available large-scale datasets including single cell RNAseq of 2,054,005 cells and Visium of 228 slides and 539,664 spots. These large and multimodal datasets were integrated using variational inference-based deep learning method. The integrative analysis of these two types of transcriptomics data enables to compare multiple cancer types in terms of spatial correlation of various cell types including cancer cell, T cells, B cell, myeloid cells, fibroblasts and endothelial cells. Spatial correlation of cell types in HCC showed that T cells, B cells and myeloid cells were co-localized compared to other cancer types. These Pan-cancer spatial transcriptomics approach enables to compare differential spatial compositions of cancer cells and TMEs in multiple cancer types.



Ji Won Han

The Catholic University of Korea

Self Introduction

Prof. Ji Won Han is an Assistant Professor in the Department of Gastroenterology and Hepatology at Seoul St. Mary's Hospital, The Catholic University of Korea.

He graduated from the College of Medicine at The Catholic University of Korea with a medical degree in 2011 and completed his residency in Internal Medicine at Seoul St. Mary's Hospital in 2016. He received his Master's degree from the Graduate School of Medicine at The Catholic University of Korea (2016) and his Ph.D. from the Graduate School of Medical Science and Engineering (GSMSE) at Korea Advanced Institute of Science and Technology (KAIST) in 2020.

Dr. Han is currently involved in multiple academic societies, including the Korean Association for the Study of the Liver, Korean Liver Cancer Association, Korean Society of Gastroenterology, and Korean Society of Clinical Ultrasound.

Research Interests

Liver Immunology and HCC Immunotherapy, Machine Learning Applications in Liver Diseases

Representative Publications

1. Dynamic peripheral T-cell analysis identifies on-treatment prognostic biomarkers of atezolizumab plus bevacizumab in hepatocellular carcinoma" Liver Cancer 2024, accepted.
2. Diagnostic accuracy of the Fibrosis-4 index for advanced liver fibrosis in nonalcoholic fatty liver disease with type 2 diabetes: A systematic review and meta-analysis" Clin Mol Hepatol. 2024
3. A Machine Learning Algorithm Facilitates Prognosis Prediction and Treatment Selection for Barcelona Clinic Liver Cancer Stage C Hepatocellular Carcinoma" Clin Cancer Res. 2024
4. IFNL3-adjuvanted HCV DNA vaccine reduces regulatory T-cell frequency and increases virus-specific T-cell responses" Journal of Hepatology. 2020
5. Functions of human liver CD69+CD103-CD8+ T cells depend on HIF-2α activity in healthy and pathologic livers" Journal of Hepatology. 2020

Basic Research 2 | DAY 1: May 29 (Thu.) | ROOM 3 [2F]

Digital Spatial Protein Profiling in Liver Diseases

Ji Won Han *The Catholic University of Korea*

Spatial proteomics has emerged as a revolutionary technique in biomedical research, enabling the visualization and quantification of protein expression while preserving spatial context within tissues. This technology, recognized as Nature Methods' "Method of the Year 2024," holds particular significance for liver disease research due to the organ's complex architecture and the critical role of spatial organization in its function and pathology.[1]

This lecture introduces the principles spatial proteomics and its applications in liver disease, with emphasis on immunological contexts. We will discuss how multiplexed imaging technologies like Imaging Mass Cytometry (IMC), Co-detection by Indexing (CODEX), and Digital Spatial Profiling (DSP) enable unprecedented insights into the liver's cellular and molecular landscape at subcellular resolution. These approaches reveal spatial relationships between hepatocytes, immune cells, and stromal components that conventional bulk proteomics cannot capture.

Recent breakthroughs in liver research will be highlighted, including:[2] characterization of tumor immune microenvironments in hepatocellular carcinoma (HCC), revealing distinct immune cell distributions between NASH-associated and virus-associated HCC;[3] identification of spatially-resolved macrophage phenotypes in progressive liver fibrosis, which has yielded a six-protein signature predictive of advanced fibrosis; and[4] mapping of functional interactions between tumor-associated macrophages and T cells at tumor margins, uncovering mechanisms of immune evasion. Specifically, I will share our recent report and experience implementing the GeoMx DSP platform for liver disease research.

The lecture will also address technical challenges, data analysis approaches, and integration with other omics technologies. Future perspectives will explore how spatial proteomics may transform liver disease diagnosis, prognosis assessment, and personalized treatment selection through integration with artificial intelligence and clinical pathology workflows.

References

1. Nature Methods. (2024). Method of the Year 2024: spatial proteomics. Nature Methods, 21(12), 2195–2196.
2. Li, M., Zhang, X., Chen, H., Wong, C.C., Ren, X., Li, Y., et al. (2024). Spatial proteomics of immune microenvironment in nonalcoholic steatohepatitis-associated hepatocellular carcinoma. Hepatology, 79(3), 560–574.

3. Lee, J., Kim, C.M., Cha, J.H., Park, J.Y., Yu, Y.S., Wang, H.J., et al. (2022). Multiplexed digital spatial protein profiling reveals distinct phenotypes of mononuclear phagocytes in livers with advanced fibrosis. Cells, 11(21), 3387.
4. Guilliams, M., Bonnardel, J., Haest, B., Vanderborght, B., Wagner, C., Remmerie, A., et al. (2022). Spatial proteogenomics reveals distinct and evolutionarily conserved hepatic macrophage niches. Cell, 185(2), 379–396.e38.

THE LIVER WEEK 2025

DAY 1: May 29 (Thu.)

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

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Young Investigator Meeting

Chairs:

Joon Hyeok Lee (Sungkyunkwan Univ.)
Won Young Tak (Kyungpook National Univ.)

Su Jong Yu

Seoul National University

Self Introduction

Eduactional

1997.3.1-2001.2.26 Doctor of Medicine, College of Medicine, Dept. of Medicine, Seoul National University
2004.3.1-2006.2.24 Master of Science in Medicine, Graduate School, Seoul National University
2010.3.1-2012.2.24 Doctor of Philosophy in Medical Science, Graduate School, Seoul National University

Professional Experience

2011.3-Present Clinical Professor, Department of Internal Medicine & Liver Research Institute, SNU College of Medicine
2016-2018 Visiting Scientist, NCI, NIH (Bethesda, MD, USA)
2019.12-2021.12 Vice Secretary General & Director of the Liaison Committee, KASL
2022.7-Present Academy Affairs Director, KLCA
2021.12-Present Associate Editor, Gut and Liver

Research Interests

Hepatocellular Carcinoma, Immunotherapy, Gut Microbiome, Biomarker

Representative Publications

1. Kim SC, Kim DW, Cho EJ, Lee JY, Kim J, Kwon C, Kim-Ha J, Hong SK, Choi Y, Yi NJ, Lee KW, Suh KS, Kim W, Kim W, Kim H, Kim YJ, Yoon JH, Yu SJ, Kim YJ. A circulating cell-free DNA methylation signature for the detection of hepatocellular carcinoma. Mol Cancer. 2023 Oct 6;22(1):164.
2. Yu SJ, Ma C, Heinrich B, Brown ZJ, Sandhu M, Zhang Q, Fu Q, Agdashian D, Rosato U, Korangy F, Greten TF. Targeting the crosstalk between cytokine-induced killer cells and myeloid-derived suppressor cells in hepatocellular carcinoma. J Hepatol. 2019 Mar;70(3):449-457.
3. Kim H, Yu SJ, Yeo I, Cho YY, Lee DH, Cho Y, Cho EJ, Lee JH, Kim YJ, Lee S, Jun J, Park T, Yoon JH, Kim Y. Prediction of Response to Sorafenib in Hepatocellular Carcinoma: A Putative Marker Panel by Multiple Reaction Monitoring-Mass Spectrometry (MRM-MS). Mol Cell Proteomics. 2017 Jul;16(7):1312-1323.
4. Won JK, Yu SJ, Hwang CY, Cho SH, Park SM, Kim K, Choi WM, Cho H, Cho EJ, Lee JH, Lee KB, Kim YJ, Suh KS, Jang JJ, Kim CY, Yoon JH, Cho KH. Protein disulfide isomerase inhibition synergistically enhances the efficacy of sorafenib for hepatocellular carcinoma. Hepatology. Hepatology. 2017 Sep;66(3):855-868.
5. Yu SJ, Kim H, Min H, Sohn A, Cho YY, Yoo JJ, Lee DH, Cho EJ, Lee JH, Gim J, Park T, Kim YJ, Kim CY, Yoon JH, Kim Y. Targeted Proteomics Predicts a Sustained Complete-Response after Transarterial Chemoembolization and Clinical Outcomes in Patients with Hepatocellular Carcinoma: A Prospective Cohort Study. J Proteome Res. 2017 Mar 3;16(3):1239-1248.

Distinguished Papers by Korean Hepatologists Aged 40 Years or Younger in 2024-2025

Su Jong Yu *Seoul National University*

Over the past year, a remarkable wave of research has emerged from Korea's community of young hepatology investigators—those under the age of 40—spanning clinical, basic, and translational fields. In this session, I'd like to highlight where we currently stand, review the types of studies being conducted, and recognize a few that stand out—not only for their scientific merit, but also for their creativity, clinical relevance, and vision.

To begin with an overview: between 2024 and early 2025, more than 120 hepatology-related publications were led or co-led by Korean investigators under 40. These studies represent a well-balanced distribution—approximately 55% in clinical research, 35% in basic and translational science, and a growing segment focused on data science and epidemiology. Compared to five years ago, both the volume and thematic diversity of research have expanded, now encompassing viral hepatitis, fatty liver disease, immunotherapy, and AI-assisted liver imaging. Yet, despite this research momentum, a critical concern persists. The proportion of full KASL (Korean Association for the Study of the Liver) members under 40 has been steadily declining. This demographic imbalance has led to a "Western pear-shaped" age distribution, with a narrowing base and an increasingly top-heavy profile. If left unaddressed, this trend could hinder not only the future of hepatology research in Korea, but also the sustainability of clinical expertise and academic leadership. As of December 31, 2024, KASL had 865 regular members, of whom only 55—just 6.4%—were under 40. This sharply contrasts with the vibrant research activity of younger investigators. While their scholarly contributions are both substantial and diverse, their formal representation within the association remains disproportionately low. A closer look at the age distribution further highlights the issue. The largest segment of regular members is in their 50s (33.1%), followed by those in their 40s (29.9%) and 60s (16.5%). In contrast, individuals in their 30s account for just 6.2%, and those in their 20s and younger are nearly absent. Without stronger integration of early-career professionals, the field risks stagnation on both clinical and academic fronts. To secure a sustainable future, we must actively invest in the next generation of hepatologists. This means providing structured training programs, ensuring protected research time, fostering strong mentorship networks, and expanding access to funding. These are not optional supports—they are foundational pillars of a thriving academic community. Promoting membership and long-term engagement of early-career researchers must become a strategic imperative.

Let me now introduce four exemplary studies that showcase the innovation and depth of research emerging from this promising group. The first examines ultrasound-based surveillance strategies for hepatocellular carcinoma in patients with chronic hepatitis B, emphasizing the application of US LI-RADS visualization scoring. The second utilizes Mendelian randomization to explore how sodium-glucose cotransporter-2 (SGLT2) inhibitors influence liver-related complications in individuals with diabetes, drawing on population-based cohort data. The third takes a translational approach, identifying prognostic biomarkers in hepatocellular carcinoma patients treated with Atezolizumab and Bevacizumab, through dynamic analysis of peripheral T-cell populations. Finally, a preclinical study investigates how co-administration of polyethylene glycol with ethanol mitigates hepatic and intestinal inflammation in mice, likely by modulating ethanol absorption within the gut.

In closing, impactful science begins with curiosity and a question that matters. While recognition may take time, meaningful work flourishes in environments where good ideas are supported by strong mentorship and sustained by communities that believe in the next generation.

Min Kyung Park

Seoul National University

Self Introduction

Prof. Park holds a Ph.D. in Stem Cell Biology from Seoul National University College of Medicine (2021-2023). She also obtained an M.D. Master Degree of Medicine from the same institution (2013-2017) and a B.S. in Biology from Seoul National University (2008-2012).

She completed a medical internship (2017-2018) and a residency in Internal Medicine (2018-2021) at Seoul National University Hospital. She served as a Research and Clinical Fellow at the Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine (2018-2022). Following this, she became a Clinical Assistant Professor at the Department of Internal Medicine, Seoul National University Hospital (2022-2023), and currently holds the same position at Seoul National University Bundang Hospital (2023-).

Research Interests

Prof. Park is deeply interested in all aspects of hepatology. Her primary research areas include investigating the pathogenesis, treatment, and prevention of hepatitis B and C in the context of viral hepatitis, as well as exploring the mechanisms, diagnosis, and therapeutic approaches for metabolic dysfunction-associated steatotic liver disease (MASLD) in the field of fatty liver disease.

Representative Publications

1. Park MK*, Hur MH*, Moon HS*, et al. Extrahepatic malignancies in metabolic dysfunction-associated fatty liver disease: A nationwide cohort study. Liver Int. Published online January 17, 2024. (* co-first authors)
2. Park MK*, Lee DH*, Hur BY, et al. Effectiveness of US Surveillance of Hepatocellular Carcinoma in Chronic Hepatitis B: US LI-RADS Visualization Score. Radiology. 2023;307(5):e222106. (* co-first authors)
3. Hur MH*, Park MK*, Cheuk-Fung Yip T*, Chen CH*, Lee HC*, Choi WM*, et al. Personalized antiviral drug selection in chronic hepatitis B patients using a machine learning model: a multinational study. [published online ahead of print, 2023 Mar 7]. Am J Gastroenterol. (* co-first authors)
4. Park MK, Lee YB, Moon H, Choi NR, Kim MA, Jang H, Nam JY, Cho EJ, Lee JH, Yu SJ, Kim YJ, Yoon JH. Effectiveness of Lenvatinib Versus Sorafenib for Unresectable Hepatocellular Carcinoma in Patients with Hepatic Decompensation. Dig Dis Sci. 2022 Jan 20. (First authors)
5. Chung SW*, Park MK*, Cho YY*, et al. Effectiveness of Transarterial Chemoembolization-First Treatment for Advanced Hepatocellular Carcinoma: A Propensity Score Matching Analysis. J Hepatocell Carcinoma. 2021;8:587-598. Published 2021 Jun 15. (* co-first authors)

Young Investigator Meeting | DAY 1: May 29 (Thu.) | ROOM 3 [2F]

Introduction of Representative Studies:
[Clinical Study 1] Effectiveness of US Surveillance of Hepatocellular Carcinoma in Chronic Hepatitis B: US LI-RADS Visualization Score

Min Kyung Park *Seoul National University*

Background: US is a standard surveillance tool of hepatocellular carcinoma (HCC) but its effectiveness varies depending the degree of fibrosis or steatosis and the etiologies of liver disease.

Purpose: To evaluate the detection power of US and the occurrence of HCC according to the US Liver Imaging Reporting and Data System (LI-RADS) visualization score in chronic hepatitis B (CHB).

Materials and Methods: Consecutive patients with CHB undergoing regular US surveillance of HCC at a tertiary referral hospital were retrospectively included in this study. During the follow-up, all patients underwent regular HCC surveillance mainly with US and, in some cases, alternative CT or MRI. Outcomes of interest included cumulative incidence of HCC and false-negative rate of US in the optimal (LI-RADS visualization A) vs. suboptimal groups (visualization B/C). Cox regression analysis was conducted to calculate the hazard ratio (HR) of HCC occurrence.

Results: A total of 2002 patients (median age=54 years [IQR, 46–60 years]; 1192 men) were included: 972 and 1030 in the optimal and suboptimal groups, respectively. Causes of suboptimal visualization included parenchymal heterogeneity from advanced cirrhosis (n=489), limited penetration from fatty liver (n=200), and limited window from overlying organ shadow (n=341). During a median follow-up of 75 months (IQR, 69–77 months), 163 patients developed HCC. Compared with the optimal group, the suboptimal group had a higher risk of HCC (2.38%/yr vs. 0.48%/yr: HR=4.93, 95% CI: 3.28, 7.41, P<.001) and higher odds of false-negative rate of US (43.9% vs. 16.7%: odds ratio=3.90, 95% CI: 1.02, 15.00, P=.04).

Conclusions: Among patients with chronic hepatitis B, those with suboptimal US LI-RADS visualization of B or C had a higher risk of hepatocellular carcinoma (HCC) and higher odds of false-negative rates of US for detecting HCC than those with optimal visualization of A.

Sung Won Chung

University of Ulsan

Self Introduction

Prof. Sung Won Chung is an Assistant Professor of the Department of Internal Medicine, Ulsan University College of Medicine.

He graduated from Seoul National University College of Medicine with his medical degree in 2014 and completed his internship and residency at the Department of Internal Medicine at Seoul National University Hospital.

Research Interests

MASLD, HCC

Representative Publications

1. SW Chung, JS Kim, W-M Choi, J Choi, D Lee, JH Shim, Y-S Lim, HC Lee and KM Kim, Synergistic Effects of Transarterial Chemoembolization and Lenvatinib on HIF-1a Ubiquitination and Prognosis Improvement in Hepatocellular Carcinoma. Clinical Cancer Research.2025; accepted.
2. SW Chung, HJ Um, W-M Choi, J Choi, D Lee, JH Shim, KM Kim, Y-S Lim, HC Lee, Tenofovir is Associated with a Better Prognosis Than Entecavir for Hepatitis B Virus-Related Hepatocellular Carcinoma. Clinical Gastroenterology and Hepatology. 2025; 23(2):300-309
3. SW Chung, H-S Moon, H Shin, H Han, S Park, HJ Cho, MK Park, S-H Won, YB Lee, EJ Cho, SJ Yu, DK Kim, J-H Yoon, J-H Lee, YJ Kim, Inhibition of sodium-glucose cotransporter-2 and liverrelated complications in individuals with diabetes: A Mendelian randomization and population-based cohort study. Hepatology. 2024. Doi:10.1097/HEP.0000000000000837. Online ahead of print
4. D Jeon, HR Cha, SW Chung, J Choi, D Lee, JH Shim, KM Kim, Y-S Lim, HC Lee, SW Lee, W-M Choi. Association between statin use and the prognosis of hepatocellular carcinoma after resection: A nationwide cohort study. eClinicalMed. 2023;65:102300.doi:10.1016/j.eclinm.2023.102300
5. Lee DH, SW Chung, J-H Lee, HY Kim, GE Chung, M-S Kim, BR Yang, JY Nam, YB Lee, YJ Kim, J-H Yoon. Associations of Chronic Hepatitis B Infection and Antiviral Treatment with the Development of the Extrahepatic Malignancies: A Nationwide Cohort Study. J Clin Oncol. 2022 Oct;40(29): 3394– 3405.doi:10.1200/JCO.21.01285

Introduction of Representative Studies:
[Clinical Study 2] Inhibition of Sodium-Glucose Cotransporter-2 and Liver-Related Complications in Individuals with Diabetes: A Mendelian Randomization and Population-Based Cohort Study

Sung Won Chung *University of Ulsan*

Despite the increasing burden of steatotic liver diseases (SLD) in individuals with type 2 diabetes mellitus (T2DM), no pharmacotherapy has been definitively proven to reduce liver-related clinical outcomes. This study aimed to investigate the association between sodium-glucose cotransporter-2 (SGLT2) inhibition and the risk of liver-related events.

A two-pronged approach was employed. First, Mendelian randomization (MR) analyses were conducted using genetic risk scores (GRS) for SGLT2 inhibition, derived from six single nucleotide polymorphisms in the UK Biobank (n=337,138) and validated in the FinnGen cohort (n=218,792). Second, a nationwide population-based cohort study using the Korean National Health Insurance Service (NHIS) database compared liver-related outcomes between individuals with T2DM and SLD treated with SGLT2 inhibitor (SGLT2i) (n=13,208) and those treated with dipeptidyl peptidase-4 inhibitors (DPP4i) (n=70,342), matched by propensity scores.

MR analyses demonstrated that genetically predicted SGLT2 inhibition was associated with a lower risk of cirrhosis development (adjusted odds ratio [OR] = 0.83, 95% CI 0.70–0.98; p=0.03; replicated in FinnGen, OR=0.73, 95% CI 0.60–0.90; p=0.003). In the Korean NHIS cohort, the SGLT2i group was associated with a 12% reduced risk of liver-related complications compared to the DPP4i group (adjusted hazard ratio [HR] = 0.88, 95% CI 0.79–0.97; p=0.01). These findings remained consistent across multiple sensitivity analyses. Potential mechanisms include weight loss,[2] improvement in insulin sensitivity,[2] activation of AMPK pathways,[3] and increased adiponectin levels.[4] Consistent evidence from two large-scale European MR studies and a Korean nationwide cohort suggests that SGLT2 inhibition may confer protection against liver-related complications in individuals with T2DM and SLD.

These findings support the consideration of SGLT2i as a preferred second-line therapy in this high-risk population to prevent liver disease progression.

References

1. Chung SW, Moon HS, Shin H, et al. Inhibition of sodium-glucose cotransporter-2 and liver-related complica-

tions in individuals with diabetes: a Mendelian randomization and population-based cohort study. Hepatology. Sep 1 2024;80(3):633-648. doi:10.1097/hep.0000000000000837
2. Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type 2 diabetes mellitus - mechanisms and treatments. Nat Rev Gastroenterol Hepatol. Sep 2021;18(9):599-612. doi:10.1038/s41575-021-00448-y
3. Li L, Li Q, Huang W, et al. Dapagliflozin Alleviates Hepatic Steatosis by Restoring Autophagy via the AMPK-mTOR Pathway. Front Pharmacol. 2021;12:589273. doi:10.3389/fphar.2021.589273
4. Gamberi T, Magherini F, Modesti A, Fiaschi T. Adiponectin Signaling Pathways in Liver Diseases. Biomedicines. May 7 2018;6(2)doi:10.3390/biomedicines6020052

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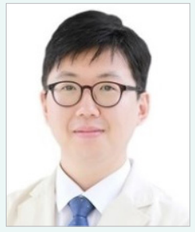


Ji Won Han

The Catholic University of Korea

Self Introduction

Prof. Ji Won Han is an Assistant Professor in the Department of Gastroenterology and Hepatology at Seoul St. Mary's Hospital, The Catholic University of Korea.

He graduated from the College of Medicine at The Catholic University of Korea with a medical degree in 2011 and completed his residency in Internal Medicine at Seoul St. Mary's Hospital in 2016. He received his Master's degree from the Graduate School of Medicine at The Catholic University of Korea (2016) and his Ph.D. from the Graduate School of Medical Science and Engineering (GSMSE) at Korea Advanced Institute of Science and Technology (KAIST) in 2020.

Dr. Han is currently involved in multiple academic societies, including the Korean Association for the Study of the Liver, Korean Liver Cancer Association, Korean Society of Gastroenterology, and Korean Society of Clinical Ultrasound.

Research Interests

Liver Immunology and HCC Immunotherapy, Machine Learning Applications in Liver Diseases

Representative Publications

1. Dynamic peripheral T-cell analysis identifies on-treatment prognostic biomarkers of atezolizumab plus bevacizumab in hepatocellular carcinoma" Liver Cancer 2024, accepted.
2. Diagnostic accuracy of the Fibrosis-4 index for advanced liver fibrosis in nonalcoholic fatty liver disease with type 2 diabetes: A systematic review and meta-analysis" Clin Mol Hepatol. 2024
3. A Machine Learning Algorithm Facilitates Prognosis Prediction and Treatment Selection for Barcelona Clinic Liver Cancer Stage C Hepatocellular Carcinoma" Clin Cancer Res. 2024
4. IFNL3-adjuvanted HCV DNA vaccine reduces regulatory T-cell frequency and increases virus-specific T-cell responses" Journal of Hepatology. 2020
5. Functions of human liver CD69+CD103-CD8+ T cells depend on HIF-2α activity in healthy and pathologic livers" Journal of Hepatology. 2020

Young Investigator Meeting | DAY 1: May 29 (Thu.) | ROOM 3 [2F]

Introduction of Representative Studies: [Basic/Translational Study 1] Dynamic Peripheral T-Cell Analysis Identifies On-Treatment Prognostic Biomarkers of Atezolizumab plus Bevacizumab in Hepatocellular Carcinoma

Ji Won Han *The Catholic University of Korea*

Introduction: Variability in response to atezolizumab plus bevacizumab (AB) treatment of hepatocellular carcinoma (HCC) underscores the critical need for the development of effective biomarkers. We sought to identify peripheral blood biomarkers reflecting response to AB treatment.

Methods: We analyzed dynamic changes in peripheral blood mononuclear cells from a prospective, multicenter cohort of 65 patients with HCC, using flow cytometry to evaluate the T-cell population before and 3 weeks after the first AB treatment.

Results: We found a unique response of the CD8+ T cells in terms of both frequency and phenotype, in contrast to CD4+ T cells and regulatory T cells. Notably, CD8+ T cells showed significant changes in expression of Ki-67 and T-cell immunoreceptors with Ig and ITIM domains (TIGIT). These distinct responses were observed particularly in the programmed cell death receptor-1 (PD-1)+ subpopulation of CD8+ T cells. Interestingly, the baseline differentiation status of PD-1+CD8+ T cells, particularly the central memory T-cell subset, correlated positively with greater proliferation (higher Ki-67 expression) of PD-1+CD8+ T cells after treatment. Moreover, effector memory cells expressing CD45RA correlated negatively with the increase in TIGIT+/PD-1+CD8+ T cells. The increase in TIGIT+/CD8+ T cells was associated with the development of immune-related adverse events, whereas increase in Ki-67+/PD-1+CD8+ T cells was associated with the better objective response rate. Importantly, dynamic shifts of Ki-67+/PD-1+CD8+ T cells and TIGIT+/CD8+ T cells significantly predicted progression-free survival and overall survival, as confirmed by multivariate analysis.

Conclusion: These findings highlight the potential of dynamic changes in CD8+ T cells as an on-treatment prognostic biomarker. Our study underscores the value of peripheral blood profiling as a noninvasive and practical method for predicting the clinical outcomes of AB treatment in patients with HCC.

References

1. Han, Ji Won, et al. "Dynamic peripheral T-cell analysis identifies on-treatment prognostic biomarkers of atezolizumab plus bevacizumab in hepatocellular carcinoma." Liver Cancer 14.1 (2025): 104-116.

Tom Ryu

Soonchunhyang University

Self Introduction

Prof. Tom Ryu is an assistant professor at the Division of Gastroenterology and Hepatology, Department of Internal Medicine at Soonchunhyang University College of Medicine, Seoul, Korea.

He earned his Doctor of Medicine from Soonchunhyang University, Master's degree from Soonchunhyang University, and a Ph.D. from KAIST. He completed his clinical training at Soonchunhyang University Hospital, where he served as a clinical fellow and clinical assistant professor.

He has held roles in academic societies, including membership in The Korean Association for the Study of the Liver (KASL), and The Korean Association of Clinical Ultrasound. He is a recipient of awards, such as the Prof. Mindie H. Nguyen Award at The Liver Meeting 2024 by the AASLD, and the Best Presentation Award at The Liver Week 2024 by the KASL..

Research Interests

Liver Fibrosis, MASLD, and Alcohol-Associated Liver Disease

Representative Publications

1. Ryu T, Chang Y, Yoo JJ, Lee SH, Jeong SW, Kim SG, Kim YS, Kim HS, Yang K, Jang JY. Glucosamine supplementation attenuates progression of metabolic dysfunction-associated steatotic liver disease and related comorbidities. Clinical Nutrition. 2025, 47, 119-128
2. Ryu T, Chang Y, Jeong SW, Yoo JJ, Lee SH, Kim SG, Kim YS, Kim HS, Kim SU, Jang JY. Adverse impact of metabolic dysfunction on fibrosis regression following direct-acting antiviral therapy: A multicenter study for chronic hepatitis C. Clinical and Molecular Hepatology. 2025 Jan 9.
3. Ryu T, Yang K, Choi BY, Cho WG, Chung BS. Co-administration of polyethylene glycol with binge ethanol reduces markers of intestinal and hepatic inflammation in C57BL/6J mice by diminishing ethanol absorption through the intestinal wall. Alcohol Clinical and Experimental Research. 2025 Jan 6.
4. Yang K, Ryu T, Chung BS. Psyllium fiber improves hangovers and inflammatory liver injury by inhibiting intestinal drinking. Frontiers in Pharmacology, 2024 Jun 28. Volume 15.
5. Ryu T, Kim K, Choi SE, Chung KPS, Jeong WI. New insights in the pathogenesis of alcohol-associated liver disease: the metabolic, immunologic, and neurologic pathways. Liver Research. 2023 Mar. Volume 7, Issue 1: 1-8.

Introduction of Representative Studies: [Basic/Translational Study 2] Co-Administration of Polyethylene Glycol with Binge Ethanol Reduces Markers of Intestinal and Hepatic Inflammation in C57BL/6J Mice by Diminishing Ethanol Absorption through the Intestinal Wall

Tom Ryu *Soonchunhyang University*

Background: Binge alcohol consumption is a major global health issue that contributes to significant morbidity, including gut barrier dysfunction, hepatic inflammation, and systemic metabolic disturbances.[1] Excessive ethanol intake disrupts intestinal integrity and promotes bacterial translocation, leading to the activation of inflammatory pathways in the liver.[2] Chronic alcohol use is strongly associated with gut dysbiosis, which further exacerbates hepatic inflammation through gut-derived endotoxins.[3] Recent study has highlighted the importance of intestinal ethanol metabolism in alcohol-related toxicity.[4] Another study investigated the role of intestinal interventions in preventing alcohol-induced inflammation, emphasizing the gut-liver axis as a crucial therapeutic target.[5] Despite the widespread prevalence of alcohol-related liver disease, effective therapeutic options for preventing binge drinking-induced intestinal and hepatic injury remain unclear.

Polyethylene glycol (PEG) is a non-absorbable, non-metabolizable polymer with well-established osmotic properties.[6] PEG has been widely used as a laxative to facilitate colonic cleansing, but its potential role in modulating ethanol absorption and metabolism has not been well explored. The present study investigates whether co-administration of PEG with binge ethanol drinking could reduce ethanol-induced gut and liver inflammation, and hangover symptoms by limiting ethanol absorption at the intestinal level.

Methods: Male C57BL/6J mice were divided into control and treatment groups. The treatment group received an oral administration of ethanol (4 g/kg body weight) with or without PEG (2 g/kg body weight). Mice of control group received an equivalent volume of vehicle without ethanol. Behavioral changes were evaluated using cylinder and footprint tests to assess motor coordination impairment caused by binge drinking. Blood ethanol, acetaldehyde, and acetone levels were quantified using gas chromatography.

To assess tissue-specific ethanol metabolism and its effects, hematoxylin and eosin staining, immunohistochemistry, and quantitative real-time polymerase chain reaction were conducted to evaluate mark-

ers of inflammation and ethanol-metabolizing enzymes in both the intestine and liver. Additionally, liver mononuclear cells were isolated to assess immune cell infiltration, and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured as indicators of hepatic injury.

Results: Mice subjected to binge ethanol exposure exhibited significant intestinal damage, as evidenced by histological findings showing epithelial detachment and increased expression of ethanol-metabolizing enzymes in the gut barrier. Serum ALT and AST levels were elevated in the ethanol-treated group. Increased inflammatory cytokine expression, including tumor necrosis factor-α and C-X-C motif chemokine ligand 1, was observed in both the intestine and liver, further confirming the presence of alcohol-induced inflammation. Behavioral analyses revealed that ethanol-treated mice exhibited impaired motor function compared to the control group, as demonstrated by a reduced number of forelimb touches in the cylinder test and shorter stride length with increased stride width in the footprint test.

Intriguingly, co-administration of PEG with ethanol significantly reduced blood ethanol and acetaldehyde concentrations, suggesting that PEG effectively inhibited ethanol absorption in the intestine. Histological analyses demonstrated that PEG preserved intestinal barrier integrity by reducing gut epithelial injury and suppressing the upregulation of CYP2E1 and ADH1. In the liver, PEG-treated mice showed lower serum ALT and AST levels, decreased hepatic immune cell infiltration, and reduced neutrophil recruitment. Behavioral analyses revealed that PEG treatment recovered ethanol-induced motor impairment, as evidenced by an increased number of forelimb touches in the cylinder test and normalized stride length in the footprint test.

Conclusion: This study provides several evidences that PEG could be an effective intervention against binge ethanol-induced intestinal and hepatic injury. By reducing ethanol absorption at the intestinal level, PEG reduces the systemic effects of ethanol, leading to decreased hepatic inflammation and improved motor function. These findings suggest that PEG has therapeutic potential for preventing alcohol-induced gut-liver axis dysfunction and associated complications. Further studies are required to evaluate the clinical applicability of PEG in human populations at risk for alcohol-related diseases.

References

1. Osna NA, Donohue TM, Jr., Kharbanda KK. Alcoholic Liver Disease: Pathogenesis and Current Management. Alcohol Res 2017;38:147-161.
2. Sosnowski K, Przybylkowski A. Ethanol-induced changes to the gut microbiome compromise the intestinal homeostasis: a review. Gut Microbes 2024;16:2393272.
3. Bajaj JS. Alcohol, liver disease and the gut microbiota. Nat Rev Gastroenterol Hepatol 2019;16:235-246.
4. Ryu T, Yang K, Chung BS. Defecation alleviates hangover by terminating intestinal drinking. Arch Med Sci 2023;19:1909-1912.
5. Yang K, Ryu T, Chung BS. Psyllium fiber improves hangovers and inflammatory liver injury by inhibiting intestinal drinking. Front Pharmacol 2024;15:1378653.
6. Alper A, Pashankar DS. Polyethylene glycol: a game-changer laxative for children. J Pediatr Gastroenterol Nutr 2013;57:134-140.

THE LIVER WEEK 2025

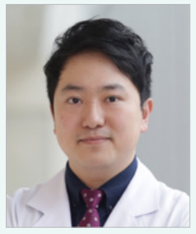
THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Research Assistant Program

Chairs:

Moon Seok Choi (Sungkyunkwan Univ.)
Jong Eun Yeon (Korea Univ.)



Joon Seo Lim

Asan Medical Center

Self Introduction

Dr. Lim graduated from Brown University with a degree in Biology in 2010 and completed his PhD in Medical Science at KAIST in 2015. Subsequently, Dr. Lim served as a postdoctoral researcher at the Graduate School of Public Health at Seoul National University.

Since 2017, he has been working as a Scientific Editor at the Scientific Publications Team in Asan Medical Center, helping researchers in writing and publishing biomedical research in international journals. Drawing on his extensive experience, Dr. Lim has delivered over 200 seminars on the intricacies of manuscript writing. These seminars cover specific guidelines for logically structuring the Introduction and Discussion sections, common scientific expressions that Korean researchers often misuse, and the appropriate application of generative artificial intelligence.

Research Interests

Scientific Publication, Medical Research

Representative Publications

1. Hwang SI, Lim JS*, Lee RW, Matsui Y, Iguchi T, Hiraki T, Ahn H. Is ChatGPT a "Fire of Prometheus" for Non-Native English-Speaking Researchers in Academic Writing? Korean Journal of Radiology (2023) (IF: 7.1)
2. Lim JS, Moon C, Lee J. Subretinal fluid disturbs the retinal venous blood flow in central serous chorioretinopathy. Scientific Reports (2022) (IF: 5.0)
3. Bae S, Lim JS, Kim JY, Jung J, Kim SH. Transmission characteristics of SARS-CoV-2 that hinder effective control (Review). Immune Network (2021)
4. Ra SH, Lim JS, Kim GU, Kim MJ, Jung J, Kim SH. Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection. Thorax (2020)

Research Assistant Program | DAY 1: May 29 (Thu.) | ROOM 3 [2F]

Artificial Intelligence Tools to Power Academic Research and Publication

Joon Seo Lim *Asan Medical Center*

In this seminar, I will introduce the multifaceted applications of advanced artificial intelligence, particularly ChatGPT, across three critical domains: English language enhancement, workplace productivity, and academic research. It systematically explores practical techniques for leveraging GPT technology to improve writing fluency, optimize business workflows, and elevate the quality of scholarly outputs. Emphasizing both the transformative potential of AI and the challenges inherent in its use, the talk examines the phenomenon of AI "hallucinations"—the generation of inaccurate or misleading information—and offers detailed strategies to diagnose and mitigate these errors.

In the realm of English language usage, we will see how GPT-powered systems can serve as robust writing aides. This includes refining grammar, enhancing stylistic expression, and generating diverse textual variants to suit different contexts—from academic papers to business communications. Detailed demonstrations illustrate how users can input rough drafts or bullet points into the model and receive polished, coherent, and contextually appropriate outputs. The discussion emphasizes that while AI can significantly reduce the burden on non-native speakers and even native English authors, users must remain vigilant about reviewing and verifying the content to ensure accuracy and nuance. Guidance is provided on employing specific command prompts to elicit targeted improvements in writing style, tone, and clarity.

Regarding workplace applications, I present how AI tools can drive efficiency and innovation in various business environments. For instance, ChatGPT can be integrated into daily workflows to automate routine tasks such as drafting emails, generating meeting summaries, or preparing reports. This automated support allows employees to focus on strategic decision-making and creativity, thereby increasing overall productivity. The session outlines best practices for deploying AI in corporate settings, including the development of custom prompts tailored to industry-specific jargon and operational procedures. It also highlights how automation in workplace communications can foster collaboration, reduce administrative burdens, and streamline project management processes. In emphasizing these applications, I provide real-world examples where GPT solutions have been successfully adopted, accompanied by a discussion on the potential pitfalls if AI-generated outputs are taken at face value without critical hu-

man oversight.

In terms of academic research, I will show how GPT can be effectively harnessed to aid in literature reviews, idea generation, and even in drafting and revising sections of research papers. The tool's ability to synthesize large volumes of data and provide structured insights makes it an invaluable resource for researchers contending with the increasing volume of scientific literature. However, one significant challenge addressed is the AI hallucination phenomenon, wherein the model produces plausible-sounding but factually incorrect information. The talk categorizes hallucinations into several types—such as factual inaccuracies, synthesis errors, and context misinterpretations—and explores their underlying causes, which include overgeneralization, biases in training data, and limitations in contextual understanding.

To manage and mitigate these hallucination issues, we should perform cross-verification with primary sources. A set of specific commands for academic writing is provided, including prompts for creating structured outlines, generating literature summaries, and drafting hypothesis-driven research sections. While such commands can substantially accelerate the manuscript preparation process, they also require a high level of discernment, foresight, and vision. Researchers are encouraged to view these tools as complementary—supporting but not replacing the critical thinking and meticulous verification that underpin robust scientific inquiry.

Further, this talk emphasizes the importance of having "eye for quality" and vision" when deploying GPT in research settings. This means that while the technology can offer a rapid proliferation of content and ideas, the academic community must exercise rigorous review and critical analysis to distinguish genuine insights from automated fabrications. I urge researchers to adopt a "wise GPT usage" strategy, wherein the benefits of streamlined workflow and creative aid are balanced with the necessity for manual cross-checking and ethical consideration. I will present some examples of integration of AI significantly enhanced research outputs without compromising the scholarly rigor expected in academic publications.

I will also talk about AI content detectors. In the current climate of AI-assisted writing, distinguishing between human and machine-generated text has become increasingly important. The talk surveys several cutting-edge AI detectors, such as those developed by OpenAI, Copyleaks, Originality.AI, and GPTZero, which are designed to assess the authenticity and originality of academic texts. However, these tools are limited in terms of sensitivity and specificity.

In summary, this presentation provides a comprehensive review of how ChatGPT and similar AI technologies can transform English language proficiency, workplace productivity, and academic research. It also offers a balanced discussion on the inherent challenges—particularly AI hallucinations—and presents a strategic framework for mitigating such issues through targeted commands and the use of AI

detection tools. Ultimately, the talk advocates for a judicious yet innovative approach to AI integration, underscoring that when combined with human insight and rigorous oversight, these advanced technologies can lead to significant advancements in both professional and academic fields.

Danielle Lee

Asan Medical Center

Self Introduction

Danielle Lee earned her Bachelor's degree in Cell Biology from the University of East Anglia in 2015 and completed a Master's degree in Neuroscience at King's College London in 2018.

She began her career at BioMed Central, where she worked for 1 year and gained valuable insight into editorial workflows and the publication processes of a scientific publishing house. She then spent 3 years as a Senior Editor at OPEN Health, where she was responsible for editing a range of deliverables, including manuscripts, abstracts, posters, and slide decks for conferences, and also led training sessions on scientific writing and visual presentation development.

For the past 4 and a half years, she has been working as a Scientific Editor in the Scientific Publications Team at Asan Medical Center. In this role, she edits manuscripts written by Korean researchers, delivers seminars on scientific writing for non-native English speakers, and provides consultations on manuscript development and conference presentation preparation.

Effective English Presentation and Communication in a Medical Conference

Danielle Lee *Asan Medical Center*

Delivering an effective English presentation at an international medical conference is a multifaceted skill that encompasses not only language proficiency but also the ability to communicate ideas clearly, engage with a diverse audience, and navigate professional social interactions with confidence. This lecture is designed to provide a comprehensive guide to improving both formal presentation delivery and informal communication, focusing especially on practical strategies for medical professionals who use English as a second language.

The first part of the session will address the elements that make a presentation impactful. One of the central themes is the transition from reading a prepared script to delivering fluid, natural speech through the use of structured talking points. Rather than memorizing content verbatim, presenters are encouraged to internalize key points and use them as prompts. This approach enables the speaker to maintain better eye contact, vary intonation, and connect more authentically with the audience. A prepared script can still be useful, especially during the rehearsal stage, as it allows the speaker to become familiar with the overall flow and structure of the presentation. However, strict adherence to memorized text can result in a robotic tone and increased anxiety if the speaker forgets a line.

A core strategy discussed in the lecture is the use of discourse markers and filler phrases. These linguistic tools, such as "so", "well", "now", or "alright", may be considered informal in academic writing, but they serve an important function in spoken language. When used sparingly and appropriately, they can smooth transitions between topics, give the speaker time to think, and help the audience follow the structure of the presentation. Phrases like "Right, let's move on to the Methods" or "So, now I'd like to introduce a new concept" add a conversational quality to the talk, making it more engaging and accessible.

Interactive speech is another technique that will be emphasised. This includes expressions that draw the audience's attention to specific content, such as "If you take a look at this figure here" or "As you can see on the right-hand side of the slide". These phrases do more than describe visuals; they help orient the listener and establish a shared focus. In addition, posing rhetorical or semi-interactive questions, such as "How many of us have been in this situation?" or "What would you consider the most important

factor here?", encourages mental engagement and fosters a sense of dialogue.

Another important component of the lecture will focus on common mistakes in English presentations. For example, translating Korean discourse markers like "그러면" directly as "then" rather than "so" can lead to unnatural phrasing. Phrases like "Then, let's move onto the results" are less natural in English than "So, let's move onto the results". Similarly, casual vocabulary, such as using "guys" instead of "everyone", can be inappropriate in formal academic settings. These small distinctions can make a significant difference in maintaining professional tone and clarity.

The second part of the session will shift to the topic of small talk and informal communication in conference settings. While often overlooked in professional training, these interactions are essential for networking, building rapport, and establishing professional credibility. Participants will be introduced to several realistic scenarios, such as initiating a conversation with a high-profile researcher during a coffee break, chatting with a fellow attendee before a session begins, or joining a networking lunch.

Through role-play examples and model dialogues, attendees will learn how to initiate conversations politely, express genuine interest, and guide discussions towards professional topics. For instance, when approaching someone new, a typical structure might include a friendly greeting, a brief self-introduction, a compliment or comment, and a soft invitation to converse: "Hi there, my name is Danielle Lee, and I work at Asan Medical Center in Seoul. I really admire your work—do you have a moment to talk?"

The lecture will also provide strategies for reading and using body language effectively. Open body language, such as eye contact, a relaxed posture, and visible hands, invites interaction, while closed body language, such as crossed arms, avoidance of eye contact, or facing away, can deter others from engaging. Understanding these non-verbal cues allows participants to enter conversations more confidently and make others feel comfortable in return.

To support continued engagement in small talk, participants will be introduced to neutral and context-appropriate conversation starters. These include questions about travel ("Is this your first time in Seoul?"), the conference itself ("Which speaker are you most looking forward to today?"), or professional background ("What sort of research are you currently working on?"). When ending the conversation, polite expressions such as "Well, I won't take any more of your time" or "Would you be happy to exchange business cards?" help conclude the interaction on a professional and respectful note.

In closing, the lecture will stress the importance of clarity, authenticity, and preparation in both formal and informal settings. While linguistic perfection is not the goal, speakers should aim for effective communication that reflects professionalism, interest in others, and confidence in sharing their own ideas. Attendees will be reminded that native-like fluency is not a prerequisite for success; rather, effective communication comes from strategic preparation, cultural awareness, and the willingness to engage.

By the end of the session, participants will be better equipped to deliver compelling presentations and to connect with peers, mentors, and collaborators at international medical conferences. The skills learned will not only enhance presentation performance but also contribute to meaningful professional relationships and long-term career development.

Sangzin Ahn

Inje University

Self Introduction

Prof. Sangzin Ahn is a professor of the Department of Pharmacology, Seoul National University College of Medicine. (2016-present)

He graduated from Seoul National University College of Medicine with his medical degree in 2009 and completed his Ph.D. at the Graduate School of Biomedical Sciences of Seoul National University with the specialty of Pharmacology. (2009~2016)

His recent publications are focused in the integration of AI chatbots into medical education, application of AI tools into medical writing and publishing, and medical text data analysis using large language models (LLMs).

Research Interests

Application of LLMs in Medical Education, Writing and Medical Text Data Analysis

Representative Publications

1. Ahn, S. Large language model usage guidelines in Korean medical journals: a survey using human-artificial intelligence collaboration. Journal of Yeungnam Medical Science. 2025 Jan;42(1), 1-7.
2. Ahn S. The transformative impact of large language models on medical writing and publishing: current applications, challenges and future directions Korean J Physiol Pharmacol. 2024 Sep;28(5):393-401.
3. Ahn S. Data science through natural language with ChatGPT's Code Interpreter. Transl Clin Pharmacol. 2024 Jun;32(2):e8.
4. Ahn S. A use case of ChatGPT in a flipped medical terminology course. Korean J Med Educ. 2023 Aug;35(3):303-307.
5. Ahn S. The impending impacts of large language models on medical education. Korean J Med Educ. 2023 Mar;35(1):103-107.

Management of Literature and References for Scientific Writing

Sangzin Ahn *Inje University*

The introduction of powerful AI-based research tools have fundamentally changed how scientists process information. While Deep Research tools from ChatGPT, Perplexity, and Gemini can rapidly generate broad overviews of research fields, these summaries provide only shallow understanding—a starting point rather than a destination. True deep understanding requires deliberate engagement with primary literature through a structured workflow that balances AI assistance with active learning techniques.

The pathway to comprehensive knowledge begins by recognizing the limitations of general AI summaries. Though these tools can provide field-level orientations in minutes rather than days, they create risks of illusory understanding when relied upon exclusively. Instead, a more effective approach leverages AI as part of a multi-stage process for deep paper comprehension. This refined workflow starts with using LLMs to generate summaries of specific research papers, providing structural scaffolding for understanding. Researchers then read the full text actively, using the AI-generated summary as context while taking personal notes and annotations. The critical third step involves returning to AI tools with one's own notes, asking for feedback on gaps or misconceptions—a process that converts implicit understanding to explicit knowledge and significantly enhances memory encoding.

For sustainable knowledge management, interconnected note-taking systems like Obsidian or Notion transform isolated paper summaries into networks of ideas that facilitate natural spaced retrieval. This approach creates an evolving knowledgebase where new insights emerge at the intersection of previously unconnected concepts. The resulting system supports modular, block-based writing where thoroughly understood concepts can be efficiently assembled into manuscripts with seamless reference integration.

Researchers must remain vigilant against the three critical illusions identified by Messeri and Crockett (2024): explanatory depth, exploratory breadth, and objectivity. These cognitive biases are particularly pronounced when using AI tools for general field surveys rather than for supporting deep paper-by-paper understanding. By distinguishing between AI-enabled surface exploration and AI-assisted deep reading, researchers can maintain intellectual rigor while significantly improving both comprehension and productivity in scientific writing and knowledge management.

Reference

1. Messeri, L., & Crockett, M. J. (2024). Artificial intelligence and illusions of understanding in scientific research. Nature, 627, 49–57. https://doi.org/10.1038/s41586-024-07146-0

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 1: May 29 (Thu.)

Ultrasound Trainee Session

Chairs:

Sung Kyu Choi (Chonnam National Univ.)
Moon Young Kim (Yonsei Univ. Wonju)

Seung Kak Shin

Gachon University

Self Introduction

Education

2005-2009 M.D.,M.S., Gachon University Graduate School of medicine, Inchoen, Republic of Korea
2013-2018 Ph.D., Division of hepatology, Gachon University, Inchoen, Republic of Korea
2022-2023 Visiting Scholar, Laboratory of Cancer Immunotherapy and Immunology, University of Tsukuba

Professional Career

2023-Present Associate Professor, Gachon University Gil Medical Center, Inchoen, Republic of Korea
2018- 2023 Assistant Professor, Gachon University Gil Medical Center, Inchoen, Republic of Korea
2016-2018 Clinical Assistant Professor, Gachon University Gil Medical Center, Inchoen, Republic of Korea
2014-2016 Fellowship, Gachon University Gil Medical Center, Inchoen, Republic of Korea
2010-2014 Resident, Gachon University Gil Medical Center, Inchoen, Republic of Korea
2009-2010 Internship, Gachon University Gil Medical Center, Inchoen, Republic of Korea

Research Interests

Basic and Clinical Research of Metabolic Dysfunction-Associated Steatotic Liver Disease and Liver Fibrosis, Immune Cell Therapy for Liver Cancer, Regenerative Medicine for Liver Fibrosis and Cirrhosis

Representative Publications

1. Shin SK et al. Current Landscape of Adoptive Cell Therapy and Challenge to Develop "Off-The-Shelf" Therapy for Hepatocellular Carcinoma. J Gastroenterol Hepatol. 2025 Apr;40(4):791-807.
2. Shin SK et al. Immune signature and therapeutic approach of natural killer cell in chronic liver disease and hepatocellular carcinoma. J Gastroenterol Hepatol. 2024 Sep;39(9):1717-1727.
3. Shin SK et al. Clinical Significance of Combined Epithelial-Mesenchymal Transition Markers Expression and Role of Rac1 in Hepatocellular Carcinoma. Int J Mol Sci. 2023 Jan 16;24(2):1765.
4. Shin SK et al. Partial Virological Response after 2 Years of Entecavir Therapy Increases the Risk of Hepatocellular Carcinoma in Patients with Hepatitis B Virus-Associated Cirrhosis. Gut Liver. 2021 May 15;15(3):430-439.
5. Shin SK et al. Exogenous 8-hydroxydeoxyguanosine ameliorates liver fibrosis through the inhibition of Rac1-NADPH oxidase signaling. J Gastroenterol Hepatol. 2020 Jun;35(6):1078-1087.

What Is an Abdominal Ultrasound?

Seung Kak Shin *Gachon University*

Abdominal ultrasound is a non-invasive imaging technique that utilizes high-frequency sound waves to produce real-time images of the organs and structures within the abdominal cavity. In abdominal exams, transducers typically operate at frequencies between 2 and 5 MHz, with lower frequencies offering greater penetration for deep organs, and higher frequencies providing better resolution for superficial structures.

This modality allows for the evaluation of major abdominal organs, including the liver, gallbladder, bile duct, pancreas, spleen, kidneys, and large blood vessels such as the aorta and inferior vena cava. It can also assess ascites, lymph nodes, and intra-abdominal masses.

When sound waves encounter tissues of different densities—such as organs, blood, or fluid—they are partially reflected back to the transducer. The returning echoes are processed by the ultrasound machine to generate real-time images of internal structures. The timing and intensity of the reflected waves determine the depth and brightness of each structure on the screen. Solid organs such as the liver or spleen reflect more sound and appear brighter (echogenic). Fluid-filled structures such as the gallbladder or cysts transmit sound without reflection and appear dark (anechoic). Gas and bone impede sound transmission and may create shadowing artifacts.

One of the key advantages of abdominal ultrasound is that it does not involve ionizing radiation, making it suitable for repeated use, including in pediatric and pregnant patients. The examination is typically performed with the patient in a fasting state to reduce bowel gas interference and to better visualize organs like the gallbladder and pancreas.

The accuracy of the examination depends greatly on the operator's experience and the patient's body habitus. Limitations include poor visualization in cases of obesity or excessive bowel gas.

In summary, abdominal ultrasound is an essential, first-line diagnostic tool, offering real-time, radiation-free imaging that contributes significantly to patient care and clinical decision-making.

References

1. P N Wells. Abdominal ultrasound diagnosis. Br Med Bull. 1980 Sep;36(3):257-60.
2. Juan Torres-Macho, Christine M Schutzer. Point-of-Care Ultrasound in Clinical Care: Abdomen. Med Clin North Am. 2025 Jan;109(1):31-45.
3. Rumack CM, et al. Diagnostic Ultrasound, 5th ed. Elsevier; 2017.

Woo Sun Rou

Chungnam National University

Self Introduction

Educational

2006 M.D., Chungnam National University College of Medicine, Daejeon, Korea
2016 M.S., Graduate School, Chungnam National University College of Medicine, Daejeon, Korea
2022 Ph.D., Graduate School, Chungnam National University College of Medicine, Daejeon, Korea

Professional Experience

2006-2007 Internship, Inje University Paik Hospital
2007-2011 Residency, Inje University Paik Hospital
2014-2015 Fellowship, Chungnam National University Hospital, Daejeon, Korea
2020-2024 Clinical Assistant Professor, Chungnam National University Sejong Hospital, Sejong, Korea
2024-Present Assistant Professor, Chungnam National University Sejong Hospital, Sejong, Korea

Research Interests

MASLD, Viral Hepatitis, Hepatocellular Carcinoma

Representative Publications

1. Woo Sun Rou, Hong Jae Jeon, Hyuk Soo Eun, et al. Association of Survival with Radiologic-Pathologic Discordance in Patients with Hepatocellular Carcinoma: A Nationwide Cohort Study Based on the Primary Liver Cancer Registry in Korea. Gut Liver. 2025 Apr 1. doi: 10.5009/gnl240393.
2. Woo Sun Rou. Assessment of Hepatic Steatosis Using Ultrasound-Based Techniques: Focus on Fat Quantification. Clinical Ultrasound. 2024;9:1-17
3. Woo Sun Rou, Hyuk Soo Eun, Sorim Choung, et al. Prognostic Value of Erythroblastic Leukemia Viral Oncogene Homolog 2 and Neuregulin 4 in Hepatocellular Carcinoma. Cancers. 2023;15(9):2634
4. Suk-Yong Jang, Woo Sun Rou, Seok Hyun Kim, Byung Seok Lee, Hyuk Soo Eun. Association between new-onset liver cirrhosis and suicide risk in South Korea: A nationwide cohort study. Clin Mol Hepatol. 2021;27(2):283-294

Ultrasound Scanning Techniques: Liver

Woo Sun Rou *Chungnam National University*

Introduction

Upper abdominal ultrasonography is a reproducible imaging modality that does not involve radiation exposure or contrast-related adverse effects. Since April 2018, expanded coverage under the national health insurance system in Korea has improved access to upper abdominal ultrasound. This modality is employed to evaluate the liver, gallbladder, biliary tract, pancreas, and spleen. Liver ultrasound is frequently used as a first-line diagnostic tool when liver disease is suspected, as it allows effective detection of structural abnormalities and hepatic lesions. It is widely used for both the diagnosis and follow-up of diffuse liver diseases and focal hepatic lesions. However, the accuracy of lesion detection and interpretation can vary depending on the operator's experience. Therefore, a comprehensive understanding of liver anatomy and a systematic scanning approach are essential.

1. Pre-examination Preparation

Ingested food and intestinal gas produced during digestion can scatter or absorb ultrasound waves, thereby compromising the visualization of abdominal organs. Furthermore, postprandial contraction of the gallbladder may obscure findings such as gallstones, polyps, or cholecystitis. Therefore, patients are required to fast for at least eight hours prior to the examination and to refrain from chewing gum. If an endoscopy is scheduled on the same day, the ultrasound should be performed beforehand.

2. Liver Segmentation

The most widely accepted liver segmentation system in ultrasonography is Couinaud's classification, which divides the liver into eight segments numbered in a counterclockwise manner starting from the caudate lobe. Segmental boundaries are defined by hepatic veins, while the portal vein runs centrally within each segment. The right hepatic vein separates the right anterior (S5, S8) and right posterior (S6, S7) segments. The middle hepatic vein delineates the boundary between the left medial segment (S4) and the right anterior segments, whereas the left hepatic vein and the umbilical portion of the left portal vein separate the left medial (S4) and lateral (S2, S3) segments.

3. Liver Scanning Technique

A 3.0–3.5 MHz transducer is optimal for most patients. In obese individuals or those with hepatic steatosis, a lower-frequency transducer (2.5 MHz) may be preferable, while high-frequency probes (e.g., 5 MHz) are suitable for thin patients. Adherence to a standardized and systematic scanning protocol is crucial to avoid missed lesions. Scanning typically begins in the supine position and may be adjusted to the left lateral decubitus position if necessary. The basic scanning method for liver examination mainly includes transverse, longitudinal, subcostal, and intercostal scans. To enhance organ visibility, patients are instructed to inhale deeply and hold their breath or to push out their abdomen, thereby lowering the liver below the costal margin.

(1) Transverse Scan

The transducer is positioned slightly left of the epigastrium. From the umbilical portion of the left portal vein, two branches course nearly in parallel toward the lateral segment—one running ventrally and the other dorsally. These branches supply the inferior-anterior segment (S3) and the superior-posterior segment (S2) of the left lateral segment, respectively. The left hepatic vein courses between these two segments. When the transducer is shifted slightly to the right, the transverse portion of the left portal vein and its branch to S4 become visible. The caudate lobe (S1) is demarcated from the lateral segment of the left lobe by the echogenic fissure for the ligamentum venosum. This scan provides a view of the portal vein branches to segments 2, 3, and 4, the origin and umbilical portion of the left portal vein, forming a pattern resembling a recumbent capital "H". The ligamentum teres, appearing as a hyperechoic structure between the medial (S4) and lateral (S2, S3) segments, may mimic a hepatic hemangioma.

(2) Longitudinal Scan

Starting at the far left of the epigastric area, the left lobe is evaluated. Directing the probe to the far left reveals the lateral margin, and moving it medially shows cross-sections of portal vein branches to S2 and S3 and the course of the left hepatic vein. Advancing the probe rightward visualizes the umbilical portion of the portal vein and a round ligament anterior-inferior to it. Further movement to the right displays the middle hepatic vein and the boundary between the left and right lobes. In the anterior or mid-axillary line, a subcostal longitudinal scan shows the inferior part of the right lobe and the longitudinal section of the right kidney, allowing comparison of liver and renal cortical echogenicity.

(3) Subcostal Scan

To examine the hepatic dome—often overlooked—the probe should be placed flat beneath the right costal margin. Deep inspiration and abdominal protrusion lower the diaphragm and liver, improving visualization. Gradually angling the transducer more vertically reveals the right, middle, and left hepatic veins draining into the inferior vena cava. Slightly further down, the bifurcation of the right and left portal veins can be observed, with the caudate lobe and the ligamentum venosum located posterior to it.

As the scan continues further inferiorly, the right portal vein divides into anterior and posterior branches, and at a lower level, the posterior branch is seen splitting into the portal vein branches to segments 6 and 7.

(4) Intercostal Scan

This scan allows visualization of the right hepatic lobe, particularly useful when subcostal views are suboptimal, such as in obese patients, cirrhosis-related atrophy, or Chilaiditi syndrome. Proper breathing techniques facilitate the visualization of the diaphragm obscured by the lungs. The transducer is placed in the 7th to 9th intercostal spaces and tilted during scanning. At the 7th intercostal space, the anterior branches of the right portal vein can be clearly visualized, along with the superiorly directed portal branch of S8 and the inferiorly directed portal branch of S5 located near the gallbladder. Additionally, the right hepatic vein, which divides the anterior and posterior segments, can be observed as it drains into the inferior vena cava. Scanning in the 8th and 9th intercostal spaces allows for visualization of the portal vein branch to S6 and S7.

4. Considerations During Liver Scanning

Due to its anatomical location, certain regions of liver—such as the hepatic dome, the inferior margin of the right lobe, and the lateral tip of the left lobe—may be difficult to visualize. Appropriate patient positioning and respiratory maneuvers can mitigate these limitations. The hepatic dome and the inferior margin of the right lobe can be more effectively visualized using subcostal or intercostal scanning in the left lateral decubitus position. For the lateral tip of the left lobe, scanning from the left subcostal area, gently angling or advancing the transducer may improve visualization.

5. Standard Liver Imaging in Upper Abdominal Ultrasound According to National Health Insurance Reimbursement Guidelines in Korea

(1) Routine Liver Ultrasound

- Longitudinal scan of the left hepatic lobe (S1, S2, S3, ligamentum venosum)
- Transverse scan of the left hepatic lobe (S1, S2, S3, S4, ligamentum venosum, umbilical portion of left portal vein)
- Subcostal scan of the hepatic veins (left hepatic vein, middle hepatic vein, right hepatic vein)
- Transverse scan of the right hepatic lobe (S5, S6, S7)
- Intercostal scan of the right hepatic lobe (S5, S6, S7, S8)
- Coronal scan of the inferior right lobe and right renal cortex
- Scan of the superior (dome) portion of the right hepatic lobe

(2) Detailed Liver Ultrasound

In addition to the standard images obtained during routine liver ultrasound:

- Transverse scan of the right and left portal vein bifurcation
- Intercostal scans of the right hepatic lobe including: the right portal vein; right hepatic vein

Conclusion

Ultrasonography is a valuable diagnostic tool for evaluating the upper abdominal organs. Given its operator-dependent nature, a thorough knowledge of abdominal anatomy and adherence to standardized scanning techniques are essential for acquiring high-quality and reliable images.

Reference

1. Aya Kamaya, Jade Wong-You-Cheong. Diagnostic Ultrasound, 2nd ed. Philadelphia: Elsevier, 2022, 6-19.
2. Adrian K.P. Lim, Matteo Rosselli. Liver Ultrasound. New York: Wiley, 2024, 27-52.
3. Berthold Block. The Practice of Ultrasound. 2nd ed. New York: Thieme, 2004, 43-86
4. 심찬섭. 복부초음파아틀라스. 4th ed. 서울: 한국의학, 2012, 2-91.
5. 보건복지부 고시 제2018 - 66호, 2018년 3월 29일

Chang Hun Lee

Jeonbuk National University

Self Introduction

Educational

2008 Doctor of Medicine, Jeonbuk National University Medical School
2018 Master of Science in Internal Medicine, Jeonbuk National University Graduate School
2020 Doctor of Science in Internal Medicine, Jeonbuk National University Graduate School

Professional Experience

2018.5 Clinical professor – The division of Gastroenterology and Hepatology, Department of Internal n Medicine, Jeonbuk National University Hospital
2022.3 Endowed assistant professor – The division of Gastroenterology and Hepatology, Department of Internal Medicine, Jeonbuk National University Medical School
2023.9 Assistant professor – The division of Gastroenterology and Hepatology, Department of Internal Medicine, Jeonbuk National University Medical School

Society Activities

2024-2025 Member, Publication Committee, KASL
2024-2025 Member, Medical Policy Committee, KASL

Research Interests

Hepatology - Alcoholic Liver Disease, Nonalcoholic Fatty Liver Disease, Viral Hepatitis

Representative Publications

1. Lee CH, You GR, Jo HG, Jun CH, Cho EY, Kim IH, Choi SK, Yoon JH. Albumin-Bilirubin Grade as a Valuable Predictor of Recurrence and Prognosis in Patients with Hepatocellular Carcinoma Following Radiofrequency Ablation. Cancers (Basel). 2024 Dec 13;16(24):4167.
2. Lee CH, Kim IH, Jeong SH. Correspondence on Letter Regarding "Contemporary Awareness of Viral Hepatitis between 2012 and 2022 among Korean Adults" Clin Mol Hepatol. 2025; 31(2): e149-e151.
3. Kang MG, Lee CH, Shen C, Kim JS, Park JH. Longitudinal changes in fatty liver index are associated with risk of hepatocellular carcinoma: A nationwide cohort study in Korea. J Hepatol. 2024 May;80(5):e216-e218.
4. Lee CH, Choi GH, Choi HY, Han S, Jang ES, Chon YE, Chang Y, Kim KA, Kim DY, Yim HJ, Kim HL, Jeong SH, Kim IH. Core indicators related to the elimination of hepatitis B and C virus infection in South Korea: A nationwide study. Clin Mol Hepatol. 2023 Jul;29(3):779-793.
5. Lee CH, Kang HJ, Yu SY, Seo SY, Kim SH, Kim SW, Lee SO, Lee ST, Kim IH. Initial treatment response and short-term mortality of spontaneous bacterial peritonitis in cirrhotic patients with hepatocellular carcinoma. Sci Rep. 2023 Apr 13;13(1):6067.

Ultrasound Scanning Techniques: Pancreato-Biliary

Chang Hun Lee *Jeonbuk National University*

Ultrasound is a safe and easily accessible modality to examine the pancreato-biliary system, providing real-time images without radiation exposure. It also allows bedside application and dynamic scanning, setting it apart from other imaging methods such as CT or MRI. These benefits make it especially useful for both initial assessments and follow-up examinations. In this session, we will review the basic techniques for scanning the pancreato-biliary system with ultrasound, focusing on practical approaches for key organs such as the gallbladder, bile duct, pancreas, and spleen.

Gallbladder Scanning

The gallbladder is one of the easiest organs to visualize on ultrasound, but it can be challenging to fully assess from the neck to the fundus. Since it is located beneath the liver, it moves significantly with respiration and can be obscured by duodenal gas. Scanning usually starts with the patient in a fasting state and in the supine position, but additional views in the left lateral decubitus or upright positions can improve visualization. In the right subcostal view, the gallbladder appears as a branch-like anechoic structure extending from the common hepatic duct, which can be found by tracing along the right side of the main portal vein. In the right intercostal view, it is seen ventral to the right portal vein, and in the right longitudinal scan, it lies ventral to the portal vein origin. To visualize the entire gallbladder, it is important to adjust the probe direction, apply gentle pressure to displace bowel gas, and use fan-shaped scanning along with respiratory control. Multiple scanning planes (longitudinal, transverse, and oblique) are recommended to ensure a complete evaluation.

Bile Duct Scanning

Visualization of the bile duct begins at the porta hepatis. The transducer is placed in the right upper quadrant, using oblique or subcostal approaches to follow the ductal course. The bile duct runs anterior to the portal vein and can be traced distally toward the pancreas. Color Doppler is helpful to distinguish vascular structures from the duct. Slight changes in patient positioning, such as a right posterior oblique position, can improve visualization. The intrahepatic bile ducts run alongside the portal vein branches and are usually visible up to the segmental branches. These segmental branches typically measure about 1 mm in diameter, and larger sizes may suggest dilatation. The left hepatic duct can be visualized

ventral to the left branch of the portal vein, especially on the right subcostal, substernal transverse, or longitudinal scans by following the portal vein branches to segments II, III, and IV. The right hepatic duct appears ventral to the right portal vein and can be observed in the right subcostal scan by tracing the anterior and posterior branches, and in the right intercostal scan by following the portal branches to segments V, VI, VII, and VIII. The caudate lobe branch (segment I) is often not visualized. The left and right hepatic ducts join to form the common hepatic duct, which runs caudally and can be identified as a tubular structure, about 6 mm or less in diameter, ventral to the origin of the portal vein in the right longitudinal or oblique scans.

Pancreas Scanning

Pancreatic scanning is challenging due to overlying bowel gas. The patient is scanned in the supine or semi-erect position, and drinking water can help as an acoustic window. Placing the transducer in the epigastric area and applying graded compression helps move bowel loops. Scanning in both transverse and longitudinal planes allows for a comprehensive evaluation. In the transverse scan, the splenic vein serves as a key landmark. The pancreas lies just anterior to the splenic vein, and by following the vein from its confluence with the superior mesenteric vein toward the spleen, the pancreas can be traced from head to tail. In the longitudinal scan, trace the portal vein caudally to the superior mesenteric vein, where the pancreas can be visualized at the level of the neck. In this view, sliding or angling the probe toward the right upper abdomen facilitates visualization of the pancreatic head, while directing the probe toward the left side of the abdomen allows visualization of the body and tail of the pancreas, with the splenic vein serving as a useful landmark.

Spleen Scanning

The spleen is located just below the left lung and diaphragm, which makes the left intercostal approach particularly effective for visualization. Placing the transducer along the 8th to 9th intercostal spaces and angling it from the left abdomen toward the back aligns with the long axis of the spleen. When the patient is positioned in the right lateral decubitus position, the intercostal spaces widen, providing a better acoustic window. If the intercostal window is limited, a subcostal approach can serve as an alternative view. Instructing the patient to take a deep breath moves the spleen below the rib cage, which improves its visibility.

Jun Sik Yoon

Inje University

Self Introduction

Prof. Jun Sik Yoon is a Professor in the Department of Internal Medicine at Inje University College of Medicine. He currently serves as the associate professor at Busan Paik Hospital.

He graduated from Hanyang University College of Medicine with his medical degree in 2008 and completed his internship and residency at the Department of Internal Medicine at Hanyang University Hospital.

Since 2019, he has been working as a professor at Busan Paik Hospital. The academic societies currently participated in are as follows:
The Korean Liver Cancer Association
The Korean Association of Clinical Ultrasound
The Busan-Ulsan-Gyeongnam Liver Association
Convergence Liver Cancer Study Group

Research Interests

Liver Cancer, MASLD

Representative Publications

1. Kim et al. Risk of cardiovascular disease with high-dose versus low-dose use of non-steroidal anti-inflammatory drugs in ankylosing spondylitis. Ann Rheum Dis. 2024 Jul 15;83(8):1028-1033.
2. Yoon et al. High-dose proton pump inhibitor treatment is associated with a higher mortality in cirrhotic patients: A multicentre study. Aliment Pharmacol Ther. 2024 Apr;59(8):973-983.
3. Yoon et al. Impact of HBeAg on Hepatocellular Carcinoma Risk During Oral Antiviral Treatment in Patients With Chronic Hepatitis B. Clin Gastroenterol Hepatol. 2022 Jun;20(6):1343-1353.e16.
4. Yoon et al. Toward a complete cure for chronic hepatitis B: Novel therapeutic targets for hepatitis B virus. Clin Mol Hepatol. 2022 Jan;28(1):17-30.
5. Yoon et al. Empirical Treatment With Carbapenem vs Third-generation Cephalosporin for Treatment of Spontaneous Bacterial Peritonitis. Clin Gastroenterol Hepatol. 2021 May;19(5):976-986.e5.

Ultrasound Findings of Common Liver Diseases

Jun Sik Yoon *Inje University*

Ultrasound is a cornerstone imaging modality for the diagnosis and management of common liver diseases due to its non-invasive nature, cost-effectiveness, and widespread availability. This presentation reviews key ultrasound findings associated with prevalent liver conditions, including non-alcoholic fatty liver disease (NAFLD), viral hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). In NAFLD, ultrasound reveals increased echogenicity indicative of steatosis, while viral hepatitis may present with hepatomegaly and altered parenchymal texture. Cirrhosis is characterized by a nodular liver surface, splenomegaly, and signs of portal hypertension, such as ascites and varices, detectable via Doppler ultrasound. HCC typically appears as hypoechoic or heterogeneous lesions, often requiring contrast-enhanced ultrasound for further characterization. Emerging techniques, such as elastography, enhance diagnostic precision by quantifying liver stiffness to assess fibrosis severity. Despite its advantages, ultrasound faces challenges, including operator variability and limitations in obese patients. This presentation highlights the critical role of ultrasound in identifying hallmark features of liver diseases and discusses its evolving applications in clinical practice.

Keywords: Ultrasound, Liver Diseases, NAFLD, Cirrhosis, Hepatocellular Carcinoma, Elastography

References

1. Castera L, et al. Noninvasive Assessment of Liver Disease in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019;156(5):1264-1281.
2. Berzigotti A, et al. Ultrasound in Portal Hypertension: From Diagnosis to Treatment Monitoring. Hepatology. 2021;73(3):1045-1058.
3. Kudo M, et al. Contrast-Enhanced Ultrasound in the Diagnosis of Hepatocellular Carcinoma: WFUMB Guidelines. Ultrasound Med Biol. 2022;48(6):981-997.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!

LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

THE LIVER WEEK 2025

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LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 1: May 29 (Thu.)

Ultrasound Trainer Session 1

Chair:

Soon Koo Baik (Yonsei Univ. Wonju)

Tae-Suk Kim

Kangwon National University

Self Introduction

Educational

2013.93-2020.98 Ph.D., in Clinical Medical Science Kangwon National University College of Medicine, Chuncheon-si, Korea

2010.93-2012.98 M.S., in Clinical Medical Science Kangwon National University College of Medicine, Chuncheon-si, Korea

2003.93-2008.92 M.D., in Medicine Kangwon National University College of Medicine, Chuncheon-si, Korea

Current Position

2022.03-Present Assistant Professor, Division of Gastroenterology, Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon, Korea

Professional Experience

KASL Committee of Education

Research Interests

Alcoholic Liver Disease, Liver Cirrhosis, Abdominal US

Representative Publications

1. Kim, Tae Suk, et al. "Metformin and dichloroacetate suppress proliferation of liver cancer cells by inhibiting mTOR complex 1." International Journal of Molecular Sciences 22.18 (2021): 10027.
2. Kim, Tae Suk, et al. "Reappraisal of sepsis-3 and CLIF-SOFA as predictors of mortality in patients with cirrhosis and infection presenting to the emergency department: A multicenter study." Clinical and molecular hepatology 28.3 (2022): 540.
3. Kim, Tae Suk, and Dae Hee Choi. "Liver Dysfunction in Sepsis." The Korean Journal of Gastroenterology= Taehan Sohwagi Hakhoe chi 75.4 (2020): 182-187.

Ultrasound Trainer Session 1 | DAY 1: May 29 (Thu.) | ROOM 7 [1F]

Current Condition of Ultrasound Education in Training Hospitals

Tae-Suk Kim *Kangwon National University*

Ultrasound (US) is an essential diagnostic tool in almost every medical area. However, US education for physicians has been conducted only in some university hospitals that directly perform abdominal US examinations in internal medicine, or some education is provided with the help of radiologists. US technology continues to become increasingly widespread, portable, and miniaturized. Furthermore, point-of-care US, i.e., US executed at the patient's bedside to obtain real-time objective information for diagnostic and clinical monitoring purposes or to guide invasive procedures, has been incorporated in many specialties. An educational accreditation system for trainers of ultrasonography in the internal medicine field was developed in 2018, but there is a lack of accredited ultrasound trainers, equipment, and space for ultrasound training.

Training of Abdominal ultrasound in Korea faces four major challenges:

(i) **Providing more specific programs and educational opportunities for residents:** There's a need to develop tailored educational programs that provide residents with comprehensive training in ultrasound techniques. This could involve creating standardized curricula that include hands-on practice and simulations.

(ii) **Expansion of manpower and quality control of the certification system:** An increase in certified trainers and a robust certification system are necessary to ensure high-quality training and practice. This could involve setting up accreditation bodies and continuous professional development programs for trainers.

(iii) **Training with advanced diagnostic ultrasonography: I**ncorporating training on advanced ultrasound technology and techniques will help practitioners stay updated with the latest developments. This could include workshops, seminars, and access to cutting-edge equipment.

(iv) **Expansion into medical student curricula:** Introducing ultrasound education early in medical training will help students develop proficiency and comfort with the technology. Integrating it into the standard curriculum can prepare future practitioners to effectively use ultrasound in clinical settings.

This topic highlights the growing importance of ultrasound (US) as a diagnostic tool across various medical disciplines, including its applications in point-of-care settings. However, it also identifies several challenges in Korea related to ultrasound training, particularly in internal medicine.

Nae-Yun Heo

Inje University

Self Introduction

Prof. Nae-Yun Heo graduated from Pusan National University College of Medicine for Bachelor's degree in 2001. Then, He got the Mater's and Doctor's degree in University of Ulsan College of Medicine. Also, He had a resident training in Internal Medicine and fellowship in the Department of Gastroenterology in Asan Medical Center, Seoul, Korea. He is affiliated to Inje University Haeundae Paik Hospital since 2011.

He is deeply interested in the hepatology including acute and chronic viral hepatitis, liver cirrhosis, hepatocellular carcinoma, and liver abscess.

Research Interests

- Chronic viral hepatitis (HBV, HCV)
- Liver Cirrhosis
- Hepatocellular Carcinoma
- Liver Abscess

Representative Publications

1. Efficacy and safety of biphenyl dimethyl dicarboxylate and ursodeoxycholic acid combination in chronic hepatitis related to metabolic syndrome components. Korean J Gastroenterol 2021;77:179-189
2. Current status of amebic liver abscess in Korea comparing with pyogenic liver abscess. Korean J Gastroenterol 2020;76:28-36
3. Hepatitis E virus: epidemiology, diagnosis, and management. Korean J Gastroenterol 2019;74:130-136
4. Long-term patient and graft survival of kidney transplant recipients with hepatitis C virus infection in the United States. Transplantation 2018;102:454-460
5. The prevalence of colonic neoplasm in cryptogenic pyogenic liver abscess: a prospectively enrolled cross-sectional study. Korean J Gastroenterol 2016;68:195-201

Ultrasound Trainer Session 1 | DAY 1: May 29 (Thu.) | ROOM 7 [1F]

Point-of-Care Ultrasound (POCUS): An Invaluable Tool in the Field of Medical Procedure Services

Nae-Yun Heo *Inje University*

Point-of-Care Ultrasound (POCUS) is a rapidly evolving bedside imaging modality that empowers clinicians to make immediate, informed decisions during patient care. Particularly in the hepatobiliary field, POCUS has become increasingly relevant in diagnosing, managing, and guiding procedures in patients with liver-related diseases.

Key Applications in Hepatobiliary Practice

1. **Ascites Evaluation:** POCUS allows for accurate detection and assessment of ascites, even in low-volume states, enhancing diagnostic sensitivity.
2. **Paracentesis Guidance:** It improves safety and success rates of paracentesis by localizing fluid pockets and avoiding vascular structures.
3. **Liver and Spleen Assessment:** POCUS enables rapid estimation of liver size, surface nodularity, and splenomegaly, which are crucial for diagnosing cirrhosis and portal hypertension.
4. **Gallbladder and Biliary Tree Evaluation:** Bedside ultrasound aids in detecting gallstones, wall thickening, pericholecystic fluid, and biliary ductal dilatation.
5. **Vascular Assessment:** Visualization of the portal vein, hepatic veins, and IVC contributes to volume status evaluation and portal flow assessment.

Advantages of POCUS in Procedure Services

- **Real-Time Guidance:** Enhances accuracy and safety of procedures such as paracentesis, thoracentesis, and central venous catheterization.
- **Rapid Clinical Decision-Making:** Facilitates immediate interpretation and integration into clinical workflows.
- **Educational Impact:** Empowers non-radiologists, including hepatologists and trainees, to perform focused assessments and interventions.

Comparison to Conventional Ultrasound While conventional ultrasound provides high-resolution,

comprehensive imaging interpreted by radiologists, POCUS offers rapid, focused, and clinician-performed imaging that augments physical examination and accelerates care. Both are complementary in delivering optimal patient outcomes.

Challenges and Implementation Barriers such as equipment availability, variability in training, and institutional support must be addressed. Structured education, faculty development, and inclusion in hepatology training curricula are key to sustainable POCUS integration.

Conclusion POCUS is a transformative tool in hepatobiliary medicine. It enhances diagnostic efficiency, procedural safety, and bedside clinical acumen. Integrating POCUS into standard practice is essential for the future of hepatobiliary care.

References

1. Moore CL, Copel JA. Point-of-care ultrasonography. N Engl J Med 2011;364:749-757.
2. Ma IWY, Arishenkoff S, Wiseman J, et al. Internal medicine point-of-care ultrasound curriculum: consensus recommendations from the Canadian Internal Medicine Ultrasound (CIMUS) group. J Gen Inern Med 2017;32:1052-1057.
3. Mercaldi CJ, Lanes SF. Ultrasound guidance decreases complications and improves the cost of care among patients undergoing paracentesis. J Ultrasound Med. 2013;32:1889–1895.

Se Young Jang

Kyungpook National University

Self Introduction

Prof. Se Young Jang is an associate professor in the Division of Gastroenterology and Hepatology, Department of Internal Medicine at Kyungpook National University Hospital and Kyungpook National University School of Medicine.

She received her M.D. in 2008 and Ph.D. in 2015 from Kyungpook National University School of Medicine. She completed her internship, residency, and fellowship in the Department of Internal Medicine at Kyungpook National University Hospital.

She is a member of several academic societies, including the Korean Association of Internal Medicine, the Korean Association for the Study of the Liver (KASL), the Korean Liver Cancer Association, the Korean Society of Gastrointestinal Endoscopy, and the Korean Society of Clinical Ultrasound. She has also held key academic roles such as Public Relations Committee Member (2016–2017) and IT Committee Member (2017–2018) of KASL, Editorial Board Member of the Korean Liver Cancer Association (2018–2019), and Education Committee Member of KASL (2020–2021).

Research Interests

MASLD, HCC, Tumor Microenvironment, Liver Fibrosis, Biomarker

Representative Publications

1. Jang SY, Yoon KT, Cho YY, Jo HG, Baek YH, Moon SY, Jo AJ, Kweon YO, Park SY, Lee YR, Jun DW, Tak WY. Aspartate aminotransferase-to-platelet ratio index outperforms Fibrosis-4 in 2843 Korean patients with metabolic dysfunction-associated steatotic liver disease. Hepatol Res. 2025 Apr;55(4). doi: 10.1111/hepr.14143. Epub 2024 Nov 29.
2. Jang SY, Park SY, Kweon YO, Lee YR, Ryeom HK, Cha JG, Kim S, Lee WK, Jo AJ, Tak WY. Temporal trends and long-term outcomes of radiofrequency ablation for hepatocellular carcinoma within the Milan criteria. Sci Rep. 2024 Aug 27;14(1):19815. doi: 10.1038/s41598-024-70494-4.
3. Moon SY, Baek YH*, Jang SY*, Jun DW, Yoon KT, Cho YY, Jo HG, Jo AJ. Proposal of a Novel Serological Algorithm Combining FIB-4 and Serum M2BPGi for Advanced Fibrosis in Nonalcoholic Fatty Liver Disease. Gut Liver. 2024 Mar 15;18(2):283-293. doi: 10.5009/gnl230128. Epub 2023 Aug 14.(*corresponding author)
4. Jang SY, Chang JY, Kim HJ. Association of changes in body mass index and waist circumference with cardiovascular risk in non-alcoholic fatty liver disease: A nationwide study. Dig Liver Dis. 2023 Nov;55(11):1509-1514. doi: 10.1016/j.dld.2023.06.006. Epub 2023 Jul 5.
5. Kim G, Han JR, Park SY, Tak WY, Kweon YO, Lee YR, Han YS, Park JG, Kang MK, Lee HW, Lee WK, Kim D, Jang SY*, Hur K*. Circular noncoding RNA hsa_circ_0005986 as a prognostic biomarker for hepatocellular carcinoma. Sci Rep. 2021 Jul 22;11(1):14930. (*corresponding author)

Role of Ultrasound Methods for the Assessment of Metabolic Dysfunction-Associated Steatotic Liver Disease

Se Young Jang *Kyungpook National University*

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as the most prevalent chronic liver condition worldwide and is now recognized as a hepatic manifestation of metabolic syndrome. Given its asymptomatic nature and progressive potential, early and accurate detection of hepatic steatosis is essential. Among the available diagnostic tools, ultrasound-based techniques offer non-invasive, cost-effective, and point-of-care advantages, making them integral to MASLD evaluation in both primary and specialty care settings.

Conventional ultrasound is the most commonly used modality for initial screening of steatosis. It identifies hepatic steatosis based on increased echogenicity compared to the renal cortex, blurring of vascular margins, and posterior beam attenuation. However, its diagnostic utility is limited by low sensitivity, particularly in detecting mild steatosis and in patients with obesity. Moreover, Conventional ultrasound provides only a subjective, semiquantitative assessment and cannot quantify liver fat content. Consequently, current clinical practice guidelines from the AASLD and EASL caution against using Conventional ultrasound as a definitive diagnostic tool for steatosis.

To address these limitations, the Controlled Attenuation Parameter (CAP), an ultrasound-derived quantitative measurement obtained via vibration-controlled transient elastography (VCTE), has been introduced. CAP quantifies hepatic steatosis by measuring the attenuation of ultrasound signals as they pass through the liver, expressed in dB/m. CAP provides a semi-quantitative assessment of steatosis (grades S1 to S3) with moderate accuracy, and it is especially useful in primary care settings for secondary risk assessment when elevated FIB-4 scores suggest a higher risk of advanced disease. Despite its advantages, CAP also has limitations, such as reduced accuracy in individuals with high BMI or advanced fibrosis, and it may not be suitable for tracking longitudinal changes in liver fat.

In summary, ultrasound methods—particularly Conventional ultrasound and CAP—play a pivotal role in the initial detection and risk stratification of MASLD. While Conventional ultrasound remains a widely available screening tool, its diagnostic limitations necessitate the use of more advanced ultrasound-based technologies like CAP. Optimizing the use of these tools in clinical workflows will be key to improving MASLD diagnosis and management, particularly in resource-limited settings.

References

1. Loomba R, Sanyal AJ. (2013). The global NAFLD epidemic. Nature Reviews Gastroenterology & Hepatology, 10(11), 686–690.
2. Rinella ME, et al. (2023). AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology, 77(5), 1797–1835. https://doi.org/10.1097/HEP.0000000000000323
3. EASL, EASD, EASO. (2024). EASL-EASD-EASO Clinical Practice Guidelines on the management of MASLD. Journal of Hepatology, 81(3), 492–542. https://doi.org/10.1016/j.jhep.2024.04.0314.
4. Paige JS, et al. (2017). A pilot comparative study of quantitative ultrasound, conventional ultrasound, and MRI for predicting histology-determined steatosis grade. AJR Am J Roentgenol, 208, W168–W177.
5. Lin SC, et al. (2015). Noninvasive diagnosis and liver fat quantification using a new quantitative ultrasound technique. Clin Gastroenterol Hepatol, 13(7), 1337–1345.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
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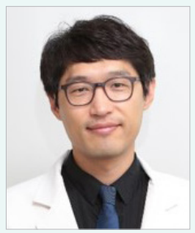

Jung Gil Park

Yeungnam University

Self Introduction

Education

2004 M.D., Kyungpook National University School of Medicine, Daegu, Korea
2015 M.S., Kyungpook National University School of Medicine, Daegu, Korea
2019 PhD., Kyungpook National University School of Medicine, Daegu, Korea

Professional Experience

- Associate Professor, Gastroenterology & Hepatology, Yeungnam University Hospital, Daegu, Korea
- Member, Committee of the Editorial Board in the KASL
- Editor in Chief, Clinical Ultrasound
- University of California San Diego, NAFLD Research Center, 2020.02-2021.02

Research Interests

MASLD, ArLD, Hepatocellular Carcinoma, ncRNA, Biomarker

Representative Publications

1. Liver stiffness by magnetic resonance elastography is associated with increased risk of cardiovascular disease in patients with non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2021;53(9):1030-1037.
2. Long-term effects of the changes in hepatic steatosis status on the risk of incident type 2 diabetes mellitus: A 15-year community-based prospective cohort study. Diabetes Res Clin Pract. 2022;184:109208
3. Impact of metabolic factors on risk of cardiovascular disease in nondiabetic metabolic dysfunction-associated fatty liver disease. Hepatol Int. 2023;17(3):626-635.
4. Fibrosis-4 index as a predictor for mortality in hospitalised patients with COVID-19: a retrospective multicentre cohort study. BMJ Open. 2020;10(11):e041989.
5. Expression of the Long Noncoding RNA GAS5 Correlates with Liver Fibrosis in Patients with Nonalcoholic Fatty Liver Disease. Genes (Basel). 2020;11(5):545.

Ultrasound Trainer Session 1 | DAY 1: May 29 (Thu.) | ROOM 7 [1F]

Liver Fibrosis Stages Using Ultrasound Technology

Jung Gil Park *Yeungnam University*

Liver fibrosis is a significant health concern, often resulting from chronic liver diseases such as viral hepatitis and metabolic dysfunction-associated steatotic disease (MASLD). Early detection and staging of liver fibrosis are crucial for effective management and treatment. Traditionally, liver biopsy has been considered the gold standard for assessing fibrosis. However, non-invasive techniques like ultrasound elastography have gained prominence due to their safety and ease of use.

Ultrasound-based elastography techniques including Transient Elastography (TE), point Shear Wave Elastography (p-SWE), and 2D Shear Wave Elastography (2D-SWE), have demonstrated promising results in staging liver fibrosis.[1]

TE, also known as FibroScan®, measures liver stiffness, which correlates with the degree of fibrosis. Studies have shown that TE is effective in distinguishing between different stages of liver fibrosis, particularly in advanced stages (F3 and F4).[2]

P-SWE (also called acoustic radiation force impulse) focuses on measuring shear wave speed at specific points within the liver. This technique offers high accuracy in quantifying liver stiffness and has been shown to be effective in identifying different stages of fibrosis.[3]

2D-SWE offers 2D imaging capabilities, allowing for the visualization of liver stiffness over a larger area. This method enhances the accuracy of fibrosis staging by providing a comprehensive overview of liver elasticity.[4] Thus, 2D-SWE has demonstrated greater diagnostic accuracy than pSWE, particularly in cases where liver fibrosis is heterogeneous.[3]

Despite these advancements, challenges remain in standardizing ultrasound elastography techniques due to variations in equipment and operator dependency.[5] Nevertheless, ultrasound elastography is increasingly integrated into clinical practice for liver fibrosis assessment, providing a non-invasive, patient-friendly alternative to liver biopsy.[6]

In conclusion continued research and technological enhancements are expected to improve the accuracy and reliability of these methods, further solidifying their role in liver fibrosis management.

References

1. Kim MN, Han JW, An J, et al. KASL clinical practice guidelines for noninvasive tests to assess liver fibrosis in chronic liver disease. Clin Mol Hepatol 2024;30(Suppl):S5-S105. doi: 10.3350/cmh.2024.0506 [published Online First: 2024/08/20]
2. Foucher J, Chanteloup E, Vergniol J, et al. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. Gut 2006;55(3):403-8. doi: 10.1136/gut.2005.069153 [published Online First: 2005/07/16]
3. Barr RG, Wilson SR, Rubens D, et al. Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement. Radiology 2020;296(2):263-74. doi: 10.1148/radiol.2020192437 [published Online First: 2020/06/10]
4. Shiina T, Nightingale KR, Palmeri ML, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: basic principles and terminology. Ultrasound Med Biol 2015;41(5):1126-47. doi: 10.1016/j.ultrasmedbio.2015.03.009 [published Online First: 2015/03/26]
5. Boursier J, Zarski JP, de Ledinghen V, et al. Determination of reliability criteria for liver stiffness evaluation by transient elastography. Hepatology 2013;57(3):1182-91. doi: 10.1002/hep.25993 [published Online First: 2012/08/18]
6. Anstee QM, Castera L, Loomba R. Impact of non-invasive biomarkers on hepatology practice: Past, present and future. Journal of hepatology 2022;76(6):1362-78. doi: 10.1016/j.jhep.2022.03.026 [published Online First: 2022/05/20]

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 1: May 29 (Thu.)

Ultrasound Trainer Session 2

Chair:

Jae Young Jang (Soonchunhyang Univ.)

Moon Hyung Lee

Kyung Hee University

Self Introduction

Prof. Moonhyung Lee is an Assistant Professor in the Department of Gastroenterology and Hepatology at Kyung Hee University Hospital at Gangdong, Seoul, Korea.

She earned medical degree from Kyung Hee University College of Medicine.

Research Interests

Prof. Moonhyung Lee's clinical and research interests include hepatocellular carcinoma, portal hypertension, metabolic dysfunction-associated steatotic liver disease (MASLD) and big-data analysis using common data models.

Representative Publications

1. Lee M, Kim M, Cha JM. Risk of Lower Gastrointestinal Bleeding in NSAID and Proton Pump Inhibitor Users Compared with NSAID-Only Users: A Common Data Model Analysis. Gut and Liver. Published online January 3, 2025. https://doi.org/10.5009/gnl240247
2. Lee M, Myung SK, Lee SH, Chang Y. Smoking and Risk of Fatty Liver Disease: A Meta-Analysis of Cohort Studies. Gastroenterology Insights. 2025;16(1):1. https://doi.org/10.3390/gastroent16010001
3. Lee M, Cha JM. Real-World Bleeding Risk of Anticoagulant and NSAID Combotherapy versus Anticoagulant Monotherapy. Gut and Liver. Published online May 10, 2024. https://doi.org/10.5009/gnl230541
4. Lee M, Shin HP. Efficacy of Transarterial Chemoembolization (TACE) for Early-Stage Hepatocellular Carcinoma. Medicina. 2023;59(12):2174. https://doi.org/10.3390/medicina59122174

Follow-Up of Benign Neoplasm of Liver: Role of Abdominal Ultrasound

Moon Hyung Lee *Kyung Hee University*

Background

Benign hepatic neoplasms, such as hepatic hemangiomas, focal nodular hyperplasia (FNH), and hepatocellular adenomas (HCA), are commonly encountered incidental findings during abdominal imaging. Although these lesions are generally asymptomatic and carry a favorable prognosis, appropriate follow-up is essential for accurate diagnosis, identification of atypical features, and early detection of potential malignant transformation. The selection of an optimal surveillance strategy should balance the risks of unnecessary interventions with the need for patient safety.

Abdominal Ultrasound as a Primary Imaging Tool

Abdominal ultrasound (US) remains the first-line imaging modality for the detection and follow-up of benign liver lesions due to its safety, accessibility, and cost-effectiveness. Conventional grayscale US, Doppler US, and contrast-enhanced ultrasound (CEUS) offer valuable diagnostic information for characterizing liver masses. Grayscale US can identify classic echogenic patterns—such as the homogenous hyperechogenicity of hemangiomas—while Doppler imaging can assess vascular flow patterns in lesions like FNH. CEUS, with its real-time microvascular imaging capabilities, has dramatically improved the diagnostic confidence for differentiating benign from malignant lesions.

Lesion-Specific Follow-up Strategies

Hepatic hemangiomas, the most frequent benign liver tumors, generally require no follow-up if <3 cm and asymptomatic. However, atypical or giant hemangiomas (>5 cm) may require periodic US to monitor for growth or complications such as rupture or thrombosis. FNH typically presents as a well-defined, isoechoic or slightly hypoechoic lesion with a central scar visible on CEUS. As FNH is considered a hyperplastic lesion without malignant potential, routine follow-up is often unnecessary unless atypical imaging features are present. Hepatocellular adenomas, however, require individualized management. Given the risk of hemorrhage or malignant transformation, particularly in women of reproductive age or anabolic steroid users, routine monitoring with US every 6–12 months may be warranted. Subtyping using MRI or biopsy can guide risk stratification.

Clinical Scenarios and Limitations

While abdominal US is a highly useful modality, its limitations include operator dependency, reduced sensitivity in obese patients, and challenges in evaluating lesions in deep hepatic segments. In ambiguous cases, cross-sectional imaging (CT or MRI) may be necessary. Nonetheless, US remains an invaluable tool for longitudinal assessment, particularly when integrated with clinical history, laboratory data, and other imaging modalities.

Future Directions

Recent advances in elastography and artificial intelligence (AI)-driven US image interpretation may enhance the diagnostic performance and predictive accuracy of ultrasound in benign liver neoplasm assessment. Standardized follow-up protocols and integration of ultrasound biomarkers could further refine surveillance strategies.

Conclusion

Abdominal ultrasound plays a pivotal role in the follow-up of benign liver tumors. Its non-invasive nature, combined with evolving technological advancements, ensures that it will remain central to clinical practice. A tailored follow-up approach based on lesion type, imaging characteristics, and patient risk factors is essential for optimal outcomes.

Keywords: benign liver tumor, abdominal ultrasound, hepatic hemangioma, focal nodular hyperplasia, hepatocellular adenoma, CEUS, liver imaging, follow-up strategy

References

1. Ronot M, Vilgrain V. Imaging of benign liver tumors. Semin Liver Dis. 2008;28(3):349–360.
2. Bartolotta TV, et al. Focal liver lesion characterization with contrast-enhanced ultrasound. World J Radiol. 2011;3(4):159–172.
3. van Aalten SM, et al. Systematic review of hepatocellular adenoma: incidence, risk factors and outcome. Liver Int. 2012;32(5):622–628.
4. Kim TK, et al. Hepatic hemangiomas: spectrum of US appearances on grayscale, power Doppler, and contrast-enhanced US. Abdom Imaging. 2005;30(3):325–332.
5. Wilson SR, Burns PN. Microbubble-enhanced US in body imaging: what role? Radiology. 2010;257(1):24–39.

SAMSUNG's Liver Solution

Jiyoon Kim *Samsung Medison*

Self Introduction

Jiyoon Kim graduated from Gacheon University with her Radiation technician degree in 2007 and had worked as a Radiology technician as well as a sonographer in GI application till 2017.

Since 2017, Jiyoon Kim has been taking a number of roles in SAMSUNG Medison, including Clinical overseas manager of East Asia, North America, Middle East and so on. Currently working for Clinical insight lab of CX Team.

Soo Young Park

Kyungpook National University

Self Introduction

Educational

2011.2-2015.6 Assistant Professor, Internal Medicine, Department of Gastroenterology, Kyungpook National University Hospital
2015.6-2020.7 Associate Professor Internal Medicine, Department of Gastroenterology, Kyungpook National University Hospital
2020.7-Present Professor, Internal Medicine, Department of Gastroenterology, Kyungpook National University Hospital
2018.8-2019.8 Visiting Scientist, NAFLD Research Center

Research Interests

Translational Research, Biomarker Study, Cancer Diagnostics, Chemotherapeutics, and Viral Hepatitis

Representative Publications

1. Shin H, Hur MH, Song BG, Park SY, Kim GA, Choi GH, Nam JY, Kim MA, Park Y, Ko Y, Park J, Lee HA, Chung SW, Choi NR, Park MK, Lee YB, Sinn DH, Kim SU, Kim HY, Kim JM, Park SJ, Lee HC, Lee DH, Chung JW, Kim YJ, Yoon JH, Lee JH. AI model using CT-based imaging biomarkers to predict hepatocellular carcinoma in patients with chronic hepatitis B. J Hepatol. 2024 Dec 20:S0168-8278(24)02784-3.
2. Kang MK, Lee YR, Jang SY, Tak WY, Kweon YO, Song JE, Loomba R, Park SY, Park JG. Impact of metabolic factors on risk of cardiovascular disease in nondiabetic metabolic dysfunction-associated fatty liver disease. Hepatol Int. 2023 Jun;17(3):626-635.
3. Yoo JJ, Park SY, Moon JE, Lee YR, Lee HA, Lee J, Kim YS, Seo YS, Kim SG. Long-term prognosis and the need for histologic assessment of chronic hepatitis B in the serological immune-tolerant phase. Clin Mol Hepatol. 2023 Apr;29(2):482-495.
4. Kang MK, Song JE, Kweon YO, Tak WY, Park SY, Lee YR, Park JG. Visceral Obesity and Its Association with Severe Coronary Artery Calcification in Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease. Diagnostics (Basel). 2024 Oct 17;14(20):2305
5. Kang MK, Baek JH, Kweon YO, Tak WY, Jang SY, Lee YR, Hur K, Kim G, Lee HW, Han MH, Choi JH, Park SY, Park JG. Association of Skeletal Muscle and Adipose Tissue Distribution with Histologic Severity of Non-Alcoholic Fatty Liver. Diagnostics (Basel). 2021 Jun 9;11(6):1061.
6. Chon YE, Kim SU, Seo YS, Lee HW, Lee HA, Kim MN, Roh YH, Park JY, Kim DY, Ahn SH, Tak WY, Park SY, Kim BK. Long-term effects of entecavir and tenofovir treatment on the fibrotic burden in patients with chronic hepatitis B. J Gastroenterol Hepatol. 2022 Jan;37(1):200-207.

Comparative Clinical Utility of Sonovue and Sonazoid in Contrast-Enhanced Ultrasound for Liver Imaging

Soo Young Park *Kyungpook National University*

Contrast-enhanced ultrasound (CEUS) has become an important imaging modality for evaluating liver lesions due to its real-time imaging capability, safety profile, and non-invasiveness. Among the second-generation ultrasound contrast agents, Sonovue (sulfur hexafluoride microbubbles) and Sonazoid (perfluorobutane microbubbles) are widely used with distinct pharmacologic properties and imaging characteristics. This review provides a comparative analysis of these two agents with a focus on their composition, contrast dynamics, and clinical applications, particularly in the context of hepatocellular carcinoma (HCC) diagnosis and surveillance. Sonovue provides high-resolution intravascular imaging during the arterial, portal venous, and late phases, while Sonazoid offers a unique postvascular Kupffer phase through selective phagocytosis by hepatic macrophages. Understanding the differences between these agents is essential for appropriate selection in various clinical scenarios.

Introduction

Contrast-enhanced ultrasound (CEUS) has been increasingly integrated into the diagnostic algorithm for focal liver lesions due to its high temporal resolution and dynamic evaluation of microvascular perfusion. In the liver, CEUS provides real-time vascular characterization of hepatic nodules, aiding in the differentiation of hepatocellular carcinoma (HCC), metastases, hemangiomas, and other lesions. Among the second-generation ultrasound contrast agents, Sonovue and Sonazoid have become essential tools, each with distinct properties that influence their diagnostic performance and clinical applications. This review aims to compare and contrast these two agents, elucidating their strengths and limitations in liver imaging.

Pharmacologic and Physical Properties

Sonovue is composed of sulfur hexafluoride gas encapsulated by a phospholipid shell, forming microbubbles that remain strictly within the vascular compartment. It is metabolized and excreted via the lungs and provides optimal contrast during the arterial, portal venous, and late vascular phases. Its contrast duration is limited to a few minutes, which is adequate for dynamic perfusion analysis but precludes delayed-phase imaging.

Sonazoid, in contrast, contains perfluorobutane gas and a phosphatidylserine-based shell that allows selective uptake by Kupffer cells in the liver. This results in a distinct Kupffer phase that begins approximately 10 minutes after administration and can persist for up to 30 minutes or longer. This phase enables prolonged liver parenchyma imaging and enhances the detection of lesions lacking Kupffer cells, such as HCC or metastases.

Imaging Characteristics and Phase Comparison

Sonovue's imaging utility is primarily based on its intravascular distribution. It provides real-time visualization of arterial enhancement and washout patterns, which are particularly useful in evaluating HCC. The hallmark findings include arterial phase hyperenhancement (APHE) and late or mild washout, which are key features in CEUS LI-RADS classification. However, the absence of a postvascular or tissue phase limits its use in lesion detection, especially for small or hypovascular nodules.

Sonazoid enables both vascular phase imaging and parenchymal imaging during the Kupffer phase. This dual-phase capability allows not only lesion characterization but also lesion detection in high-risk populations. In the Kupffer phase, normal liver tissue appears uniformly enhanced, while lesions lacking Kupffer cells appear as defects. This feature significantly improves sensitivity in detecting early-stage or small HCCs.

Clinical Applications in Liver Lesions

In HCC diagnosis, Sonovue and Sonazoid both demonstrate high diagnostic performance in detecting typical enhancement patterns. Sonazoid provides additional information through Kupffer phase imaging, which can improve confidence in detecting atypical or small lesions. For example, dysplastic nodules or early HCCs, which may appear isovascular during the vascular phase, may be more conspicuous as defects in the Kupffer phase with Sonazoid.

Metastatic lesions typically show early washout and hypoenhancement in both agents. However, Sonazoid facilitates clearer detection in the Kupffer phase due to its defect-based contrast mechanism. In contrast, hemangiomas and focal nodular hyperplasia (FNH) are often more readily diagnosed with Sonovue due to characteristic enhancement patterns (e.g., peripheral nodular enhancement and spoke-wheel pattern, respectively) observed in the vascular phase.

Surveillance and Screening Utility

One of the major advantages of Sonazoid over Sonovue lies in its potential utility in HCC surveillance. Due to its prolonged Kupffer phase, Sonazoid enables whole-liver screening in a single contrast injection, which is particularly valuable for high-risk populations such as patients with cirrhosis. Several studies have shown improved sensitivity for small HCCs using Sonazoid-enhanced surveillance compared to conventional B-mode ultrasound. In contrast, Sonovue is generally not used for surveillance due to its lack of delayed parenchymal imaging.

Agent Selection and Practical Considerations

Sonovue is widely approved and used in the United States, Europe, and Asia, with versatility across multiple organ systems. Its short duration of enhancement and safety profile make it suitable for rapid dynamic imaging. Sonazoid, while approved only in selected countries such as Japan, South Korea, and China, offers unique advantages for liver-specific imaging and surveillance protocols. However, arterial phase imaging with Sonazoid requires precise timing, and the need for specific contrast imaging settings (e.g., intermediate mechanical index) must be considered.

Ultimately, the choice between Sonovue and Sonazoid should be based on the clinical context, diagnostic objective, patient characteristics, and institutional experience.

Conclusion

Sonovue and Sonazoid are complementary ultrasound contrast agents with unique features that cater to different diagnostic needs in liver imaging. Sonovue excels in vascular characterization of liver lesions during dynamic phases, while Sonazoid offers the added benefit of Kupffer phase imaging for lesion detection and surveillance. Recognizing the strengths and limitations of each agent is essential for optimizing CEUS-based liver imaging and improving diagnostic outcomes in hepatology practice.

References

1. Kono Y, Lyshchik A, Cosgrove D, et al. Contrast-enhanced ultrasound (CEUS) Liver Imaging Reporting and Data System (LI-RADS) 2017: A review of important differences compared to CT/MRI. Abdom Radiol (NY) 2018;43:127–142.
2. Takahashi H, Maruyama H, Shimada T, et al. Characterization of focal liver lesions with contrast-enhanced ultrasound using Sonazoid. World J Radiol 2010;2:249–256.
3. Korean Association for the Study of the Liver (KASL). KASL clinical practice guidelines for the management of hepatocellular carcinoma: 2022 update. Clin Mol Hepatol 2022;28:583–705.
4. Jang HJ, Kim TK, Burns PN, Wilson SR. CEUS of hepatocellular carcinoma: Advantages and limitations. Abdom Imaging 2015;40:52–60.
5. Wilson SR, Burns PN. Microbubble-enhanced US in body imaging: What role? Radiology 2010;257:24–39.
6. Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver - Update 2012: A WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, and FLAUS. Ultraschall Med 2013;34:11–29.
7. Liver Imaging Reporting and Data System (LI-RADS) v2017. American College of Radiology. Available from: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS

Sae Hwan Lee

Soonchunhyang University

Self Introduction

Education

1999 Graduated with M.D. Degree, College of Medicine Chung-Ang University, Seoul, Korea
2010 Graduated with Ph.D. Degree in Medicine
2007 Residency, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea
2009 Clinical Fellow, Gastroenterology
2015 Research Fellow, GI Unit, Massachusetts General Hospital, Boston, MA

Professional Experience

American Association of Cancer Research
Korean Society of Gastroenterology
Korean Association for the Study of the Liver

Research Interests

HCC, Viral Hepatitis

Representative Publications

1. Inhibition of P2RX7 contributes to cytotoxicity by suppression of glycolysis and AKT activation in human hepatocellular carcinoma. BMB Report 2024
2. Effect of antiviral therapy in patients with low HBV DNA level on transarterial chemoembolization for hepatocellular carcinoma. J Viral Hepat 2021

Ultrasound Trainer Session 2 | DAY 1: May 29 (Thu.) | ROOM 7 [1F]

Advanced Abdominal Ultrasound Considerations

Sae Hwan Lee *Soonchunhyang University*

Liver biopsy is the standardized procedure for obtaining hepatic tissue samples for the sake of histopathological examination. Ultrasound guidance is far superior to the blind approach, as it has shown to lower complication rates and increase success rates of the diagnostic yields of the procedure. The relative contraindications that should be considered at a case-by-case basis include the following: morbid obesity causing functional limitation to the operator, mild-to-moderate ascites. Bleeding is by far the most frequent serious adverse effect. The most significant risk factors for bleeding have been shown to be older age, the presence of malignancy, increased number of biopsy passes, and coagulation disorders.

Ultrasound shear wave elastography (SWE) is a non-invasive, low risk technology allowing the assessment of tissue stiffness. Point shear wave and 2D-shear wave elastography use sound energy to generate the applied perpendicular force. An early example is a 2006 study evaluating the relationship between liver stiffness and advanced liver disease of various etiologies in over 700 patients. Half of the enrolled patients had concomitant liver biopsies. In this study, shear stiffness values of 7.2 kPa, 12.5 kPa, and 17.6 kPa predicted moderate fibrosis, severe fibrosis, and cirrhosis, respectively, with a positive predictive value of at least 90% in each case. The impact of silent liver disease can be seen in a recent study involving over 7000 patients with non-alcoholic fatty liver disease (NAFLD), where a liver stiffness value greater than 10 kPa was shown to confer a substantial mortality risk over a 10 year period.

References

1. Alturkistani H, Alsergani AH, Alzeer M et al. Ultrasound-guided percutaneous liver biopsy: A review of what operators need to know. Medicine (Baltimore). 2024:26;103:e38673.
2. Suffredini G, Gao WD, Dodd-o JM. Ultrasound Shear Wave Elastography Evaluation of the Liver and Implications for Perioperative Medicine. J. Clin. Med. 2024:13;3633

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DAY 2: May 30 (Fri.)

KASL Special Interest Group 1.
The KASL Steatotic Liver Disease Study Group

Challenges to Overcome in the Era of MASLD

Chairs:

Byoung Kuk Jang (Keimyung Univ.)
Su Jong Yu (Seoul National Univ.)

Mi Na Kim

Yonsei University

Self Introduction

Education

M.D., Yonsei University College of Medicine, Seoul, Republic of Korea
Master Degree, Medicine, Graduate School, Yonsei University, Seoul, Republic of Korea
Ph.D., Medicine, Graduate School, Yonsei University, Seoul, Republic of Korea

Professional Training & Appointments

- Internship, Residency, Fellowship & Clinical Research Assistant Professor, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
- Assistant Professor & Associate Professor, Department of Internal Medicine, CHA University School of Medicine, Seongnam-si, Korea
- Postdoc Research Fellow, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, U.S.A.

Current position

Associate Professor, Division of Gastroenterology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

Research Interests

MASLD and Chronic Viral Hepatitis: Treatment Strategies and Factors Influencing Long-Term Prognosis

Representative Publications

1. Kim MN, Han JW, An J, Kim BK, Jin YJ, Kim SS, Lee M, et al. KASL clinical practice guidelines for noninvasive tests to assess liver fibrosis in chronic liver disease. Clin Mol Hepatol 2024;30:S5-s105.
2. Kim MN, An J, Kim EH, Kim HY, Lee HA, Yu JH, Jin YJ, et al. Vibration-controlled transient elastography for significant fibrosis in treatment-naïve chronic hepatitis B patients: A systematic review and meta-analysis. Clin Mol Hepatol 2024;30:S106-s116.
3. Han W, Han K, Hwang SG, Ahn SH, Kim MN. Association of physical activity, including amount and maintenance, with the risk of HCC among patients with type 2 diabetes. JHEP Rep 2024;6:101166.
4. Kim MN, Lee JS, Lee HW, Kim BK, Park JY, Kim DY, Ahn SH, et al. ALT Is Not Associated With Achieving Subcirrhotic Liver Stiffness and HCC During Entecavir Therapy in HBV-Related Cirrhosis. Clin Gastroenterol Hepatol 2023;21:2278-2287.e2275.
5. Kim MN, Han K, Yoo J, Hwang SG, Zhang X, Ahn SH. Diabetic MAFLD is associated with increased risk of hepatocellular carcinoma and mortality in chronic viral hepatitis patients. Int J Cancer 2023;153:1448-1458.

KASL Special Interest Group 1. | DAY 2: May 30 (Fri.) | ROOM 1 [3F]

Best Strategies to Assess Advanced Fibrosis in MASLD

Mi Na Kim *Yonsei University*

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the leading cause of chronic liver disease worldwide. Among patients with MASLD, the presence of advanced fibrosis (≥ stage F3) is the most critical predictor of liver-related outcomes, including hepatocellular carcinoma, liver failure, and mortality. Therefore, the accurate and early identification of advanced fibrosis is essential for patient management, risk stratification, and therapeutic decision-making.

Liver biopsy has been considered the gold standard for assessing fibrosis. However, its invasiveness, risk of complications, and sampling variability, have led to the development of non-invasive tests. Current strategies to assess advanced fibrosis are based on the combined use of serum biomarkers and imaging modalities, enabling effective risk stratification while minimizing the need for biopsy.

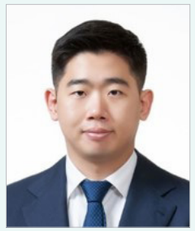
Among serum biomarkers, simple scoring systems such as the fibrosis-4 index (FIB-4) and the NAFLD fibrosis score are widely used. These scores are calculated using readily available clinical and laboratory parameters, offering a practical and inexpensive first-line approach. However, their diagnostic performance is modest, particularly in the intermediate ranges. More specialized biomarker panels, such as the Enhanced Liver Fibrosis test, provide improved accuracy but may not be accessible in all clinical settings. Imaging-based elastography techniques have significantly advanced the non-invasive assessment of liver fibrosis. Vibration-controlled transient elastography measures liver stiffness and has been extensively validated in MASLD populations. It is widely available, rapid, and reproducible, although factors such as obesity and hepatic inflammation can affect measurement accuracy. Magnetic resonance elastography offers the highest diagnostic accuracy among non-invasive imaging modalities but is limited by high cost and lower accessibility. Ultrasound-based shear wave elastography is another promising modality, offering quantitative liver stiffness measurements with good performance characteristics.

The current recommended strategy for assessing advanced fibrosis in MASLD involves a sequential two-step approach. Initial risk stratification is performed using simple serum-based scores such as FIB-4. Patients with low-risk scores may be managed conservatively without further evaluation, while those with indeterminate or high-risk scores needs to undergo confirmatory testing with imaging-based elastography. This approach optimizes resource utilization, reduces unnecessary referrals for liver biopsy, and increases the detection rate of true advanced fibrosis.

In this lecture, we will review these strategies in detail, discussing their advantages, limitations, and practical application in clinical practice.

References

1. Sohn W, Lee YS, Kim SS, et al. KASL clinical practice guidelines for the management of metabolic dysfunction-associated steatotic liver disease 2025. Clin Mol Hepatol 2025;31(Suppl):S1-s31. (In eng). DOI: 10.3350/cmh.2025.0045.
2. Kim MN, Han JW, An J, et al. KASL clinical practice guidelines for noninvasive tests to assess liver fibrosis in chronic liver disease. Clin Mol Hepatol 2024;30(Suppl):S5-s105. (In eng). DOI: 10.3350/cmh.2024.0506.
3. Hagström H, Shang Y, Hegmar H, Nasr P. Natural history and progression of metabolic dysfunction-associated steatotic liver disease. Lancet Gastroenterol Hepatol 2024;9(10):944-956. (In eng). DOI: 10.1016/s2468-1253(24)00193-6.
4. EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024;81(3):492-542. (In eng). DOI: 10.1016/j.jhep.2024.04.031.
5. Åsberg A, Lian IA, Løfblad L, Mikkelsen G. Personalized risk assessment of advanced liver fibrosis in patients with MASLD. J Hepatol 2025 (In eng). DOI: 10.1016/j.jhep.2025.02.014.



Joonyub Lee

The Catholic University of Korea

Self Introduction

Prof. Joonyub Lee is a Professor in the Division of Endocrinology and Metabolism, Department of Internal Medicine at Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea.

He earned his medical degree from the Catholic University College of Medicine in 2012 and completed his internship and residency in Internal Medicine at Seoul St. Mary's Hospital. Following his clinical training, he pursued an M.D.-Ph.D. program at KAIST (Korea Advanced Institute of Science and Technology). He is currently serving as an Assistant Professor at Seoul St. Mary's Hospital.

His clinical and translational research interests focus on metabolic dysfunction-associated steatotic liver disease (MASLD) and β-cell physiology.

Research Interests

Diabetes Mellitus, Pancreatic β-Cell Physiology, Metabolic Dysfunction Associated Steatotic Liver Disease

Representative Publications

1. Multiparity increases the risk of diabetes by impairing the proliferative capacity of pancreatic β cells. Experimental & Molecular Medicine 2023;55:2269-2280
2. PRMT1 Is Required for the Maintenance of Mature β-Cell Identity. Diabetes. 2020;69(3):355-68.
3. Efficacy and Safety of Alogliptin-Pioglitazone Combination for Type 2 Diabetes Mellitus Poorly Controlled with Metformin: A Multicenter, Double-Blind Randomized Trial. Diabetes Metab J 2024; doi: 10.4093/dmj.2023.0259
4. Opening the Precision Diabetes Care through Digital Healthcare. Diabetes Metab J 2023; doi: 10.4093/dmj.2022.0386
5. β cell replacement therapy for the cure of diabetes. J Diabetes Investig 2022; doi: 10.1111/jdi.13884

Use of Anti-Diabetic Drugs in MASLD: Can We Kill Two Birds with One Stone?

Joonyub Lee *The Catholic University of Korea*

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a progressive metabolic disorder that frequently coexists with diabetes mellitus (DM) and increases the risk of cardiovascular (CV) disease. This association urges the need for early and active intervention for MASLD. Biopsy-based studies have demonstrated that pioglitazone and GLP-1 receptor agonists can induce MASH resolution and fibrosis improvement. These agents provide a comprehensive benefit, simultaneously addressing glycemic control, liver disease, and cardiovascular risk. Emerging therapies, particularly dual and triple incretin-based treatments, hold further promise for optimizing outcomes. A post hoc analysis of tirzepatide revealed that MASH resolution and fibrosis improvement were strongly associated with body weight reduction and improved glycemic control across the overall population. MASH resolution benefits were observed in both T2D and non-T2D populations, whereas fibrosis improvement was more pronounced in T2D patients. Additionally, resmetirom has emerged as a complementary and independent therapeutic option distinct from anti-diabetic agents, offering further opportunities for comprehensive MASLD management. This presentation will explore the evolving therapeutic landscape for MASLD and its intersection with cardiometabolic disease, highlighting future strategies for integrated patient care.

Shang-Chin Huang

National Taiwan University, Taiwan

Self Introduction

Education

2007-2014 M.D., College of Medicine, National Yang-Ming University, Taipei, Taiwan
2021-Present Ph.D. student, Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan

Academic Honor

2022 APASL STC on HCC: Young Investigator Award
2022 APASL STC on HCC: Outstanding Abstract Award
2022 Liver Disease Prevention & Treatment Research Foundation: Liver Disease Research Award
2022 Taiwan Digestive Disease Week (TDDW): Young Investigator Award
2023 APASL Annual Meeting: Young Investigator Award
2023 APASL Annual Meeting: The Best Poster of YI
2023 TDDW: Young Investigator Award
2024 APASL STC on MAFLD: Young Investigator Award
2024 Taiwan Association for the Study of the Liver (TASL): Distinguished Young Scholar Award
2024 APAGE Research Programme Award (Co-investigator)
2025 APASL Rising Star Award

Representative Publications

1. SC Huang, TH Su, TC Tseng et al. All-cause and cause-specific mortality in patients with chronic hepatitis B and concurrent steatotic liver disease J Hepatol. 2025 (in press): S0168-8278(24)02763-6.
2. SC Huang, TH Su, TC Tseng et al. Pre-Existing and New-Onset Metabolic Dysfunctions Increase Cirrhosis and Its Complication Risks in Chronic Hepatitis B Am J Gastroenterol. 2025 Feb 1;120(2):401-409.
3. SC Huang, TH Su, TC Tseng et al. Metabolic Dysfunction-Associated Steatotic Liver Disease Facilitates Hepatitis B Surface Antigen Seroclearance and Seroconversion Clin Gastroenterol Hepatol. 2024 Mar;22(3):581-590.e6.
4. SC Huang, TH Su, TC Tseng et al. Distinct effects of hepatic steatosis and metabolic dysfunction on the risk of hepatocellular carcinoma in chronic hepatitis B. Hepatol Int. 2023 Oct;17(5):1139-1149.
5. SC Huang, CJ Liu. Chronic hepatitis B with concurrent metabolic dysfunction-associated fatty liver disease: Challenges and perspectives. Clin Mol Hepatol. 2023 Apr;29(2):320-331

Relationship between MASLD and Chronic Hepatitis B: Friends or Foes

Shang-Chin Huang *National Taiwan University, Taiwan*

Chronic hepatitis B (CHB) affects over 300 million people globally. With the rising prevalence of metabolic syndrome, steatotic liver disease (SLD), particularly metabolic dysfunction-associated SLD (MASLD), is increasingly observed in CHB patients. This overlap introduces new clinical complexity, highlighting the need to understand how steatosis and metabolic dysfunction influence the natural course of CHB.

SLD Suppresses HBV Activity and Promotes Functional Cure

Contrary to common assumptions, hepatic steatosis may have a suppressive effect on HBV replication. CHB patients with SLD show lower HBV DNA and HBsAg levels and are likely to be HBeAg-negative. In large untreated HBeAg-negative cohorts, MASLD independently increases the likelihood of HBsAg seroclearance and seroconversion. This suggests that steatosis may enhance host control of HBV.

Paradoxical Protection: SLD Reduces Cirrhosis, HCC, and Mortality in CHB

SLD may also confer broader liver protection in CHB. In several cohort studies, CHB patients with SLD had significantly lower risks of cirrhosis, HCC, and all-cause mortality compared to those without SLD. These benefits were observed after adjusting for metabolic risk factors, suggesting that steatosis itself may represent a favorable disease phenotype in selected patients.

The Other Side of the Coin: Metabolic Dysfunctions Exacerbate Liver Disease Progression

In contrast, metabolic abnormalities such as diabetes, hypertension, and overweight worsen liver outcomes. Both pre-existing and new-onset metabolic dysfunctions increase the risks of cirrhosis, HCC, and liver-related death in a dose-dependent manner. Diabetes, in particular, is a strong risk factor for liver disease progression in CHB.

Incorporating SLD and Metabolic Risk Assessment into CHB Management

SLD and metabolic dysfunction have distinct, often opposing, effects in CHB. While SLD may reduce HBV activity and liver complications, metabolic dysfunctions significantly worsen prognosis. Routine assessment of both components should be incorporated into CHB management to optimize surveillance,

risk prediction, and intervention strategies.

References

1. Mak LY, Hui RW, Fung J et al. Diverse effects of hepatic steatosis on fibrosis progression and functional cure in virologically quiescent chronic hepatitis B. J Hepatol. 2020;73(4):800-806.
2. Huang SC, Su TH, Tseng TC et al. Metabolic Dysfunction-Associated Steatotic Liver Disease Facilitates Hepatitis B Surface Antigen Seroclearance and Seroconversion. Clin Gastroenterol Hepatol. 2024;22(3):581-590 e586.
3. Huang SC, Su TH, Tseng TC et al. All-cause and cause-specific mortality in patients with chronic hepatitis B and concurrent steatotic liver disease. J Hepatol. 2024 Dec 14: S0168-8278(24)02763-6. doi: 10.1016/j.jhep.2024.12.009. Online ahead of print.
4. Huang SC, Liu CJ. Chronic hepatitis B with concurrent metabolic dysfunction-associated fatty liver disease: Challenges and perspectives. Clin Mol Hepatol. 2023;29(2):320-331.
5. Huang SC, Su TH, Tseng TC et al. Pre-Existing and New-Onset Metabolic Dysfunctions Increase Cirrhosis and Its Complication Risks in Chronic Hepatitis B. Am J Gastroenterol. 2025;120(2):401-409.
6. Mak LY, Hui RW, Lee CH et al. Glycemic burden and the risk of adverse hepatic outcomes in patients with chronic hepatitis B with type 2 diabetes. Hepatology. 2023;77(2):606-618.
7. Wong YJ, Nguyen VH, Yang HI et al. Impact of fatty liver on long-term outcomes in chronic hepatitis B: a systematic review and matched analysis of individual patient data meta-analysis. Clin Mol Hepatol. 2023;29(3):705-720.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

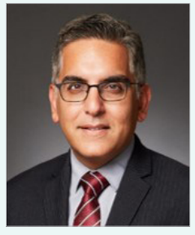
DAY 2: May 30 (Fri.)

KASL-AASLD Joint Symposium 1

Randomized Controlled Trials (RCTs) in Hepatology

Chairs:

W. Ray Kim (Mayo Clinic, USA)
Yoon Jun Kim (Seoul National Univ.)



Sumeet Asrani

Baylor University, USA

Self Introduction

Dr. Sumeet Asrani, MD, MSc is the Chief of Hepatology and Liver Transplantation at the Baylor Simmons Transplant Institute in Dallas and Fort Worth. He received his medical degree from Baylor College of Medicine in Houston. He did his internship and residency at Washington University School of Medicine in St. Louis, MO. He went on to complete fellowships in gastroenterology, hepatology and transplant hepatology at the Mayo Clinic in Rochester, Minnesota before joining the transplant hepatology team at Baylor University Medical Center in 2013.

He has published over 200 peer reviewed publications and has mentored more than 35 trainees to help advance their medical careers. He previously served as an associate editor for the American Journal of Transplantation (AJT) and as an associate editor for Liver Transplantation (LT). He is actively involved in national and international collaborations to improve care for patients with liver disease and authored AASLD guidelines on non-invasive liver disease assessment and acute on chronic liver failure.

Research Interests

Alcohol Associated Liver Disease, Kidney Dysfunction and Cirrhosis, Liver Transplantation Predictive Models, Critically Ill Cirrhosis

Representative Publications

1. Burden of liver diseases in the world
2. Development of quality measures in cirrhosis by the Practice Metrics Committee of the American Association for the Study of Liver Diseases
3. Reducing the global burden of alcohol - associated liver disease: a blueprint for action
4. Meeting report: the Dallas consensus conference on liver transplantation for alcohol associated hepatitis
5. AASLD Practice Guidance on Acute-on-chronic liver failure and the management of critically ill patients with cirrhosis

Practical Tips for Designing and Conducting Successful RCT

Sumeet Asrani *Baylor University, USA*

The patient population of interest needs to be considered. One needs to be mindful of the cirrhosis population that is aging, has multiple chronic conditions, and suffers from relevant complications. For most studies, support is built around transplant centers but burden of disease is in the community. Industry investment is limited in cirrhosis. There are enrollment challenges for trials, protocol nonadherence, and wide gap between the population enrolled in idealized efficacy trials and those encountered in clinical practice. Hence, there is a need to lower the barrier to entry for clinical trials

There are 3 aspects to cover in the realm of conducting an RCT in Hepatology.

Considerations should be given to the following during **design** phase

1. Relevant question: Will intervention change clinical practice
2. Criteria: equilibrium between strict and selective criteria (standardized patient group) and more heterogeneous conditions (external validity of the results).
3. Feasible: Timeline
4. Mirror reality: The RCT will be completed only in a relatively small percentage of all potentially eligible population
5. Novel designs such as pragmatic clinical trials should be considered.

During **conducting** phase of the trial, on needs to consider the importance of the primary site as being the leader in recruitment. There should be an assumption that there will be site drop off or reduction in recruitment. Data collection needs to be easy to complete and not burdensome. One must anticipate that roadblocks will happen with funding, site performance and personnel turnover.

To ensure **success**, one must establish cadence and structure for meeting milestones. There should be accountability. Several perspectives need to be considered from staff, patient, recruitment extenders as well as operations.

Reference

Implementing pragmatic clinical trials in hepatology
Elliot B Tapper, Marina Serper, David S Goldberg
Hepatology 2024

Inkyung Jung

Yonsei University

Self Introduction

Prof. Inkyung Jung is a Professor of Biostatistics in the Department of Biomedical Systems Informatics at Yonsei University College of Medicine. She currently serves as Chair of the department and Director of the Biostatistics Collaboration Unit within the College of Medicine.

She earned her B.S. (1998) and M.S. (2000) degrees in Statistics from Seoul National University. She received her Ph.D. in Biostatistics from the University of North Carolina at Chapel Hill. Following her doctoral training, she completed a post-doctoral fellowship at Harvard Medical School and subsequently held a faculty position as Assistant Professor at the University of Texas Health Science Center at San Antonio. She joined Yonsei University College of Medicine in 2010.

In her role as a biostatistician, she has also contributed as a statistical editor for several clinical journals, including Clinical and Molecular Hepatology, Archives of Plastic Surgery, Intestinal Research, and Vascular Specialist International.

Research Interests

Statistical Learning, Statistical Methods for Spatial Epidemiology and Pharmacoepidemiology, Clinical Trial, Health Claims Data Analysis

Representative Publications

1. Signal detection statistics of adverse drug events in hierarchical structure for matched case–control data. Biostatistics 2024; 25(5):1112-1121
2. Real-world incidences and risk factors of immune-related adverse events in patients treated with immune checkpoint inhibitors: A nationwide retrospective cohort study. Cancer Letters 2024; 596:216998.
3. Optimizing the maximum reported cluster size for the multinomial-based spatial scan statistic. International Journal of Health Geographics 2023; 22:30.
4. Stability selection for LASSO with weights based on AUC. Scientific Reports 2023; 13:5207.
5. A decrease in the incidence of encephalitis in South Korea during the COVID-19 pandemic: A nationwide study between 2010 and 2021. Journal of Medical Virology 2023; 95:e28490.

KASL-AASLD Joint Symposium 1 | DAY 2: May 30 (Fri.) | ROOM 1 [3F]

Biases, Challenges, and Innovations in RCT Statistics

Inkyung Jung *Yonsei University*

Randomized Controlled Trials (RCTs) are widely regarded as the gold standard for evaluating clinical interventions, offering methodological rigor through randomization, blinding, and control. However, both statistical and practical challenges limit their effectiveness in real-world clinical decision-making. Common misconceptions—such as assuming randomization eliminates all bias, or overinterpreting p-values as definitive proof of clinical relevance—persist among clinicians and researchers alike.

From a statistical perspective, RCTs face a range of technical hurdles: underpowered sample sizes, baseline imbalances despite randomization, inflated type I error due to multiplicity, and missing data that may threaten internal validity. Beyond statistics, traditional trial designs often lack generalizability, suffer from high screen failure rates, and encounter difficulties in patient recruitment and retention. These challenges are especially evident in hepatology research, where trials in conditions like non-alcoholic steatohepatitis (NASH) frequently span long durations with limited success, partly due to rigid inclusion criteria and reliance on invasive endpoints.

In response, innovative trial designs such as platform and pragmatic trials are gaining attention. Platform trials enable the evaluation of multiple therapies within a unified and adaptive framework, optimizing efficiency and resource use. Pragmatic trials embed research within routine clinical care, improving the applicability of findings to everyday practice. Case studies from recent hepatology trials—including the PRIORITIZE pragmatic trial in hepatitis C and emerging platform trials for NASH—illustrate how these models can overcome limitations of traditional designs.

This talk examines common biases, statistical challenges, and recent innovations in RCT design, with a focus on their implications for clinical research in hepatology.

Kris V. Kowdley

Washington State University, USA

Self Introduction

Prof. Kris V. Kowdley, is Director of Liver Institute Northwest and professor, Elson S. Floyd College of Medicine at Washington State University. He received his B.S. in Biology and Anthropology from Columbia University, and his medical degree from Mount Sinai School of Medicine. He completed his internship and residency at Oregon Health Science University and a Fellowship in Gastroenterology and Hepatology at Tufts University School of Medicine.

He is internationally recognized as a clinician, educator, and researcher in liver disease. He has led several major international clinical trials of new treatments for hepatitis C, primary biliary cholangitis, primary sclerosing cholangitis and nonalcoholic steatohepatitis.

He is the author of more than 1,000 articles, book chapters, reviews, abstracts and commentaries, and his scholarly work has been cited more than 75,000 times (h-index 125), according to Google Scholar. He is on the Web of Science list of "Highly Cited Researchers" (top 1% by citations for field) for 2019-2024.

Research Interests

MASH, Hepatic Iron Overload Disorders, Cholestatic Liver Disease, Chronic Viral Hepatitis

Representative Publications

1. Sanyal AJ, Chalasani N, Kowdley KV, McCullough A, Diehl AM, Bass NM, Neuschwander-Tetri BA, Lavine JE, Tonascia J, Unalp A, Van Natta M, Clark J, Brunt EM, Kleiner DE, Hoofnagle JH, Robuck PR; NASH CRN. Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. N Engl J Med. 2010 May 6;362(18):1675-85. doi: 10.1056/NEJMoa0907929. Epub 2010 Apr 28. PMID: 20427778; PMCID: PMC2928471.
2. Kowdley KV, Bowlus CL, Levy C, Akarca US, Alvares-da-Silva MR, Andreone P, Arrese M, Corpechot C, Francque SM, Heneghan MA, Invernizzi P, Jones D, Kruger FC, Lawitz E, Mayo MJ, Shiffman ML, Swain MG, Valera JM, Vargas V, Vierling JM, Villamil A, Addy C, Dietrich J, Germain JM, Mazain S, Rafailovic D, Taddé B, Miller B, Shu J, Zein CO, Schattenberg JM; ELATIVE Study Investigators' Group; ELATIVE Study Investigators' Group. Efficacy and Safety of Elafibranor in Primary Biliary Cholangitis. N Engl J Med. 2024 Feb 29;390(9):795-805. doi: 10.1056/NEJMoa2306185. Epub 2023 Nov 13. PMID: 37962077.
3. Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, Shiffman ML, Schiff E, Ghalib R, Ryan M, Rustgi V, Chojkier M, Herring R, Di Bisceglie AM, Pockros PJ, Subramanian GM, An D, Svarovskaia E, Hyland RH, Pang PS, Symonds WT, McHutchison JG, Muir AJ, Pound D, Fried MW; ION-3 Investigators. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med. 2014 May 15;370(20):1879-88. doi: 10.1056/NEJMoa1402355. Epub 2014 Apr 10. PMID: 24720702.
4. Kowdley KV, Lawitz E, Poordad F, Cohen DE, Nelson DR, Zeuzem S, Everson GT, Kwo P, Foster GR, Sulkowski MS, Xie W, Pilot-Matias T, Liossis G, Larsen L, Khatri A, Podsadecki T, Bernstein B. Phase 2b trial of interferon-free therapy for hepatitis C virus genotype 1. N Engl J Med. 2014 Jan 16;370(3):222-32. doi:10.1056/NEJMoa1306227. PMID: 24428468.
5. Kowdley KV, Modi NB, Peltekian K, Vierling JM, Ferris C, Valone FH, Gupta S. Rusfertide for the treatment of iron overload in HFE-related haemochromatosis: an open-label, multicentre, proof-of-concept phase 2 trial. Lancet Gastroenterol Hepatol. 2023 Dec;8(12):1118-1128. doi: 10.1016/S2468-1253(23)00250-9. Epub 2023 Oct 17. PMID: 37863080.

KASL-AASLD Joint Symposium 1 | DAY 2: May 30 (Fri.) | ROOM 1 [3F]

Successes and Failures in RCT: Insights from AASLD Experiences

Kris V. Kowdley *Washington State University, USA*

Recent years have shown results from several randomized controlled trials in hepatology, and the AASLD has been the venue for presentation of the results of several of these studies. One major success has been the development of all-oral, interferon free regimens for treatment of chronic hepatitis C. The first combination therapies of sofosbuvir, an NS5b nucleotide polymerase inhibitor and ledipasvir, an NS5a inhibitor, demonstrated that an 8-week regimen of this combination resulted in almost 99% likelihood of sustained virologic response in chronic hepatitis C genotypes 1, 3 and 4. Another combination of sofosbuvir and velpatasvar, a different NS5a inhibitor showed similar efficacy across all HCV genotypes. Similarly, the combination of Glecaprevir, an NS3/4 protease inhibitor and pibrentasvir, an NS5a inhibitor has similar efficacy against HCV genotypes.

Major advances have also been made in the treatment of chronic cholestatic liver disease. UDCA was approved for treatment of primary biliary cholangitis (PBC) in 1997 in the USA and obeticholic acid, an FXR-agonist was approved as second-line treatment in 2016. This marked the first approval of a therapy for non-viral liver disease using an endpoint of improvement in serum alkaline phosphatase and bilirubin as a surrogate for improvement in clinical outcomes for PBC. In 2024, elafibranor and seladelpar, both PPAR agonists were both approved as second-line therapies for PBC in the USA. However, obeticholic acid failed to demonstrate efficacy with regard to improved clinical outcomes compared to placebo in the confirmatory COBALT trail. Therefore, obeticholic acid remains with only conditional approval in the USA and full approval of this medication will require demonstration of improvement in rates of end-stage liver disease, liver transplantation or complications of liver disease.

Treatment of metabolic dysfunction-related steatohepatitis (MASH) remains a major challenge as this disease affects 12-18 million Americans and has become a leading indication of liver transplantation in the USA. Resmetirom was approved for treatment of MASH in 2024 and several GLP1 agonists (semaglutide, tirzapetide) have shown promising results in resolution of MASH and improvement of fibrosis. Recently the ESSENCE Phase 3 trial also showed positive results for semaglutide in MASH.

The major challenge in clinical trials in chronic liver disease is the difficulty in showing clinical benefit based on "hard endpoints" such as liver transplantation or complications of liver disease given the long natural history of liver disease and the challenges of conducting trials where it may be difficult to determine the differences between drug toxicity and progression of underlying liver disease. Several liver diseases such as primary sclerosing cholangitis are sufficiently rare with heterogenous natural history making design and conduct of clinical trials more challenging.

Young-Suk Lim

University of Ulsan

Self Introduction

Prof. Young-Suk Lim currently serves as the Dean of the University of Ulsan College of Medicine and is a Professor in the Department of Gastroenterology, Asan Medical Center, South Korea. Prof. Lim is the President Elect of the Korean Association for the Study of the Liver (KASL) for the term spanning December 2025 to November 2027.

He served as the Director of the Clinical Trial Center at Asan Medical Center from April 2015 to June 2019.

Prof. Lim completed his medical degree at Seoul National University College of Medicine in 1992 and obtained his PhD from the same institution in 2002. He completed the Clinical Research Training Program at the Mayo Clinic in Rochester, Minnesota, USA, in 2008.

He received the First Leading Research Achievement Award from the Korean Association for the Study of the Liver (KASL) in 2023. Prof. Lim has been commended by the Ministry of Health and Welfare of the Korean Government on three occasions (2017, 2020, and 2022). In 2018, he was named Professor of the Year at the University of Ulsan and was also the recipient of the Academic Achievement Award from the Alumni Association of Internal Medicine at Seoul National University Hospital.

His primary research interests lie in hepatitis B and hepatocellular carcinoma. His work has been published in the world's esteemed medical journals, including Lancet Gastroenterology & Hepatology, JAMA Oncology, Gastroenterology, Journal of Hepatology, Gut, and Hepatology.

Research Interests

Prof. Lim's research interests include hepatitis B and hepatocellular carcinoma. He has published many articles in many prestigious international medical journals including Lancet Gastroenterology & Hepatology, JAMA Oncology, Gastroenterology, Journal of Hepatology, Gut, and Hepatology.

Representative Publications

1. Lim YS, Yu ML, Choi J, Chen CY, Choi WM, Kang W, et al. Early Antiviral Treatment with Tenofovir Alafenamide to Prevent Serious Clinical Adverse Events in Chronic Hepatitis B Patients with High Viremia: Interim Results from the ATTENTION Randomised Controlled Trial. Lancet Gastroenterol Hepatol. Accepted. In press.
2. Kim GA, Lim YS, Han S, Choi GH, Choi WM, Choi J, et al. Viral Load-Based Prediction of Hepatocellular Carcinoma Risk in Noncirrhotic Patients with Chronic Hepatitis B: A Multinational Study for the Development and External Validation of a New Prognostic Model. Ann Intern Med 2024:ePub ahead of print. PMID: 39284185, DOI: 10.7326/M24-0384.
3. Choi WM, Kim GA, Choi J, Choi GH, Lee YB, Sinn DH, Lim YS, et al. Non-linear association of baseline viral load with on-treatment hepatocellular carcinoma risk in chronic hepatitis B. Gut. 2023;73(4):649-65. PMID: 37813567.
4. Choi WM, Yip TC, Wong GLH, Kim WR, Yee LJ, Brooks-Rooney C, Curteis T, and Lim YS, et al. Hepatocellular carcinoma risk in patients with chronic hepatitis B receiving tenofovir-vs. entecavir-based regimens: individual patient data meta-analysis. J Hepatol 2023;78:534-542.
5. Lim YS, Gwak GY, Choi J, Lee YS, Byun KS, Kim YJ, Yoo BC, Kwon SY, Lee HC. Monotherapy with Tenofovir Disoproxil Fumarate for Adefovir-Resistant vs. Entecavir-Resistant Chronic Hepatitis B: a 5-Year clinical trial. J Hepatol 2019;71:35-44. PMID: 30876946.

Successes and Failures in RCT: Insights from KASL Experiences

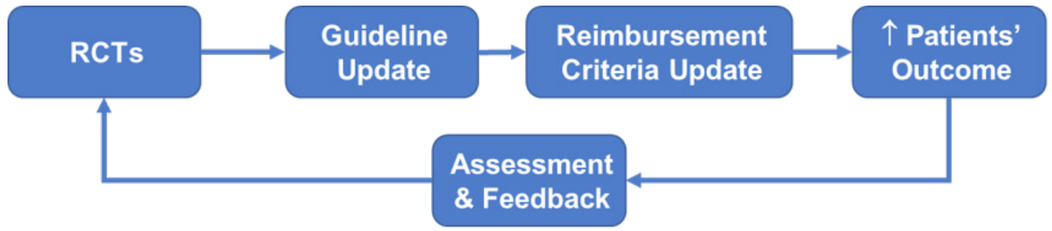
Young-Suk Lim *University of Ulsan*

Randomized controlled trials (RCTs) are widely regarded as the gold standard for evaluating the relationship between an intervention, exposure, or risk factor and an outcome. A defining feature of RCTs is randomization, which ensures that the groups being compared are balanced in all respects, apart from chance differences. This process minimizes biases by making the treatment and control groups equivalent in all characteristics except for the treatment assignment. When randomization is executed properly, any difference observed in outcomes can be confidently attributed to the intervention itself.

The key distinction between RCTs (experimental studies) and observational studies (non-experimental studies) lies in the random allocation of interventions, which is absent in the latter. While RCTs inherently control for biases and confounders through randomization, observational studies do not automatically address these issues. Consequently, observational studies may exhibit significant differences in both observed and unobserved participant characteristics between treatment and control groups, leading to biased estimates of treatment effects. Bias and confounding are particularly pronounced in case-control studies and, to a lesser extent, in cohort studies. These issues can either create false associations between intervention and outcome or mask true differences that exist. To establish causality in observational studies, researchers must carefully consider and account for alternative explanations.

RCTs, however, require substantial financial, temporal, and logistical resources. Therefore, it is critical for researchers to thoroughly review prior observational studies related to their topic before designing an RCT. Observational study can provide valuable insights that help shape the hypothesis, refine study design, and optimize resource allocation for RCTs.

By offering the highest level of evidence, RCTs play a pivotal role in informing updates to clinical practice guidelines and determining reimbursement criteria by healthcare insurance systems. Recent RCTs conducted in Korea have achieved notable success, demonstrating the country's growing contribution to global clinical research.[1-12]



References

1. Lim YS, Yu ML, Choi J, et al. Early Antiviral Treatment with Tenofovir Alafenamide to Prevent Serious Clinical Adverse Events in Chronic Hepatitis B Patients with High Viremia: Interim Results from the ATTENTION Randomised Controlled Trial. Lancet Gastroenterol Hepatol 2025;In press.
2. Choi J, Lim YS, Kim JH, et al. Tenofovir Alafenamide for Multiple Drug-Resistant Chronic Hepatitis B: A 3-Year Clinical Trial. Clin Gastroenterol Hepatol 2023;21:3185-3187.
3. Byun KS, Choi J, Kim JH, et al. Tenofovir Alafenamide for Drug-Resistant Hepatitis B: A Randomized Trial for Switching From Tenofovir Disoproxil Fumarate. Clin Gastroenterol Hepatol 2022;20:427-437 e425.
4. Lim YS, Gwak GY, Choi J, et al. Monotherapy with tenofovir disoproxil fumarate for adefovir-resistant vs. entecavir-resistant chronic hepatitis B: A 5-year clinical trial. J Hepatol 2019;71:35-44.
5. Yoon SM, Ryoo BY, Lee SJ, et al. Efficacy and Safety of Transarterial Chemoembolization Plus External Beam Radiotherapy vs Sorafenib in Hepatocellular Carcinoma With Macroscopic Vascular Invasion: A Randomized Clinical Trial. JAMA Oncol 2018;4:661-669.
6. Lim YS, Lee YS, Gwak GY, et al. Monotherapy with tenofovir disoproxil fumarate for multiple drug-resistant chronic hepatitis B: 3-year trial. Hepatology 2017;66:772-783.
7. Kim SY, An J, Lim YS, et al. MRI With Liver-Specific Contrast for Surveillance of Patients With Cirrhosis at High Risk of Hepatocellular Carcinoma. JAMA Oncol 2017;3:456-463.
8. An J, Lim YS, Kim GA, et al. Telbivudine versus entecavir in patients with undetectable hepatitis B virus DNA: a randomized trial. BMC Gastroenterol 2017;17:15.
9. Lim YS, Yoo BC, Byun KS, et al. Tenofovir monotherapy versus tenofovir and entecavir combination therapy in adefovir-resistant chronic hepatitis B patients with multiple drug failure: results of a randomised trial. Gut 2016;65:1042-1051.
10. Lim YS, Byun KS, Yoo BC, et al. Tenofovir monotherapy versus tenofovir and entecavir combination therapy in patients with entecavir-resistant chronic hepatitis B with multiple drug failure: results of a randomised trial. Gut 2016;65:852-860.
11. Lim YS, Lee JY, Lee D, et al. Randomized trial of the virologic response during up to two years of entecavir-adefovir combination therapy in multiple-drug-refractory chronic hepatitis B virus patients. Antimicrob Agents Chemother 2013;57:3369-3374.
12. Lim YS, Lee JY, Lee D, et al. Randomized trial of entecavir plus adefovir in patients with lamivudine-resistant chronic hepatitis B who show suboptimal response to lamivudine plus adefovir. Antimicrob Agents Chemother 2012;56:2941-2947.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

State-of-the-Art Lecture

Chair:

Masao Omata (The Univ. of Tokyo, Japan)

Chun-Jen Liu

National Taiwan University, Taiwan

Self Introduction

Prof. Chun-Jen LIU is a Professor at the Department of Internal Medicine, and Director of the Hepatitis Research Center, Clinical Trial Center, and Division of Gastroenterology & Hepatology, National Taiwan University College of Medicine and Hospital. He achieved his MD and PhD at the National Taiwan University. He has been actively involved in clinical trials for the treatment of various liver diseases, and delivered the JGH Foundation Emerging Leader Lecture in APDW 2013.

Recently, he received NTUH outstanding Research Award 2022. He is now the President of the Taiwan Association for the Study of the Liver, and the associate editor of the Journal of the Formosan Medical Association and Journal of Microbiology, Immunology and Infection. He has authored 400 papers in international peer-reviewed journals.

Research Interests

Prof. LIU's interests include chronic hepatitis B and C, HCC, and metabolic dysfunction-associated steatotic liver disease (MASLD), where his studies focus on the role of treatment and trial interventions for chronic viral hepatitis, MASLD and HCC.

Representative Publications

1. Liu CJ, Chuang WL, Sheen IS, et al. Efficacy of ledipasvir and Sofosbuvir Treatment of HCV Infection in Patients Coinfected with HBV. Gastroenterology 2018;154:989-997.
2. Liu CJ, Chuang WL, Lee CM, et al. Peginterferon alfa-2a plus ribavirin for the treatment of dual chronic infection with hepatitis C and B viruses. Gastroenterology 2009;136:496-504.
3. Liu CJ, Lee PH, Lin DY, et al. Heparanase inhibitor PI-88 as adjuvant therapy for hepatocellular carcinoma after curative resection: A randomized phase II trial for safety and dose-finding. J Hepatol 2009;50:958-968.
4. Liu CJ, Lo SC, Kao JH, et al. Transmission of occult hepatitis B virus by transfusion to adult and pediatric recipients in Taiwan. J Hepatol 2006;44:39-46.
5. Liu CJ, Chen PJ, Lai MY, et al. A prospective study characterizing full-length hepatitis B virus genomes during acute exacerbation. Gastroenterology 2003;124:80-90.

Hepatitis B Virus with Co-Existing Liver Diseases: The Interactions between Viral Hepatitis C, MAFLD, and Hepatitis B Virus

Chun-Jen Liu *National Taiwan University, Taiwan*

Viral hepatitis due to chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection and metabolic dysfunction-associated fatty liver disease (MAFLD) are common liver diseases worldwide. Therefore, in clinical practice, we may encounter subjects with dual etiology of liver diseases such as co-existing HBV/HCV and MAFLD/HBV. In my presentation, the clinical features and mutual interactions of HBV with co-existing HCV will be reviewed first. From the experience of these interactions between HBV and HCV, the impact of MAFLD on the clinical presentations of liver diseases and treatment outcomes in patients with chronic viral hepatitis B, and the clinical questions to be addressed regarding dual etiology will be discussed.

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May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

KASL Symposium 2

The Immunological Horizon Towards Curing Viral Hepatitis and Beyond

Chairs:

Chun-Jen Liu (National Taiwan Univ., Taiwan)
Sang Hoon Ahn (Yonsei Univ.)

Won-Mook Choi

University of Ulsan

Self Introduction

Prof. Won-Mook Choi is an Assistant Professor of the Department of Gastroenterology, Asan Medical Center

He graduated from Seoul National University College of Medicine with his medical degree in 2010 and graduated from KAIST with his PhD degree in 2019. He completed his internship and residency at the Department of Internal Medicine at Seoul National University Hospital in 2015 and completed his fellowship at the Department of Gastroenterology at Asan Medical Center in 2021.

Since 2022, he has held several roles, including Scientific Committee Member and Assistant Director of the Medical Policy Committee of the Korean Association for the Study of the Liver (2024–), as well as Member of the Publication and Planning Committees of the Korean Liver Cancer Association (2024–).

Research Interests

Chronic Hepatitis B, Hepatocellular Carcinoma, Portal Hypertension

Representative Publications

1. Heo S, Yang J, Park J, Hui RW, Song BG, Song IH, Yoon YI, Cheung TT, Chung SW, Choi J, Lee D, Shim JH, Kim KM, Lim YS, Lee HC, Seto WK, Lee JH, Choi WM (corresponding). Association Between Viral Replication Activity and Postoperative Recurrence of HBV-Related Hepatocellular Carcinoma. Aliment Pharmacol Ther. 2025 Mar 16. doi: 10.1111/apt.70085. Online ahead of print.
2. Chung SW, Um HJ, Choi WM (corresponding), Choi J, Lee D, Shim JH, Kim KM, Lim YS, Lee HC. Tenofovir is associated with a better prognosis than entecavir for hepatitis B virus-related hepatocellular carcinoma. Clin Gastroenterol Hepatol. 2025 Feb;23(2):300-309.e9.
3. Choi WM (first), Yip TC, Kim WR, Yee LJ, Brooks-Rooney C, Curteis T, Clark LJ, Jafry Z, Chen CH, Chen CY, Huang YH, Jin YJ, Jun DW, Kim JW, Park NH, Peng CY, Shin HP, Shin JW, Yang YH, Wong GL, Lim YS. Chronic Hepatitis B baseline viral load and on-treatment liver cancer risk: A multinational cohort study of HBeAg-Positive patients. Hepatology. 2024 Aug 1;80(2):428-439.
4. Choi WM (first), Kim GA, Choi J, Choi GH, Lee YB, Sinn DH, Lim YS. Non-linear association of baseline viral load with on-treatment hepatocellular carcinoma risk in chronic hepatitis B. Gut. 2024 Mar 7;73(4):649-658.
5. Choi WM (first), Kim GA, Choi J, Han S, Lim YS. Increasing on-treatment hepatocellular carcinoma risk with decreasing baseline viral load in HBeAg-positive chronic hepatitis B. J Clin Invest. 2022 May 16;132(10):e154833.

KASL Symposium 2 | DAY 2: May 30 (Fri.) | ROOM 1 [3F]

Pipelines for Curing Hepatitis B Using Immunological Targets: Successes and Failures

Won-Mook Choi *University of Ulsan*

Hepatitis B virus (HBV) is among the oldest known human pathogens, with viral sequences found in Neolithic human remains over 7,000 years old. This long coadaptation with the human host has shaped HBV into a virus that is uniquely adept at evading immune responses, which in turn makes chronic HBV infection particularly resistant to cure. When acquired in adulthood, HBV infection typically induces robust adaptive immune responses, resulting in self-limited acute hepatitis and life-long immunity in over 95% of cases. In contrast, perinatal or early childhood infections often lead to immune tolerance and lifelong chronic infection. This tolerance is driven, in part, by the overwhelming presence of non-infectious subviral particles composed of HBsAg, which outnumber infectious virions by more than 1,000-fold and contribute to immune exhaustion. These features highlight the need for immune-restorative therapies in HBV cure strategies.

While the ideal endpoint of sterilizing cure—complete elimination of both cccDNA and integrated HBV DNA—remains beyond reach with current technology, functional cure has emerged as a more realistic and clinically meaningful goal. Functional cure is defined as sustained (≥24 weeks off-treatment) loss of HBsAg and undetectable HBV DNA, with or without anti-HBs seroconversion. This outcome is associated with significant reductions in risks for cirrhosis, hepatocellular carcinoma, and liver-related mortality. Recently, a partial cure defined by sustained HBsAg levels <100 IU/mL has also gained acceptance as an intermediate milestone. Approved therapies—nucleos(t)ide analogues (NUCs) and pegylated interferon-alpha (Peg-IFN-α)—are effective at suppressing viral replication but rarely achieve functional cure. NUCs such as entecavir and tenofovir provide long-term viral suppression and have excellent safety profiles, but they have no effect on cccDNA or integrated HBV DNA, and thus require lifelong administration. HBsAg clearance with NUC monotherapy is observed in only 2–5% of patients even after a decade of treatment. Peg-IFN-α offers the possibility of finite treatment but is limited by poor tolerability and low response rates, particularly in Asian patients who predominantly carry non-genotype A HBV.

Novel therapies for HBV cure fall into two major categories: virus-targeting agents and immunomodulators. While many antiviral agents—such as siRNAs, capsid assembly modulators (CAMs), and entry inhibitors—have shown promising reductions in HBV DNA and HBsAg, they are unlikely to achieve sustained

immune control as monotherapy. Thus, immunomodulatory approaches are gaining traction as the potential keystone of future HBV cure strategies. Immunotherapies aim to restore or stimulate HBV-specific immune responses. Key strategies include: 1) **Checkpoint Inhibitors** (e.g., anti-PD1/PDL1 such as envafolimab, nivolumab): These agents have demonstrated HBsAg reductions particularly in patients with low baseline HBsAg levels, 2) **Therapeutic Vaccines** (e.g., VTP-300, BRII-179): Designed to induce HBV-specific T-cell responses; their standalone efficacy is modest, but they may enhance responses in combination regimens, and 3) **Toll-Like Receptor Agonists** (e.g., TLR7/8 agonists such as selgantolimod and ruzotolimod): These stimulate innate immunity but have shown limited impact on HBsAg levels in clinical trials.

To date, most immune-based approaches have not produced high rates of HBsAg seroclearance. Multiple challenges remain: HBV-specific T-cell exhaustion, persistence of HBsAg production from integrated DNA, and variable responses by genotype and ethnicity. Additionally, ALT flares and virologic relapse following treatment withdrawal remain safety concerns. While combinations of siRNA with Peg-IFN-α or immune modulators have shown synergistic effects, they require further validation in larger trials with long-term follow-up. Future HBV cure strategies must integrate virologic suppression with immune reconstitution. This will require: 1) **Immunologic profiling and patient stratification:** Treatment decisions should be informed by baseline HBsAg levels, HBV genotype, and T-cell exhaustion markers, 2) **Rational combination regimens:** Pairing RNAi agents or CAMs with immune stimulators such as therapeutic vaccines or checkpoint inhibitors may offer the most promise, and 3) **Development of novel immunomodulators:** Next-generation agents must induce durable, antigen-specific T-cell responses and overcome existing barriers of immune exhaustion and tolerance. Equally important will be the identification of robust immunologic biomarkers to monitor response and guide treatment cessation criteria.

HBV is a master of immune evasion, shaped by millennia of coevolution with humans. While functional cure remains rare with current therapies, it is now an attainable goal thanks to advances in antiviral and immune-based therapies. The future of HBV cure lies not in a single "magic bullet," but in combination approaches that suppress viral replication while reawakening host immunity. The development of innovative immunomodulators will be central to this effort.

References

1. Rehermann B. Toward a better understanding of chronic hepatitis B virus infection. J Clin Invest. 2024 Oct 1;134(19):e185568.
2. Fung S, Choi HSJ, Gehring A, Janssen HLA. Getting to HBV cure: The promising paths forward. Hepatology. 2022 Jul;76(1):233-250.
3. Hui RW, Mak LY, Fung J, Seto WK, Yuen MF. Prospect of emerging treatments for hepatitis B virus functional cure. Clin Mol Hepatol. 2025 Feb;31(Suppl):S165-181.
4. Gopalakrishna H, Ghany MG. Perspective on Emerging Therapies to Achieve Functional Cure of Chronic Hepatitis B. Curr Hepatol Rep. 2024 Jun;23(2):241-252.
5. Lok ASF. Toward a Functional Cure for Hepatitis B. Gut Liver. 2024 Jul 15;18(4):593-601.
6. Mak LY, Boettler T, Gill US. HBV Biomarkers and Their Role in Guiding Treatment Decisions. Semin Liver Dis. 2024 Nov;44(4):474-491.
7. Iannacone M, Guidotti LG. Immunobiology and pathogenesis of hepatitis B virus infection. Nat Rev Immunol. 2022 Jan;22(1):19-32.

Loey Lung-Yi Mak

The University of Hong Kong, Hong Kong

Self Introduction

Prof. Mak received primary medical education at The University of Hong Kong and completed specialty training in year 2018 in Queen Mary Hospital Hong Kong as a gastroenterologist and hepatologist. She joined the academic faculty in year 2020 and obtained the degree of Doctor of Medicine in the field of clinical liver diseases in year 2021. She has published more than 160 peer-reviewed articles in reputable journals, with >80 being first-authored/ co-first/ corresponding authored articles, highlights including publications in Journal of Hepatology, Gut, Clinical Molecular Hepatology, and Hepatology. She is an Honorary Research Fellow of The Centre for Immunology and Infectious Diseases, Blizard Institute, Queen Mary University of London since Jan 2022 to conduct research in the field of HBV immunology, and received the Croucher Fellowship for post-doctoral research. Her research group focuses on host-viral interactions in chronic hepatitis B infection. She also led the hepatitis C virus micro-elimination efforts in Hong Kong, and pioneered such strategy in persons under custody in correctional facilities. She also established the Specialty Out-Patient Clinic for Steatotic Liver Disease in Queen Mary Hospital.

She was the recipient of The Emerging Leader Award by The European Association for the Study of Liver, which is a yearly award specifically dedicated to young fellows and will be given to 2-3 young scholars. She was the Finalist for The Rising Star Award, EMMS International's inaugural Global Women in Healthcare Awards in association with the Royal College of Physicians of Edinburgh in 2024.

Research Interests

Clinical Liver Diseases in the Field of Chronic Viral Hepatitis and Steatotic Liver Disease

Representative Publications

1. Mak LY, Anderson M, Stec M, et al Longitudinal profile of plasma pregenomic RNA in patients with chronic hepatitis B infection on long-term nucleoside analogues and its interaction with clinical parameters. Clin Mol Hepatol 2024 in press
2. Mak LY, Wooddell CI, Lenz O, et al. Long-term hepatitis B surface antigen response after finite treatment of ARC-520 or JNJ-3989. Gut 2025; 74: 440-450
3. Mak LY, Cloherty G, Wong DKH, et al. HBV RNA profiles in chronic hepatitis B patients under different disease phases and anti-viral therapy. Hepatology 2021; 73:2169-2179.
4. Mak LY, Wong DKH, Pollicino T, et al. Occult hepatitis B infection and hepatocellular carcinoma: epidemiology, virology, hepatocarcinogenesis and clinical significance. J Hepatol 2020; 73:952-64.
5. Mak LY, Hui RWH, Fung J, et al. Diverse effects of hepatic steatosis on fibrosis progression and functional cure in virologically quiescent chronic hepatitis B. J Hepatol 2020; 73:800-806.

Targeting Innate Immunity as a Promising Approaches for Curing Hepatitis B

Loey Lung-Yi Mak *The University of Hong Kong, Hong Kong*

Chronic hepatitis B infection is characterized by dysfunction of the host immune system. The innate immunity, being the first line of defence to combat pathogens, is perturbed by hepatitis B virus in various aspects contributing to chronicity and liver damage. Failure to mount an adequate antiviral response at initial phase of infection, along with suppressive mechanisms on downstream adaptive immune response are central to the mechanisms of HBV pathogenesis. Key players include Kupffer cell, monocytes, NK cells and myeloid-derived suppressor cells. The adaptive immune effectors also bear innate-like properties.

As the current therapy cannot cure HBV, novel approaches for curing hepatitis B have been explored including strategies to alleviate the dysfunctional innate effectors. Among many, the three main mechanisms explored are toll-like receptors, retinoic acid-inducible-gene-I signaling, and interferon pathways. The data from the clinical trials showed induction of immune response that may or may not be accompanied by significant reduction in HBsAg levels, indicating the need to combine with virus-directing agents to optimize the potential of these strategies. As the innate effectors are enriched in the intrahepatic compartment, clinical trials should consider evaluation of the liver alongside with peripheral blood to elucidate the mechanism of action for novel agents.

References

1. Maini MK & Gehring AJ. J Hepatol 2016
2. Morikawa K et al. Ann Transl Med 2016
3. Yuen MF et al. Nat Review Dis Primers 2018
4. Janssen HLA et al. J Hepatol 2018
5. Janssen HLA et al. JHep Reports 2024
6. Gill US et al. Gut 2018

Markus Cornberg

Hannover Medical School, Germany

Self Introduction

Prof. Markus Cornberg is a Professor of Infectious Diseases with a focus on Hepatology and Deputy Director of the Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology at Hannover Medical School, Germany. Since 2019, he has also served as Clinical Director at the Helmholtz Centre for Infection Research and Director of the Centre for Individualized Infection Medicine (CIIM).

He is the Medical Executive Director of the German Liver Foundation. He has been leading the development of the German clinical guidelines for the management of hepatitis B virus (HBV) infection since 2007 and currently serves as the coordinator (panel chair) of the EASL Clinical Practice Guidelines for HBV infection.

From 2017 to 2020, he was a member of the Scientific Committee and the Governing Board of the European Association for the Study of the Liver (EASL). He was Associate Editor of the Journal of Hepatology (2019–2024) and has been serving as Associate Editor of Hepatology since 2024.

Research Interests

Prof. Cornberg basic science research focus is the investigation of cellular immune responses for disease progression and treatment response in patients with viral hepatitis. He has published >400 original scientific papers as well as review articles.

Representative Publications

1. Urbanek-Quaing M, Chou YH, Gupta MK, Steppich K, Bremer B, Schmaus H, Deterding K, Maasoumy B, Wedemeyer H, Xu CJ, Kraft ARM, Cornberg M. Enhancing HBV-specific T cell responses through a combination of epigenetic modulation and immune checkpoint inhibition. Hepatology. 2024 Dec 19. doi: 10.1097/HEP.0000000000001202.
2. Wedemeyer H, Aleman S, Brunetto MR, Blank A, Andreone P, Bogomolov P, Chulanov V, Mamonova N, Geyvandova N, Morozov V, Sagalova O, Stepanova T, Berger A, Manuilov D, Suri V, An Q, Da B, Flaherty J, Osinusi A, Liu Y, Merle U, Schulze Zur Wiesch J, Zeuzem S, Ciesek S, Cornberg M, Lampertico P; MYR 301 Study Group. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. N Engl J Med. 2023 Jul 6;389(1):22-32. doi: 10.1056/NEJMoa2213429.
3. Aliabadi E, Urbanek-Quaing M, Maasoumy B, Bremer B, Grasshoff M, Li Y, Niehaus CE, Wedemeyer H, Kraft ARM, Cornberg M. Impact of HBsAg and HBcrAg levels on phenotype and function of HBV-specific T cells in patients with chronic hepatitis B virus infection. Gut. 2022 Nov;71(11):2300-2312. doi: 10.1136/gutjnl-2021-324646.
4. Cornberg M, Lok AS, Terrault NA, Zoulim F; 2019 EASL-AASLD HBV Treatment Endpoints Conference Faculty. Guidance for design and endpoints of clinical trials in chronic hepatitis B - Report from the 2019 EASL-AASLD HBV Treatment Endpoints Conference. J Hepatol. 2020 Mar;72(3):539-557. doi: 10.1016/j.jhep.2019.11.003.
5. Rinker F, Zimmer CL, Höner Zu Siederdissen C, Manns MP, Kraft ARM, Wedemeyer H, Björkström NK, Cornberg M. Hepatitis B virus-specific T cell responses after stopping nucleos(t)ide analogue therapy in HBeAg-negative chronic hepatitis B. J Hepatol. 2018 Sep;69(3):584-593. doi: 10.1016/j.jhep.2018.05.004.

Targeting Adaptive Immunity as a Promising Approaches for Curing Hepatitis B

Markus Cornberg *Hannover Medical School, Germany*

Tatsuya Kanto

Japan Institute for Health Security, Japan

Self Introduction

Tatsuya Kanto is a researcher and hepatologist/physician with expertise in immunology in liver diseases. He got PhD degree at Osaka University and worked as a research associate for dendritic cell biology at the University of Pittsburgh, USA, from 1998 to 2001. He worked as an Associate Professor at Osaka University from 2003 to 2013 and moved to the National Center for Global Health and Medicine (NCGM). His current position is Director General at the Research Center for Hepatitis and Immunology, Japan Institute for Health Security (JIHS).

He has been working with the Ministry of Health, Labor, and Welfare to promote the Hepatitis Action Plan in Japan. His field of interest is the exploration of the pathogenesis of liver disease for the development of immune-based therapy against viral hepatitis, liver cirrhosis, and cancer. He has published more than 260 papers and invited review articles in peer-reviewed journals, such as Hepatology, Journal of Hepatology, Immunity, Journal of Immunology and Gastroenterology.

Research Interests

- Immunopathogenesis of Viral Hepatitis, MASLD/MASH, and Liver Cancer
- Development of Immune Modulators for the Treatment of Chronic HBV Infection
- Establishment of Therapeutic Strategy for Congestive Liver Disease, such as FALD
- Promotion of Hepatitis Countermeasures in Japan

Representative Publications

1. Shigeno S, Kodama T, Murai K, Motooka D, Fukushima A, Nishio A, Hikita H, Tatsumi T, Okamoto T, Kanto T, Takehara T. Intrahepatic exhausted antiviral immunity in immunocompetent mouse model of chronic hepatitis B. Cell Mol Gastroenterol Hepatol. 2025;19(1):101412 doi: 10.1016/j.jcmgh.2024.101412.
2. Kogiso T, Tokuhara D, Ohfuji S, Tanaka A, Kanto T. Evaluation of diagnostic criteria for mild-to-advanced stages of Fontan-associated liver disease: A nationwide epidemiological survey in Japan. Hepatol Res 2025;55:611-621.
3. Mino M, Kakazu E, Sano A, Tsuruoka M, Matsubara H, Kakisaka K, Kogure T, Sekine K, Aoki Y, Imamura M, Matsuda M, Yamazoe T, Mori T, Yoshio S, Inoue J, Masamune A, Kanto T. Comprehensive analysis of peripheral blood free amino acids in MASLD: the impact of glycine-serine-threonine metabolism. Amino Acids. 2024 Dec 24;57(1):3. doi: 10.1007/s00726-024-03433-2.PMID: 39718621
4. Mori T, Yoshio S, Kakazu E, Kanto T. Active role of the immune system in metabolic dysfunction-associated steatotic liver disease. Gastroenterol Rep (Oxf). 2024 Oct 15;12:goae089. doi: 10.1093/gastro/goae089. eCollection 2024. PMID: 39411101
5. Takeuchi Y, Nozawa A, Yukimoto A, Kitsuka M, Tateishi R, Kioke K, Okano K, Kanto T. Integrated policy of medical expense subsidies and clinical registry for patients with liver cancer and decompensated cirrhosis in Japan. Hepatol Res. 2024;54(8):745-752.

Development of a Novel Immune Modulator SA-5 as a Therapeutic Option for Chronic Hepatitis B

Tatsuya Kanto *Japan Institute for Health Security, Japan*

An effective method of eliminating HBV cccDNA is the elimination of HBV-infected hepatocytes by immune cells. The cure rate in adults with acute HBV infection is 95%, whereas the cure rate in patients with chronic hepatitis is markedly lower. Comparative analysis of the immune response between the two pathologies is important for obtaining a functional cure. We analyzed cured cases of acute hepatitis B and showed that the tryptophan-metabolizing enzyme indoleamine-2,3-dioxygenase (IDO) is highly expressed during the onset of hepatitis and is involved in early inhibition of HBV replication.[1] We also found that induction of chemokines such as CXCL9 and IL-21 was important in achieving HBsAg negativity in patients with acute hepatitis B, and chronic hepatitis B treated with sequential therapy (NUC and Peg-IFN-α).[2] IL-21 is produced by follicular helper T cells (Tfh) and is involved in the maturation of B cells into antibody-producing cells, and the functional improvement of HBV-specific $CD8^+$ T cells.

Various new drugs are under development to achieve a functional cure in patients with chronic hepatitis B. In addition to drugs targeting molecules involved in HBV entry and replication, immune modulators that activate the immune system are being intensively developed. The results of the Phase-II study of a TLR7 agonist (GS-9620, GS) in patients with chronic hepatitis B were reported, but the HBsAg reduction was insufficient. This is thought to be partly because effective doses could not be administered due to safety concerns.

We are developing a novel TLR7 agonist (SA-5) with enhanced in vivo targeting to the liver. In vitro, SA-5 stimulates pDCs capacity to induce IL-21-producing Tfh and B cells to produce anti-HBs antibody.[3] To clarify the in vivo anti-HBV activity, SA-5 was administered to HBV model mice with preserved immune systems. HBsAg transgenic mice were treated with SA-5 once a week for 4-8 weeks. As a result, the HBsAg-positive hepatocyte rate decreased to 40-50% of the GS-treated group. The frequency of HBsAg-specific IFN-γ-producing cells was significantly increased in the treated group. A novel HBV mouse model in which mouse hepatocytes were replaced by FAH-HBV-expressing hepatocytes using the SB-transposon system was established to investigate the effect of SA-5. Short-term administration of SA-5 caused a transient increase in ALT, and HBV DNA and HBV pgRNA were significantly reduced. Compared to the control IFN-α-treated group, ISG expression was increased in the SA-5-treated group, the cytotoxic activity of intrahepatic NK cells and $CD8^+$ T cells was stronger, and intrahepatic T cells were

differentiated into effector memory T cells.[4] These results indicate that SA-5 exerts not only activating innate immunity but also adaptive immunity. Furthermore, SA-5 treatment of cynomolgus monkeys showed a stronger and safer ability to induce ISG than the control GS-treated group. For the immune monitoring of patients with chronic hepatitis B, we developed a highly sensitive method to detect multifunctional HBs, HBV pol, and HBV core-specific $CD8^+$ T cells.[5] We are in the process of regulatory approval and aim to start an investigator/physician-initiated FIH study of SA-5 in 1Q of 2026. In this presentation, I will discuss the status of the development of immune modulators, including SA-5, against chronic hepatitis B and a possible combination of novel drugs for future HBV therapy.

References

1. S. Yoshio, M. Sugiyama, H. Shoji, Y. Mano, E. Mita, T. Okamoto, Y. Matsuura, A. Okuno, O. Takikawa, M. Mizokami, T. Kanto, Indoleamine-2 , 3-dioxygenase as an effector and an indicator of protective immune responses in patients with acute hepatitis B. Hepatology 63, 83–94 (2016).
2. S. Yoshio, Y. Mano, H. Doi, H. Shoji, T. Shimagaki, Y. Sakamoto, H. Kawai, M. Matsuda, T. Mori, Y. Osawa, M. Korenaga, M. Sugiyama, M. Mizokami, E. Mita, K. Katayama, J. Tanaka, T. Kanto, Cytokine and chemokine signatures associated with hepatitis B surface antigen loss in hepatitis B patients. JCI Insight 3(20):e12268 (2018).
3. T. Mori, S. Yoshio, S. Yoshikawa, Y. Tsustui, T. Sakata, Y. Yoshida, Y. Sakamoto, H. Kawai, Y. Osawa, T. Yamazoe, Y. Aoki, S. P. Fletcher, T. Kanto, Toll-like receptor 7 agonist, GS-986, is an immune-stimulant inducing follicular helper T cells and expanding HBs antigen-specific B cells in vitro. Liver Int. 43;1213-1224 (2023).
4. S. Shigeno, T. Kodama, K. Murai, D. Motooka, A. Fukushima, A. Nishio, H. Hikita, T. Tatsumi, T. Okamoto, T. Kanto, T. Takehara, Intrahepatic exhausted antiviral immunity in an immunocompetent mouse model of chronic hepatitis B. Cell. Mol. Gastroenterol. Hepatol., 19:101412 (2024).
5. S. Takahama, S. Yoshio, Y. Masuta, H. Murakami, R. Sakamori, S. Kaneko, T. Honda, M. Murakawa, M. Sugiyama, M. Kurosaki, Y. Asahina, T. Takehara, V. Appay, T. Kanto, T. Yamamoto, Hepatitis B surface antigen reduction is associated with hepatitis B core-specific CD8+ T cell quality. Front. Immunol. 14:1257113 (2023).

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

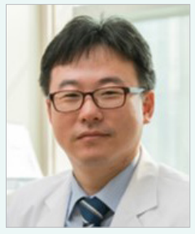
DAY 2: May 30 (Fri.)

KASL-KAHBPS-KLCA-KLTS Joint Symposium

Multidisciplinary Practices to Prevent Hepatocellular Carcinoma Occurrence and Recurrence

Chairs:

Tae Hun Kim (Ewha Womans Univ.)
Dong-Hwan Jung (Univ. of Ulsan)



Jeong Han Kim

Konkuk University

Self Introduction

Education

2021.03-Present	Professor, Konkuk University School of Medicine, Konkuk University Medical Center
2017.03-2018.02	Visiting Postdoctoral Scientist, Cedars-Sinai Medical Center, Los Angeles, CA, USA
2016.03-2021.02	Associate Professor, Konkuk University School of Medicine, Konkuk University Medical Center
2012.03-2016.02	Assistant Professor, Konkuk University School of Medicine, Konkuk University Medical Center
2011.03-2012.02	Clinical Assistant Professor, Konkuk University School of Medicine, Konkuk University Medical Center
2008.03-2011.02	Clinical Assistant Professor, Korea University Medical Center, Ansan Hospital
2007.03-2009.08	Korea University, College of Medicine, Ph.D.
2002.03-2004.02	Korea University, College of Medicine, Master
1993.03-1999.02	Korea University, College of Medicine, bachelor

Professional Experience

2023.01	International Liver Cancer Association, Member
2023.01	American Association for the Study of Liver Diseases, Regular Member
2021.01	The European Association for the Study of the Liver, Regular Member
2011.02	Asian Pacific Association of the Study of the Liver, Regular Member
2009.11	The Korean Association of the Study of the Liver
2009.01	The Korean Liver Cancer Association

Research Interests

Liver Cirrhosis, Fatty Liver, Alcoholic Liver Disease, Hepatocellular Carcinoma, Viral Hepatitis

Representative Publications

1. Global epidemiology of acute kidney injury in hospitalised patients with decompensated cirrhosis: the International Club of Ascites GLOBAL AKI prospective, multicentre, cohort study. Lancet Gastroenterol Hepatol 2025 Online first
2. Model for end-stage liver disease-3.0 vs. model for end-stage liver disease-sodium: mortality prediction in Korea. Korean J Intern Med. 2024 Mar;39(2):248-260
3. Diagnosis of Autoimmune Hepatitis. Korean J Gastroenterol 2023;81(2):66-71
4. Switching from Tenofovir-Based Combination Therapy to Tenofovir Monotherapy in Multidrug-Experienced Chronic Hepatitis B Patients: a 5-Year Experience at Two Centers. Antimicrob Agents Chemother 2022;66(8):e0027522
5. Changing Trends in Liver Cirrhosis Etiology and Severity in Korea: the Increasing Impact of Alcohol. J Korean Med Sci. 2021;36(21)e145

Etiology-Based Primary Prevention Strategies for Hepatocellular Carcinoma

Jeong Han Kim *Konkuk University*

Liver cancer is the third leading cause of cancer-related deaths globally, with incident cases expected to rise from 905,700 in 2020 to 1.4 million by 2040. Hepatocellular carcinoma (HCC) accounts for about 80% of all primary liver cancers. Viral hepatitis and chronic excessive alcohol consumption are major risk factors for HCC, but metabolic dysfunction-associated steatotic liver disease is also becoming a dominant cause. The increasing numbers of cases of HCC and changes in risk factors highlight the urgent need to for updated and targeted prevention strategies.

We will review current evidence on etiology-specific interventions, emphasizing primary, secondary, and tertiary prevention approaches tailored to the underlying risk factors.

Viral Hepatitis-Related Hepatocellular Carcinoma

Hepatitis B Virus (HBV)

HBV infection is associated with increased risk of HCC, especially in patients who are treatment-naïve, male and of older age, and those with a high HBV DNA level, core promoter mutations, cirrhosis or metabolic syndrome. The widespread adoption of the HBV vaccine and long-term nucleoside-nucleotide analogue therapy has reduced the incidence of HBV-associated HCC.

Primary Prevention: Universal HBV vaccination is the cornerstone of prevention. In Taiwan, the introduction of routine infant vaccination in 1984 reduced childhood HCC incidence by 70% within two decades. Several population-based cohort studies have shown that immunization against HBV significantly reduces prevalence of HBV infection and might reduce HCC risk.

Secondary Prevention: Antiviral therapies such as tenofovir and entecavir suppress viral replication, reducing HCC risk by 50-70% in cirrhotic patients. Long-term nucleoside analogue therapy lowers HBV DNA levels, mitigating fibrosis progression and hepatocyte dysplasia. Regular surveillance with ultrasound and alpha-fetoprotein (AFP) testing is critical for early detection in high-risk cohorts.

Tertiary Prevention: A meta-analysis of 20 studies of HBV treatment following liver resection of HCC demonstrated a reduced risk of recurrence. A study including 850 patients from Taiwan treated with ablation for HCC showed a reduction in HCC recurrence in patients treated with nucleoside analogues.

Hepatitis C Virus (HCV)

HCV-related HCC arises from chronic inflammation, insulin resistance, and viral protein interactions with host oncogenes.

Primary Prevention: While no HCV vaccine exists, harm reduction strategies—such as sterile needle programs and blood product screening—have reduced transmission rates by 80% in industrialized nations.

Secondary Prevention: Direct-acting antivirals (DAAs) that can achieve sustained virological response (SVR) against chronic HCV infection have decreased HCC risk by 70% and lowered the 5-year mortality in patients with HCC by 63%. However, cirrhotic patients remain at residual risk (1.5-3% annually post-SVR), necessitating ongoing surveillance.

Tertiary Prevention: The current evidence indicates a 50-78% reduction in the risk of HCC in patients with cirrhosis and 70-80% risk reduction in those without cirrhosis.

Metabolic and Lifestyle-Associated Hepatocellular Carcinoma

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and Metabolic Dysfunction-Associated Steatohepatitis (MASH)

MASLD-related HCC is rising globally, driven by obesity and metabolic syndrome. Up to 20% of MASLD patients progress to MASH, with annual HCC incidence of 1.5-2.6% in cirrhotic stages.

Primary Prevention: Weight reduction through caloric restriction and moderate exercise (≥150 minutes/week) reduces hepatic steatosis and inflammation. A 7-10% body weight loss reverses fibrosis in 60% of early MASH cases. Dietary interventions, such as the Mediterranean diet rich in monounsaturated fats and antioxidants, lower HCC risk by 30%.

Secondary Prevention: Pharmacotherapy targeting insulin resistance—metformin and pioglitazone—reduces HCC incidence by 40% in diabetic MASLD patients. Statins modulate the RAS/RAF/MEK pathway, decreasing hepatocyte proliferation and dysplasia.

Surveillance Challenges: Unlike viral hepatitis, MASLD-related HCC often arises in non-cirrhotic livers. Current guidelines recommend ultrasound screening for cirrhotic patients, but emerging biomarkers like PNPLA3 rs738409 polymorphisms may refine risk stratification in pre-cirrhotic cohorts.

Alcohol-Related Liver Disease (ALD)

Alcohol cessation is considered an essential strategy in HCC prevention as it decreases the risk of liver disease progression while mitigating the hepatocarcinogenic effect of alcohol. Although no supporting evidence from an RCT is available, a meta-analysis indicated that abstaining from alcohol is associated with 6-7% annual risk reduction of developing HCC for former drinkers.

Primary Prevention: Public health policies limiting alcohol availability—taxation, minimum unit pricing,

appear to have the most impact on reducing alcohol-related harm, including cirrhosis, in a UK population.

Secondary Prevention: Early fibrosis detection through transient elastography (FibroScan) enables targeted interventions. Abstinence for ≥2 years regresses fibrosis in 30% of compensated cirrhotics, lowering HCC risk to baseline.

Conclusion

Etiology-specific HCC prevention requires a multipronged approach: vaccination and antivirals for viral hepatitis, lifestyle and metabolic interventions for MASLD, and public health measures against aflatoxins and alcohol. However, global disparities in resource allocation persist, underscoring the need for equitable implementation of cost-effective interventions like HBV vaccination and aflatoxin control. Future research must address residual HCC risk in cured HCV and MASLD populations, optimizing surveillance protocols and novel therapeutics.

Min-Su Park

Kyung Hee University

Self Introduction

Educational

2013.2 Ph.D. Degree, College of Medicine, Kyung Hee University, Seoul, South Korea
2008.2 M.S. Degree, College of Medicine, Kyung Hee University, Seoul, South Korea
2003.2 M.D. Degree, College of Medicine, Kyung Hee University, Seoul, South Korea

Professional Experience

2023.9-Present Professor, Division of Hepatobiliary Surgery and Organ Transplantation
Department of Surgery, Kyung Hee University Medical Center, Seoul, South Korea
2018.9-2023.8 Associate Professor, Division of Hepatobiliary Surgery and Organ Transplantation
Department of Surgery, Kyung Hee University Medical Center, Seoul, South Korea
2014.9-2018.8 Assistant Professor, Division of Hepatobiliary Surgery and Organ Transplantation
Department of Surgery, Kyung Hee University Medical Center, Seoul, South Korea

Research Interests

- HCC Biomarker
- HCC Prognosis Predictive Model
- Ischemic-Reperfusion Injury Prevention

Representative Publications

1. Optimal tailored screening protocol after living donor liver transplantation for hepatocellular carcinoma, J Korean Med Sci. 2014.
2. Living-donor liver transplantation associated with higher incidence of hepatocellular carcinoma recurrence than deceased-donor liver transplantation. Transpl. 2014.
3. Hesperidin Ameliorates Hepatic Ischemia-Reperfusion Injury in Sprague-Dawley Rats Trasnpl. Proc 2019.

KASL-KAHBPS-KLCA-KLTS Joint Symposium | DAY 2: May 30 (Fri.) | ROOM 1 [3F]

Post-Resection Monitoring and Predictors for Hepatocellular Carcinoma Recurrence

Min-Su Park *Kyung Hee University*

Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality worldwide, with a high rate of recurrence even after curative resection. Effective post-resection surveillance and identification of reliable predictors of recurrence are critical components in improving long-term outcomes. This presentation explores the multidisciplinary approaches for post-resection monitoring and discusses current evidence on risk stratification and recurrence predictors.

Surveillance protocols typically include dynamic contrast-enhanced imaging and serial alpha-fetoprotein (AFP) measurements, but emerging biomarkers such as circulating tumor DNA (ctDNA), microRNAs, and inflammation-based scores are gaining prominence. Additionally, tumor-related factors (e.g., size, microvascular invasion, poor differentiation), liver function parameters, and host immune status are integrated into modern risk assessment models. Artificial intelligence and machine learning-based algorithms have also been introduced to enhance prediction accuracy. Furthermore, the role of antiviral therapy in patients with HBV or HCV-related HCC, and the impact of metabolic dysfunction-associated steatotic liver disease (MASLD) on recurrence patterns, are evaluated.

Through a multidisciplinary lens—encompassing hepatology, oncology, radiology, pathology, and surgery—this session underscores the importance of individualized surveillance strategies and risk-adapted interventions to prevent recurrence. Ultimately, the integration of novel biomarkers and predictive models into clinical practice holds promise for more precise, proactive post-resection management of HCC.

Hye Won Lee

Yonsei University

Self Introduction

Prof. Hye Won Lee graduated from Ewha Womans University College of Medicine and received her Ph.D. degree from Yonsei University College of Medicine. She completed her residency and fellowship at Severance hospital, where she continues to work as an Associate Professor at Yonsei University College of Medicine.

She visited the Chinese University of Hong Kong as a vising scholar for two years. She has continued to conduct her research on chronic liver disease, especially NASH and HBV. She has won several awards and grants from various institutions and academies. She is recognized as one of the outstanding young physicians in Korea.

Research Interests

Hepatocellular Carcinoma
Chronic Liver Disease Including NASH and Viral Hepatitis

Representative Publications

1. Kim DH, Kim EM, Lee JS, Kim MN, Kim BK, Kim SU, Park JY, Choi GH, Ahn SH, Lee HW, Kim DY. Cytokine-Induced Killer Cell Immunotherapy Reduces Recurrence in Patients with Early-Stage Hepatocellular Carcinoma. Cancers (Basel). 2025 Feb 7;17(4):566
2. Park K, Lee HW, Kim E, Choi WM, Lee D, Shim JH, Kim KM, Lim YS, Lee HC, Yoo C, Ryoo BY, Han S, Choi J. Risk of Variceal Bleeding in Patients Receiving Atezolizumab-Bevacizumab Treatment for Hepatocellular Carcinoma. Aliment Pharmacol Ther. 2025 Jan 28. doi: 10.1111/apt.18526
3. Yoo HJ, Kim JY, Yoo JJ, Lee HW, Kim SG, Kim YS. Lower incidence of hepatocellular carcinoma with tenofovir alafenamide in chronic hepatitis B: Evidence from a large-scale cohort. JHEP Rep . 2024 Nov 12;7(2):101268. doi: 10.1016/j.jhepr.2024.10126
4. H Lin, HW Lee, TCF Yip, E Tsochatzis, S Petta, et al. Vibration-controlled transient Elastography scores to predict liver-related events in Steatotic liver disease. JAMA. 2024 Mar 21:e241447.
5. Lee HW, Park S, Park HJ, Cho KJ, Kim DY, Hwang B, Park JY. T-Cell Dynamics Predicts Prognosis of Patients with Hepatocellular Carcinoma Receiving Atezolizumab Plus Bevacizumab. Int J Mol Sci. 2024 Oct 11;25(20):10958

Diagnosis and Multidisciplinary Management of Recurrent Hepatocellular Carcinoma after Hepatectomy

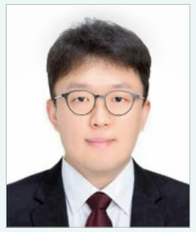
Hye Won Lee *Yonsei University*

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related death worldwide. While surgical resection provides a curative option for early-stage HCC, recurrence remains a major challenge, with up to 70% of patients experiencing relapse within five years. Recurrent HCC (rHCC) is typically classified as early or late based on timing, and as intrahepatic metastasis or multicentric recurrence based on pathogenesis. These classifications carry different prognostic implications and influence subsequent therapeutic strategies. Advances in imaging techniques, such as gadoxetic acid-enhanced MRI and contrast-enhanced ultrasound, have improved the early detection of recurrence. In addition, liquid biopsy techniques including circulating tumor DNA (ctDNA) are being explored as sensitive, non-invasive surveillance tools.

The management of rHCC requires a multidisciplinary approach involving hepatologists, surgeons, radiologists, and oncologists. Treatment options include repeat hepatectomy, salvage liver transplantation, and various locoregional therapies such as radiofrequency ablation (RFA), transarterial chemoembolization (TACE), and stereotactic body radiotherapy (SBRT). Salvage liver transplantation offers a curative option for selected patients with preserved liver function and recurrent tumors meeting transplant criteria. For patients with advanced-stage recurrence or limited treatment tolerance, systemic therapies including tyrosine kinase inhibitors and immune checkpoint inhibitors may be considered. Therapeutic decisions are guided by liver function, tumor burden, prior interventions, and validated risk stratification tools such as the modified UICC stage, ALBI grade, and FIB-4 index.

Recent efforts have focused on refining risk prediction and improving patient selection for treatment. Prognostic models that integrate clinical, imaging, and molecular factors are gaining traction in clinical practice. Moreover, emerging evidence from clinical trials suggests that adjuvant or perioperative immunotherapy may reduce recurrence risk in patients with high-risk features after resection. These developments underscore the potential value of incorporating biomarker-based strategies and immune modulation into the current treatment paradigm.

Future perspectives in the management of rHCC include the use of patient-derived organoid platforms for individualized drug testing, radiogenomic analysis to predict recurrence patterns, and artificial intelligence–driven tools to support decision-making. Together, these innovations aim to personalize and improve the care of patients with rHCC. Continued advancements in diagnostic, therapeutic, and predictive technologies are expected to enhance long-term outcomes in this challenging clinical context.



Seok-Hwan Kim

Chungnam National University

Self Introduction

Education

2006	Doctor of Medicine Chungnam National University School of Medicine
2009	M.S. in Medicine Chungnam National University Graduate School
2017	Ph.D. in Medicine Ulsan University Graduate School

Professional Experience

2014-2017	Clinical Instructor, Ulsan University College of Medicine, Asan Medical Center
2018-2022	Assistant Professor Chungnam National University School of Medicine
2023-Present	Associate Professor Chungnam National University School of Medicine
2023-Present	Vice dean for Research Chungnam National University School of Medicine

Professional Organizations

2023-Present	Director of the informatics board, Korean Society for Liver Transplantation
2022-Present	Clinical Trial Committee, Korean Society of Surgical Oncology
2021-Present	Research Committee, Korean Association of HBP Surgery
2021-Present	Education Committee, Korean Association of HBP Surgery
2021-Present	Scientific program and research Committee, Korean Society for Transplantation
2021-Present	Insurance Committee, Korean Society for Transplantation
2022-2024	Vice Secretary General, Korean Association of HBP Surgery
2021-2023	Liaison Committee, Korean Association of HBP Surgery
2021-2023	Research Committee, Korean Liver Transplantation Society
2020-2022	Editorial Committee, Korean Society of Surgical Metabolism and Nutrition

Representative Publications

1. Association of Survival with Radiologic-Pathologic Discordance in Patients with Hepatocellular Carcinoma: A Nationwide Cohort Study Based on the Primary Liver Cancer Registry in Korea Gut and Liver 2025
2. Establishment of a chronic biliary disease mouse model with cholecystoduodenal anastomosis for intestinal microbiome preservation World Journal of Gastroenterology 2024
3. Comprehensive effects of fecal microbiota transplantation on cynomolgus macaques across various fecal conditions Frontiers in Microbiology 2024
4. CX3CR1+ macrophages interact with hepatic stellate cells to promote hepatocellular carcinoma through CD8+ T cell suppression Hepatology 2024
5. Enhanced Expression of Glycolytic Enzymes and Succinate Dehydrogenase Complex Flavoprotein Subunit A by Mesothelin Promotes Glycolysis and Mitochondrial Respiration in Myeloblasts of Acute Myeloid Leukemia International Journal of Molecular Science 2024

Criteria and Workups for Liver Transplant Eligibility in Recipients Focus on Hepatocellular Carcinoma Patients

Seok-Hwan Kim *Chungnam National University*

Background

Liver transplantation is a life-saving treatment for patients with end-stage liver disease and hepatocellular carcinoma (HCC). Due to the limited supply of donor organs, strict selection criteria and thorough pre-transplant evaluation are essential to maximize outcomes and ensure fair allocation.

Aim

This presentation reviews the latest criteria and comprehensive workups for determining liver transplant eligibility, focusing on HCC patients and strategies to prevent tumor occurrence and recurrence.

Methods

Reviewing current international guidelines and recent literature emphasized general and HCC-specific eligibility criteria. The multidisciplinary evaluation process is summarized, including imaging, laboratory, cardiovascular, and psychosocial assessments.

General Eligibility Criteria

For non-HCC patients, the Model for End-Stage Liver Disease (MELD) score remains the primary tool for prioritization. The MELD score ranges from 6 to 40 and is calculated based on serum bilirubin, serum creatinine, and INR (International Normalized Ratio). It predicts mortality risk within three months, allowing clinicians to prioritize patients with the highest urgency.

HCC-Specific Eligibility Criteria

For HCC patients, the Milan criteria (single tumor ≤5cm or up to 3 tumors ≤3cm without vascular invasion) are widely used. These criteria have been shown to provide excellent post-transplant outcomes, with a recurrence rate of less than 10%. However, expanded criteria such as UCSF (University of California, San Francisco) and up-to-seven criteria are being considered in selected cases. UCSF criteria include a single tumor up to 6.5 cm or up to five tumors with a total diameter of 8 cm, while the up-to-seven criteria involve tumors with a total diameter of up to 7 cm without vascular invasion.

Pre-Transplant Evaluation

A thorough pre-transplant workup is crucial in determining eligibility and minimizing risks. This includes:

- Imaging: Dynamic CT or MRI assesses tumor size, number, and vascular invasion.
- Tumor Marker Evaluation: To evaluate tumor biology, alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) are measured.
- Viral Serology: Hepatitis B and C status are determined to guide antiviral therapy before and after transplantation.
- Cardiopulmonary Testing: Assessments such as echocardiography and pulmonary function tests evaluate the patient's cardiovascular and respiratory status.
- Psychosocial Assessment: Evaluations by social workers and psychologists determine the patient's ability to adhere to post-transplant care and support systems.

For HCC patients, additional considerations include response to locoregional therapy (such as radiofrequency ablation or transarterial chemoembolization) and downstaging protocols for those initially outside standard criteria. These strategies aim to reduce tumor burden and improve eligibility for transplantation.

Recent Advances

Recent molecular markers and imaging advances have significantly improved risk stratification and candidate selection. Molecular profiling of tumors can identify high-risk features, guiding decisions on eligibility and post-transplant surveillance. Enhanced imaging techniques, including functional MRI and PET scans, provide detailed information on tumor biology and response to therapy.

Future Directions

Future directions include the adoption of molecular profiling and artificial intelligence to personalize transplant candidate selection and management further. Artificial intelligence algorithms can analyze large datasets to predict outcomes and optimize selection criteria. This transformative approach balances urgency, benefit, and equity in liver transplantation.

Conclusion

Determining liver transplant eligibility requires a multidisciplinary approach that balances urgency, benefit, and equity. Continuous refinement of selection criteria and evaluation protocols is vital to improve outcomes and reduce HCC recurrence. The integration of molecular profiling and artificial intelligence promises to personalize candidate selection, enhancing the success rates of liver transplantation for patients with end-stage liver disease and HCC.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

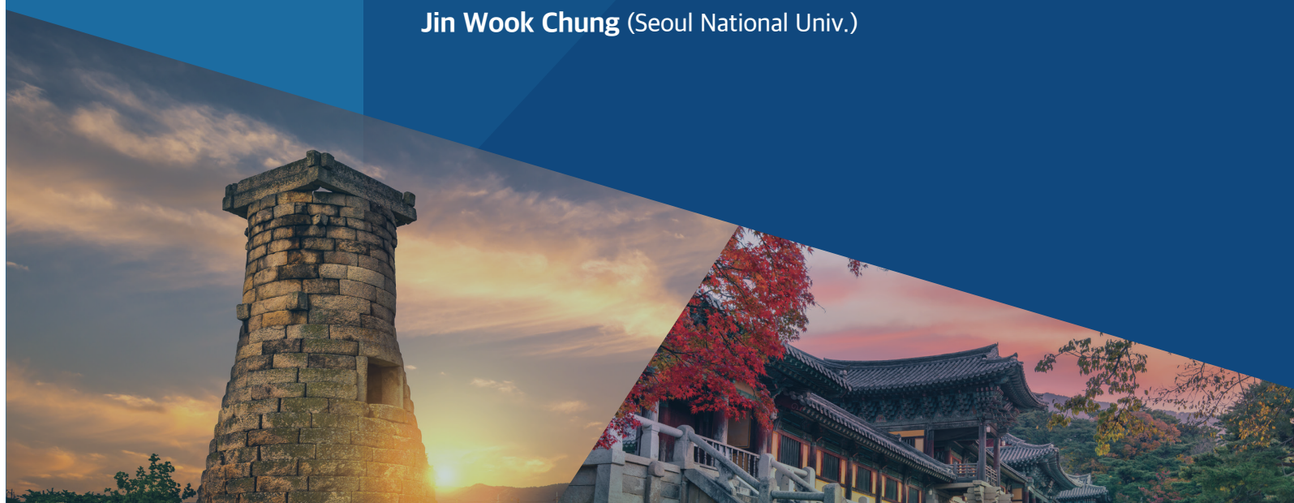
DAY 2: May 30 (Fri.)

KLCA Symposium 1

Evolving Epidemiology and Advancing Surveillance of Hepatocellular Carcinoma

Chairs:

Joong-Won Park (Myoungji Hospital, Hanyang Univ.)
Jin Wook Chung (Seoul National Univ.)



Han Ah Lee

Chung-Ang University

Self Introduction

Prof. Han Ah Lee is an assistant professor in the Department of Internal Medicine at Chung-Ang University College of Medicine, specializing in hepatology.

She graduated from Korea University College of Medicine and earned her Ph.D. in 2018.

She has been actively involved in both clinical practice and research. She currently serves as an associate editor of Clinical and Molecular Hepatology, contributing to the advancement of liver disease research and publication.

Research Interests

Metabolic Dysfunction-Associated Steatotic Liver Disease, Hepatitis B Virus, Hepatocellular Carcinoma

Representative Publications

1. A machine learning model to predict liver-related outcomes after the functional cure of chronic hepatitis B. (J Hepatol. 2025)
2. Metabolic Dysfunction-Associated Steatotic Liver Disease and Risk of Cardiovascular Disease: A Nationwide Cohort Study (Gut. 2024)
3. Identification of patients with favorable prognosis after resection in intermediate-stage hepatocellular carcinoma. (Int J Surg. 2024)
4. Non-invasive prediction of post-sustained virological response hepatocellular carcinoma in hepatitis C virus: A systematic review and meta-analysis. (Clin Mol Hepatol. 2024)
5. Assessment of the postoperative prognosis in patients with hepatocellular carcinoma using vibration-controlled transient elastography: A systemic review and meta-analysis. (Clin Mol Hepatol. 2024)

Trends from the Nationwide Cancer Registry

Han Ah Lee *Chung-Ang University*

The Korean Nationwide Cancer Registry, led by the Korea Central Cancer Registry (KCCR), provides comprehensive, population-based data on cancer incidence, mortality, survival, and treatment trends. This registry serves as a critical resource for understanding the evolving cancer burden in Korea, informing national cancer control strategies, and facilitating international comparisons.

Overall Cancer Trends in Korea

In 2023, Korea is projected to see 273,076 new cancer cases and 81,818 cancer deaths. The most common cancer sites are expected to be the lung, thyroid, breast, colon and rectum, and stomach, collectively accounting for about half of the national cancer burden.[1] Lung cancer remains the leading cause of cancer death, followed by liver, colorectal, pancreatic, and gallbladder cancers. Age-standardized incidence rates for all cancers are gradually decreasing, reflecting the impact of national screening programs and improved public health measures. However, cancer remains a leading cause of morbidity and mortality, and the absolute number of cases is expected to rise due to population aging

Liver Cancer (Hepatocellular Carcinoma, HCC) in Korea

Liver cancer, predominantly hepatocellular carcinoma (HCC), poses a substantial health challenge in Korea. In 2020, there were approximately 10,565 new HCC cases annually, with an incidence rate of 30 per 100,000 individuals.[2] HCC is the second leading cause of cancer-related death in Korea, reflecting both its high incidence and poor prognosis.

Registry and Data Collection

The KCCR, established in 1999, is a legally mandated, nationwide registry that captures nearly all incident and survival data for major cancers, including HCC. However, early registry data were limited in clinical detail, especially regarding cancer staging and treatment modalities. To address these gaps, since 2010, the KCCR and the Korean Liver Cancer Association (KLCA) have jointly implemented a systematic, two-stage sampling approach for the Korean Primary Liver Cancer Registry (KPLCR). Each year, approximately 10–15% of newly diagnosed HCC patients are randomly selected from the KCCR database, ensuring unbiased, nationally representative data collection. Trained personnel extract detailed

clinical information from medical records, which is then validated by expert clinicians and de-identified before being made available for research. This methodology overcomes the selection bias inherent in voluntary registries and complies with Korea's strict privacy regulations

Epidemiological Features

Analysis of the KPLCR data reveals important trends in HCC epidemiology and management in Korea. In 2015, the median age of HCC patients was 61 years, with 80% being male. Hepatitis B virus (HBV) infection remained the predominant etiology (58%), but the proportion of non-viral causes—such as alcohol and metabolic dysfunction-associated steatotic liver disease (MASLD)—has steadily increased.[3] At diagnosis, 45% of patients were at a very early or early stage (BCLC 0/A), but 39% were already at an advanced stage (BCLC C). The most common initial treatment was transarterial therapy (32%), followed by surgical resection (23%), best supportive care (20%), and local ablation therapy (11%). Only 35% of patients received potentially curative treatments. Adherence to BCLC guideline-recommended therapies was 34.5% overall, with lower rates in intermediate and advanced stages. The 5-year overall survival rate was 27%, with better outcomes for those diagnosed early and receiving curative treatment. The most recent data from 2016–2018 show further shifts. The median age at diagnosis increased to 63 years, and the proportion of non-viral etiologies continued to rise, while HBV-related HCC declined to 55.7%.[4] The proportion of patients with preserved liver function (Child-Turcotte-Pugh class A) increased to 74.8%. Early-stage diagnosis (BCLC 0/A) accounted for 43.7% of cases, but nearly 40% were still diagnosed at advanced stages. Initial treatment patterns evolved, with surgical resection rates rising to 25% and the use of drug-eluting bead TACE increasing. Systemic therapy was still limited, but expected to rise with the introduction of new agents. The 5-year overall survival rate improved to 44.3%, reflecting advances in early detection and treatment. However, guideline adherence remained suboptimal (43.2%), and more than half of HCC cases were still diagnosed at advanced stages, especially among elderly and non-viral etiology patients

Treatment Patterns

There has been a notable shift in initial treatment patterns for HCC in Korea. Surgical resection rates have increased, particularly laparoscopic procedures, which rose from 10.6% to 60.6% among surgical cases. Systemic therapy utilization has grown, with novel agents like atezolizumab-bevacizumab becoming the most widely used by 2022. Transarterial therapy (e.g., TACE) remains common but has decreased in relative frequency. Best supportive care has declined, reflecting improved access to active treatments. These changes are influenced by advances in clinical research, evolving reimbursement policies, and the adoption of new therapeutic options

Conclusion

The Korean nationwide cancer and HCC registries have become essential tools for tracking epidemiological trends, evaluating treatment patterns, and assessing outcomes at the population level. Continued efforts to enhance surveillance, tailor management for high-risk groups, and adapt to changing disease patterns will be crucial for further improving HCC outcomes in Korea.

References

1. Jung KW, Kang MJ, Park EH, Yun EH, Kim HJ, Kong HJ, Im JS, Seo HG. Prediction of Cancer Incidence and Mortality in Korea, 2023. Cancer Res Treat. 2023 Apr;55(2):400-407.
2. Kim BH, Yun EH, Lee JH, Hong G, Park JY, Shim JH, Kim E, Kong HJ, Jung KW, Lim YS. Advancing Korean nationwide registry for hepatocellular carcinoma: a systematic sampling approach utilizing the Korea Central Cancer Registry database. J Liver Cancer. 2024 Mar;24(1):57-61.
3. Yoon JS, Lee HA, Kim HY, Sinn DH, Lee DH, Hong SK, Cho JY, Choi J, Chang Y, Kong HJ, Kim E, Won YJ, Lee JH. Hepatocellular Carcinoma in Korea: an Analysis of the 2015 Korean Nationwide Cancer Registry. J Liver Cancer. 2021 Mar;21(1):58-68.
4. An J, Chang Y, Choi GH, Sohn W, Song JE, Shin H, Yoon JH, Yoon JS, Jang HY, Cho EJ, Han JW, Hong SK, Cho JY, Jung KW, Park EH, Kim E, Kim BH. Hepatocellular carcinoma in Korea: an analysis of the 2016-2018 Korean Nationwide Cancer Registry. J Liver Cancer. 2025 Mar;25(1):109-122.

Young Eun Chon

CHA University

Self Introduction

Prof. Young Eun Chon, currently asociate professor in CHA University.

Education

Bachelor's Degree, Yonsei University
Master's Degree Yonsei University
Doctoral Degree (Ph.D.), Yonsei University

Professional Experience

KASL Academic Secretary
KASL Insurance Commissioner

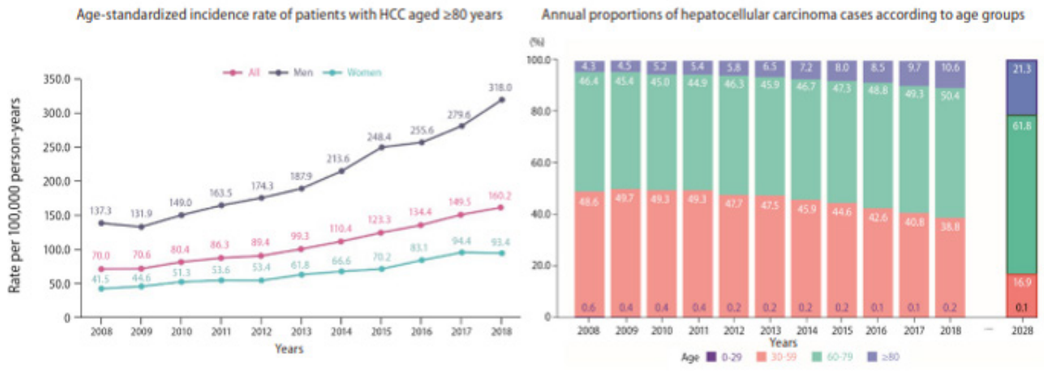
Research Interests

HCC, MASLD, HBV

Future Trends in Hepatocellular Carcinoma in Korea

Young Eun Chon *CHA University*

We aim to examine the changes in the epidemiology of hepatocellular carcinoma (HCC) in South Korea, including incidence rates, underlying diseases, and treatment methods, based on the National Health Insurance Service (NHIS) data from 2008 to 2018. First, the incidence of HCC in Korea gradually declined, however, the incidence of HCC in the elderly (patients aged ≥80 years) increased significantly (age-standardized incidence rate increased by 0.96% per year). Second, the HCC related to hepatitis B virus and hepatitis C virus is decreasing, whereas HCC attributable to alcohol and metabolic dysfunction associated steatotic liver disease is increasing. Presence of metabolic associated co-morbid diseases in HCC including type 2 diabetes mellitus, chronic kidney disease, hypertension, cardiovascular disease, cerebrovascular disease is increasing. As for primary treatment for HCC, the proportion of transarterial therapy is decreasing, whereas surgical resection, local ablation therapy, and systemic therapy are increasing. Understanding the changes in the epidemiology of HCC as it allows us to anticipate how the incidence, diagnosis, and treatment of HCC may evolve in the future, and to prepare effective interventions for vulnerable patients at risk.



Hyuk Soo Eun

Chungnam National University

Self Introduction

Prof. Hyuk Soo Eun is an Associate Professor of the Department of Internal Medicine, Chungnam National University College of Medicine.

He graduated from Chungnam National University College of Medicine with his medical degree in 2007 and completed his internship and residency at the Department of Internal Medicine at Chungnam National University Hospital.

He earned his Ph.D. in Medical Science from KAIST (Korea Advanced Institute of Science and Technology). He subsequently completed a fellowship in Gastroenterology at Chungnam National University Hospital, where he later served as a Clinical Assistant Professor and then now serve as an Associate Professor.

Since 2020, he has been serving as a member of the Scientific Committee of the Korean Association for the Study of the Liver (KASL) and as an editorial board member of the Korean Liver Cancer Association (KLCA).

Research Interests

- Molecular Mechanism of HCC Development , Liquid Biopsy for HCC
- Clinical Study of NAFLD, HCC, Autoimmune Hepatitis and Primary Biliary Cholangitis

Representative Publications

1. Rou WS, Jeon HJ, Eun HS, Lee HS, Park JH, Joo JS, Kim JS, Lee ES, Kim SH, Lee JE, Shin KS, Kim SH, Yeo MK, Lee JM, Kwon IS, Lee BS. Association of Survival with Radiologic-Pathologic Discordance in Patients with Hepatocellular Carcinoma: A Nationwide Cohort Study Based on the Primary Liver Cancer Registry in Korea. Gut Liver. 2025 Apr 1. doi: 10.5009/gnl240393. (Co-Corresponding author)
2. Jong-Min Jeong, Sung Eun Choi, Young-Ri Shim, Hee-Hoon Kim, Young-Sun Lee, Keungmo Yang, Kyurae Kim, Min Jeong Kim, Katherine Po Sin Chung, Seok-Hwan Kim, Jin-Seok Byun, Hyuk Soo Eun, Won-Il Jeong. CX3CR1+ macrophages interact with hepatic stellate cells to promote hepatocellular carcinoma through CD8+ T cell suppression Hepatology. 2024 Jul 19. doi: 10.1097/HEP (Co-Corresponding author)
3. Yujin Jeong, Seunghwan Noh, Minsang Yu, Sung-pil Chang, Hyuksoo Eun, Jinchul Kim, Youngjun Song. Liquid Metal Electrodynamic Accumulation Microfluidics System for DNA Memory and Liquid Biopsy. Adv. Func. Mater. 2023. https://doi.org/10.1002/adfm.202305680 (Co-Corresponding author)
4. Jeon HJ, Eun HS, Kwon IS, Lee BS, Lee ES, Rou WS, Sung JK, Moon HS, Kang SH, Lee HS et al: Outcomes of laparoscopic radiofrequency ablation versus percutaneous radiofrequency ablation for hepatocellular carcinoma. Surg Endosc 2023. (Co-First author)
5. Rou WS, Eun HS, Choung S, Jeon HJ, Joo JS, Kang SH, Lee ES, Kim SH, Kwon IS, Ku BJ et al: Prognostic Value of Erythroblastic Leukemia Viral Oncogene Homolog 2 and Neuregulin 4 in Hepatocellular Carcinoma. Cancers (Basel) 2023, 15(9). (Co-First author)

KLCA Symposium 1 | DAY 2: May 30 (Fri.) | ROOM 2 [3F]

Imaging and Beyond: Expanding Hepatocellular Carcinoma Surveillance Modalities

Hyuk Soo Eun *Chungnam National University*

The global landscape of hepatocellular carcinoma (HCC) is undergoing a profound transformation, driven by changing epidemiological trends and rapid advancements in surveillance technologies. Traditionally, chronic viral hepatitis B and C were the predominant causes of HCC; however, the rising prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD, formerly NAFLD) and its progressive form, metabolic dysfunction-associated steatohepatitis (MASH), is reshaping the at-risk population. Notably, a substantial proportion of HCC now arises in non-cirrhotic livers, particularly among patients with metabolic risk factors, challenging the effectiveness of existing surveillance paradigms that primarily target cirrhotic individuals.

Conventional surveillance, centered on biannual ultrasound (US) with or without alpha-fetoprotein (AFP) measurement, remains the standard of care. Yet, the sensitivity of US for early-stage HCC detection is suboptimal—especially in patients with obesity, advanced fibrosis, or hepatic steatosis, where visualization is limited. Studies indicate that US sensitivity for early HCC hovers around 63%, with even lower performance in patients with NAFLD/MASLD. These limitations have prompted the exploration of alternative and adjunctive modalities to enhance early detection, reduce false positives, and improve patient outcomes.

Recent advances in imaging are at the forefront of this evolution. Non-contrast and abbreviated MRI protocols have demonstrated markedly improved sensitivity and specificity for early-stage HCC, particularly in high-risk patients with poor US visualization. For example, non-contrast MRI can detect Barcelona Clinic Liver Cancer (BCLC) stage 0 tumors at twice the rate of US (8% vs. 3%), while also reducing unnecessary diagnostic referrals by up to 70%. The introduction of standardized reporting frameworks, such as the 2024 update of the Liver Imaging Reporting and Data System (LI-RADS), further enhances the reproducibility and clinical utility of advanced imaging modalities. Additionally, contrast-enhanced ultrasound and emerging CT-based techniques are being evaluated for their potential roles in specific clinical scenarios.

Beyond imaging, the integration of blood-based biomarkers and artificial intelligence (AI) is poised to revolutionize HCC surveillance. Biomarker panels—including the GALAD score (which combines gender, age, AFP, AFP-L3, and DCP), circulating tumor DNA, and microRNAs—are under active investiga-

tion, with several phase III trials underway. These tools may offer improved risk stratification and early detection, particularly in non-cirrhotic populations who are currently underserved by guideline-based surveillance. AI-driven algorithms, leveraging electronic health records and imaging data, show promise for individualized risk prediction and automated lesion detection, potentially reducing interobserver variability and optimizing resource allocation.

The evolving epidemiology of HCC necessitates a shift toward personalized, risk-adapted surveillance strategies. This includes the adoption of MRI-based surveillance in cirrhotic patients with inadequate US windows, and the development of biomarker-driven or AI-assisted screening protocols for non-cirrhotic individuals with metabolic risk factors. Importantly, up to 20% of HCC cases related to MASLD/MASH occur in non-cirrhotic livers, highlighting a critical gap in current surveillance guidelines and underscoring the need for broader inclusion criteria.

Future directions should prioritize the harmonization of international guidelines, cost-effectiveness analyses of advanced modalities, and strategies to ensure equitable access—especially in resource-limited settings. The integration of abbreviated imaging protocols, validated biomarkers, and digital health solutions will be essential to optimize surveillance adherence and reduce HCC-related mortality. As the field moves beyond conventional imaging, a multidisciplinary, patient-centered approach will be key to addressing the challenges of the next era in HCC surveillance.

In summary, the expanding armamentarium of HCC surveillance modalities—spanning advanced imaging, biomarkers, and AI—offers unprecedented opportunities to improve early detection and outcomes. However, successful implementation will require careful consideration of patient selection, healthcare infrastructure, and cost-effectiveness, as well as ongoing research to refine and validate emerging technologies in diverse populations.

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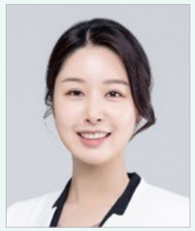

Hyo Jung Park

University of Ulsan

Self Introduction

Prof. Hyo Jung Park graduated from University of Ulsan College of Medicine with her medical degree in 2013 and completed her intership and residancy at Asan Medical Center, receiving her diploma in Radiology in 2018. She obtained a master's degree in 2022 and a doctoral degree in 2022.

She is an Assistant Professor of the Department of Radiology, University of Ulsan College of Medicine.

Research Interests

Liver Imaging, Biliopancreatic Imaging, Cancer Imaging, Personalized Medicine

Representative Publications

1. Park HJ, Shin K, You M-W, et al. Deep Learning–based Detection of Solid and Cystic Pancreatic Neoplasms at Contrast-enhanced CT. Radiology 2023 Jan 306(1):140-149
2. Park HJ, Kim KW, Won SE, et al. Definition, Incidence, and Challenges for Assessment of Hyperprogressive Disease during Cancer Treatment with Immune Checkpoint Inhibitors: A Systematic Review and Meta-analysis. JAMA Netw Open 2021; 4(3) e211136
3. Park HJ, Lee SS, Park B, Yun J, Sung YS, Shim WH, Shin YM, Kim SY, Lee SJ, Lee MG. Radiomics analysis of gadoxetic acid-enhanced MRI for staging liver fibrosis. Radiology 2019; 290:380-387
4. Park HJ, Jang HJ, Kim SY, Lee SJ, Won HJ, Byun JH, Choi SH, Lee SS, An J, Lim Y-S. Non-enhanced magnetic resonance imaging as a surveillance tool for hepatocellular carcinoma: Comparison with ultrasound. J Hepatol 2020; 72(4):718-724
5. Park HJ, Jang JK, Park SH, Park KJ, Baek S, Hong YS. Restaging abdominopeltic computed tomography before surgery after preoperative chemotherapy in patients with locally advanced rectal cancer. JAMA Oncol 2018; 4(2):259-62

The Future of Imaging-Based Hepatocellular Carcinoma Surveillance: Personalized Approaches and Artificial Intelligence

Hyo Jung Park *University of Ulsan*

Early detection of HCC remains a cornerstone strategy to reduce disease-related mortality through timely therapeutic intervention. However, HCC incidence is highly heterogeneous depending on underlying etiology, liver disease severity, and patient-specific risk factors. This necessitates a shift from a uniform surveillance paradigm to a personalized approach. Recent guidelines and real-world evidence emphasize stratifying surveillance intensity based on individual HCC risk. Recently developed risk scores such as PAGE-B, aMAP, and REACH-B have been validated to identify high-risk populations who may benefit from intensified imaging surveillance, while sparing low-risk individuals from unnecessary procedures. Emerging evidence supports the cost-effectiveness of using advanced imaging modalities—particularly abbreviated MRI (AMRI)—when selectively applied to patients with elevated annual HCC risk or those with suboptimal ultrasound visualization, such as individuals with obesity, steatotic liver disease, or poor acoustic windows. However, patients with compromised liver function (e.g., Child-Pugh B/C) may derive less benefit due to reduced image quality on MRI. Artificial intelligence (AI) has recently emerged as a transformative tool in HCC surveillance. One major application lies in improving HCC risk stratification. AI-based platforms may also guide the selection of optimal surveillance strategies by integrating clinical, imaging, and laboratory data to personalize modality choices and screening intervals. The integration of patient-specific risk modeling, imaging modality selection, and AI-based decision support can enhance optimal HCC surveillance while ensuring cost-efficiency.

References

1. Goossens N, Singal AG, King LY, et al. Cost-effectiveness of risk score–stratified hepatocellular carcinoma screening in patients with cirrhosis. Clin Transl Gastroenterol. 2017;8:e101.
2. Kim HL, An J, Lee YB, et al. Magnetic resonance imaging is cost - effective for hepatocellular carcinoma surveillance in high - risk patients with cirrhosis. Hepatology. 2019;69(4):1599-1613.
3. Nahon P, Layese R, Bourcier V, et al. Early hepatocellular carcinoma detection using magnetic resonance imaging is cost-effective in high-risk patients with cirrhosis. JHEP Rep. 2022;4(1):100390.
4. Singal AG, Chhatwal J, Parikh ND, Tapper EB. Cost-effectiveness of a biomarker-based screening strategy for hepatocellular carcinoma in patients with cirrhosis. Liver Cancer. 2024;13(3):643-654.
5. Kao SYZ, Niu B, Paik JM, et al. Cost-effectiveness of a precision hepatocellular carcinoma surveillance strategy in patients with cirrhosis. eClinicalMedicine. 2024;75:102755.
6. Singal AG, Ng M, Kulkarni A. Advancing surveillance strategies for hepatocellular carcinoma: a new era of effi-

cacy and precision. J Clin Exp Hepatol. 2024;14(1):101448.
7. Lee HW, Cho EJ, Sinn DH, et al. A machine learning model for predicting hepatocellular carcinoma risk in patients with chronic hepatitis B. Liver Int. 2023;43(9):1813-1821.
8. Zandavi SM, Jang M, Kim JY, et al. AI-powered prediction of HCC recurrence after surgical resection: personalised intervention opportunities using patient-specific risk factors. Liver Int. 2024;44(12):2724-2737.
9. Kim HY, Lampertico P, Nam JY, et al. An artificial intelligence model to predict hepatocellular carcinoma risk in Korean and Caucasian patients with chronic hepatitis B. J Hepatol. 2022;76(2):311-318.
10. Ho CT, Lee HW, Sinn DH, et al. Conventional and machine learning-based risk scores for patients with early-stage hepatocellular carcinoma. Clin Mol Hepatol. 2024;30(2):406-420.
11. Chen QF, Huang T, Wu PF, et al. Surveillance strategy for Barcelona Clinic Liver Cancer B hepatocellular carcinoma achieving complete response: an individualized risk-based machine learning study. Front Bioeng Biotechnol. 2021;9:667641.
12. Wong GLH, Chan HL, Yip TC, et al. Novel machine learning models outperform risk scores in predicting hepatocellular carcinoma in patients with chronic viral hepatitis. JHEP Rep. 2022;4(2):100441.
13. Audureau E, Carrat F, Layese R, et al. Personalized surveillance for hepatocellular carcinoma in cirrhosis – using machine learning adapted to HCV status. J Hepatol. 2020;73(6):1434-1445.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
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DAY 2: May 30 (Fri.)

Liver Biopsy in Hepatocellular Carcinoma

Chair:

Kyung Sik Kim (Yonsei Univ.)

Hae Lim Lee

The Catholic University of Korea

Self Introduction

Prof. Hae Lim Lee is a clinical assistant professor in the Department of Internal medicine, Hepatology, at The Catholic University College of Medicine.

She graduated from Ewha Womans University College of Medicine with a medical degree in 2008 and completed internship and residency at the Department of Internal medicine at The Catholic University Hospital, receiving a diploma in Internal Medicine in 2013.

She has been serving as a member of the Korean Liver Cancer Association since 2018.

Professional Experience

2021-Present	KLCA Committee of Project
2024-Present	KLCA Committee of Academy Affairs
2024-Present	KASL Committee of Public Relations
2018-2021	KLCA Committee of Public Relations
2022-2023	KASL Committee of Recruitment

Research Interests

HBV, Hepatocellular Carcinoma, Liver Cirrhosis

Representative Publications

1. Prediction of long-term HBsAg seroclearance in HBeAg-negative chronic hepatitis B patients. JHEP Rep. 2025. In press
2. Core protein inhibitors: Opportunities and challenges at the forefront of hepatitis B cure. Clin Mol Hepatol. 2024 May 14
3. A refined prediction model for survival in hepatocellular carcinoma patients treated with transarterial chemoembolization. Front Oncol. 2024 Mar
4. The role of transjugular intrahepatic portosystemic shunt in patients with portal hypertension: Advantages and pitfall. Clin Mol Hepatol. 2022 Apr
5. Anticancer Effect of Statins in Patients Undergoing Liver Transplantation for Hepatocellular Carcinoma. Liver Transpl 2022 Mar
6. Anti-fibrotic effects of branched-chain amino acids on hepatic stellate cells. Korean J Intern Med. 2022 Jan

The Role of Liver Biopsy in Hepatocellular Carcinoma Management: A KLCA Perspective

Hae Lim Lee *The Catholic University of Korea*

Liver biopsy is not routinely required for the clinical management of hepatocellular carcinoma (HCC), including diagnosis or evaluation of treatment response. This is primarily because HCC often develops in the setting of chronic liver disease or cirrhosis, typically associated with well-known risk factors such as chronic hepatitis B virus or hepatitis C virus infection and alcohol abuse. Additionally, the procedure carries inherent risks, particularly in cirrhotic patients. However, the need for pathological evaluation is increasing—not only for definitive diagnosis but also due to advancements in systemic therapies.

To assess the clinical necessity of liver biopsy in HCC management, the Korean Liver Cancer Association (KLCA) conducted a survey among HCC specialists between December 2024 and January 2025. A total of 137 physicians participated, comprising 60% internists, 19% radiologists, 14% surgeons, 5% radiation oncologists, and others. The survey revealed a low rate of liver biopsy utilization for definite diagnosis, with 49% of KLCA members performing the procedure in fewer than 10% of cases, while 5% reported not performing it at all (Figure 1). The primary reasons for this limited use included the perception that liver biopsy is unnecessary for diagnosis and treatment decision, as well as concerns about procedure-related complications, such as bleeding, tumor track seeding, and infections.

Diagnosis of HCC is based on established imaging criteria, with the Liver Imaging Reporting and Data System (LI-RADS) widely used to stratify the probability of HCC. However, approximately 10% of cases diagnosed as HCC radiologically are later identified as other conditions, such as dysplastic nodules, adenomas, or other malignancies, upon biopsy—even in LR-5.[1] A study involving patients with radiologically diagnosed advanced HCC who were eligible for systemic therapy also demonstrated a similar incidence of non-HCC tumors upon pathological evaluation. Consequently, the 2024 British Society of Gastroenterology guideline now recommends liver biopsy for patients with suspected HCC based on imaging studies who are being considered for systemic therapy.[2, 3] Findings from the KLCA survey further support this concerns, with 80.5% of responders reporting discrepancies between radiological and pathological findings in suspected HCC cases during real-world clinical practice. Such misdiagnoses may result in missed opportunities for appropriate treatment, necessitating the need for biopsy.

Significant advancements in laboratory technologies, including next-generation sequencing, have expanded our understanding of key genetic alterations, molecular pathways, the tumor microenvi-

ronment, and immune interactions involved in cancer development. Approximately 97% of recently approved oncology therapeutic products are designed to target specific molecular mechanisms, relying on an in-depth understanding of these pathways.[4] In HCC, combination immunotherapy regimens, such as atezolizumab/bevacizumab, the most widely used systemic therapy in South Korea,[5] and tremelimumab/durvalumab, have become established first-line systemic therapies, alongside multikinase inhibitors as sorafenib and Lenvatinib. However, despite these therapeutic advancements, many clinical trials investigating systemic agents for HCC have failed to identify reliable biomarkers for predicting treatment response, leading to a low response rate of 20%–30%.[6-8] Currently, ramucirumab remains the only HCC therapy guided by a biomarker (AFP levels), in contrast to the broader oncology landscape, where approximately 39% of oncology-related therapeutic agents approved between 2002 and 2022 are biomarker-based therapies.[4] The lack of available tumor tissue remains a significant barrier to biomarker research, limiting progress in precision medicine for HCC.

Despite the clinical need for liver biopsy, several limitations hinder the broader recommendation for increasing its utilization in HCC patients. First, concerns regarding potential complications must be addressed. Although the risk of bleeding and track tumor seeding, among the most significant complications, has been reported at a low incidence,[9, 10] many physicians, including most KLCA members, continue to take precautionary measures, such as transfusion or discontinuation of antiplatelet or anticoagulant agents before biopsy (Figure 2A, B). Establishing standardized procedural guidelines is essential to ensure safety and consistency. Second, the high tumor heterogeneity of HCC limits the role of liver biopsy, as small tissue samples may not fully represent the molecular and genetic complexity of the tumor. Alternative strategies such as serial biopsy following non-response or disease progression after initial treatment, as well as liquid biopsy, may provide valuable tumor-related information while mitigating some of the challenges associated with traditional tissue sampling.[11]

To advance precision and personalized medicine, obtaining pathologic insights is now essential—not only for definitive diagnosis but also for predicting and assessing treatment response. Although fewer KLCA members than expected currently support increasing liver biopsy utilization, 65% agree that the procedure should be expanded in the long term. Given these considerations, it is time for a reassessment of liver biopsy's role in HCC management, with an emphasis on enhancing safety, refining procedural guidelines, and integrating biopsy-based molecular profiling into clinical practice.

References

1. Brusset B, Jacquemin M, Teyssier Y, Roth GS, Sturm N, Roustit M, Bone A, et al. Radiological diagnosis of hepatocellular carcinoma does not preclude biopsy before treatment. JHEP Rep 2024;6:100957.
2. Childs A, Zakeri N, Ma YT, O'Rourke J, Ross P, Hashem E, Hubner RA, et al. Biopsy for advanced hepatocellular carcinoma: results of a multicentre UK audit. Br J Cancer 2021;125:1350-1355.
3. Suddle A, Reeves H, Hubner R, Marshall A, Rowe I, Tiniakos D, Hubscher S, et al. British Society of Gastroenterology guidelines for the management of hepatocellular carcinoma in adults. Gut 2024;73:1235-1268.
4. Scott EC, Baines AC, Gong Y, Moore R, Jr., Pamuk GE, Saber H, Subedee A, et al. Trends in the approval of cancer therapies by the FDA in the twenty-first century. Nat Rev Drug Discov 2023;22:625-640.
5. Han JW, Sohn W, Choi GH, Jang JW, Seo GH, Kim BH, Choi JY. Evolving trends in treatment patterns for hepatocellular carcinoma in Korea from 2008 to 2022: a nationwide population-based study. J Liver Cancer 2024;24:274-285.
6. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Kudo M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-1905.
7. Yau T, Park JW, Finn RS, Cheng AL, Mathurin P, Edeline J, Kudo M, et al. Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol 2022;23:77-90.
8. Abou-Alfa GK, Lau G, Kudo M, Chan SL, Kelley RK, Furuse J, Sukeepaisarnjaroen W, et al. Tremelimumab plus Durvalumab in Unresectable Hepatocellular Carcinoma. NEJM Evid 2022;1:EVIDoa2100070.
9. European Association for the Study of the L. EASL Clinical Practice Guidelines on prevention and management of bleeding and thrombosis in patients with cirrhosis. J Hepatol 2022;76:1151-1184.
10. Silva MA, Hegab B, Hyde C, Guo B, Buckels JA, Mirza DF. Needle track seeding following biopsy of liver lesions in the diagnosis of hepatocellular cancer: a systematic review and meta-analysis. Gut 2008;57:1592-1596.
11. Dhanasekaran R, Suzuki H, Lemaitre L, Kubota N, Hoshida Y. Molecular and immune landscape of hepatocellular carcinoma to guide therapeutic decision-making. Hepatology 2023.

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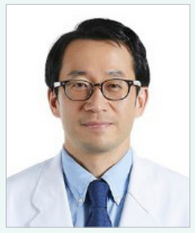
DAY 2: May 30 (Fri.)

KLCA Symposium 2

Advancing Biomarker Discovery and Translational Insights in Liver Cancer

Chairs:

Seung Kew Yoon (The Catholic Univ. of Korea)
Hee Chul Yu (Jeonbuk National Univ.)



Soung Won Jeong

Soonchunhyang University

Self Introduction

Prof. Soung Won Jeong is a Professor of the Department of Hepatology, Soonchunhyang University Seoul Hospital.

He graduated from Soonchunhyang University College of Medicine with his medical degree in 1998 and completed his internship and residency at the Department of Gastroenterology at Soonchunhyang University Seoul Hospital, receiving his diploma in Internal Medicine in 2003.

He is currently holding a position of a seretary general of Liver Cirrhosis study group of KASL, and a director of public reactions committee of the Korean Association of Clinical Ultrasound.

He has been conducting research on cell-free DNA in HCC with support from the National Research Foundation of Korea.

Research Interests

HCC, HBV, MASLD

Representative Publications

1. Aliment Pharmacol Ther. 2025 Apr;61(8):1333-1342. doi: 10.1111/apt.70004. Epub 2025 Feb 16.
   Clinical Course and Prognosis of Long-Term Survivors of Hepatocellular Carcinoma.
   Soon Sun Kim[1], Jonghyun Lee[2], Sang Bong Ahn[3], Young Eun Chon[4], Eileen Yoon[5], Soung Won Jeong[6](Correspondence), Dae Won Jun[5]
2. Clin Mol Hepatol. 2023 Jan;29(1):120-134. Hepatocellular carcinoma incidence is decreasing in Korea but increasing in the very elderly. Young Eun Chon[1], Seong Yong Park[23], Han Pyo Hong[4], Donghee Son[5], Jonghyun Lee[6], Eileen Yoon[7], Soon Sun Kim[8], Sang Bong Ahn[9], Soung Won Jeong[10](Correspondence), Dae Won Jun[7]
3. J Liver Cancer. 2022 Sep;22(2):167-177.doi: 10.17998/jlc.2022.09.19.Epub 2022 Sep 29.
   The diagnostic value of circulating tumor DNA in hepatitis B virus induced hepatocellular carcinoma: a systematic review and meta-analysis. Young Chang[1], Soung Won Jeong[1](Correspondence), Jae Young Jang[1], Hyuksoo Eun[2], Young-Sun Lee[3], Do Seon Song[4], Su Jong Yu[5], Sae Hwan Lee[6], Won Kim[7], Hyun Woong Lee[8], Sang Gyune Kim[9], Seongho Ryu[10], Suyeon Park[11,12]

Liquid vs. Tissue Biopsy to Support Treatment Decisions in Hepatocellular Carcinoma

Soung Won Jeong *Soonchunhyang University*

Liquid biopsies—including cell-free DNA (cfDNA), circulating tumor cells (CTCs), non-coding RNAs (ncRNAs), and extracellular vesicles (EVs)—have emerged as promising tools for the non-invasive diagnosis and monitoring of hepatocellular carcinoma (HCC). These techniques offer considerable advantages over conventional tissue biopsy in terms of patient comfort and procedural safety. However, several limitations remain, including suboptimal sensitivity, high cost, and limited accessibility in routine clinical practice. Traditionally, cfDNA analyses have focused on assessing the total amount, integrity, and copy number alterations. More recently, advanced techniques have been developed to evaluate tumor-specific methylation patterns, particularly within CpG islands of tumor suppressor genes, as well as somatic mutation signatures. Genomic profiling has identified mutations in genes such as TERT, CTNNB1, and TP53 as key drivers in hepatocarcinogenesis. Notably, TERT promoter and TP53 mutations have been detected in the cfDNA of more than 75% of patients with early-stage HCC[1,2] In particular, DNA methylation signatures specific to HCC have shown a sensitivity of 84.5% and a specificity of 95%, highlighting their improved potential for early detection.[3] Recent studies have also focused on the cfDNA "fragmentome," which refers to the comprehensive profile of cfDNA fragment lengths and end motifs. Since cfDNA is highly fragmented, with patterns that reflect nucleosomal organization, these fragmentomic features can provide insight into tissue-of-origin. For example, HCC patients exhibit a higher prevalence of specific 4-mer end motifs.[4] This method has demonstrated the ability to detect HBV-related HCC with 87.1% sensitivity and 88.4% specificity.[5] Moreover, the unbiased analysis of cfDNA fragmentomes may allow for the discovery of novel methylation patterns, further aiding in patient classification and early diagnosis.[6] Despite these advances, the clinical utility of cfDNA remains limited by the strong correlation between circulating tumor DNA (ctDNA) levels and tumor burden. Smaller lesions, as seen in early-stage HCC, tend to release less DNA into circulation, resulting in decreased detection sensitivity. Consequently, cfDNA may be more suitable for monitoring disease recurrence, treatment response, or the emergence of resistance, rather than for early diagnosis.

Non-coding RNAs, including microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), also represent promising biomarkers. These RNAs do not encode proteins but regulate various cellular processes such as chromatin remodeling, transcriptional control, and genomic architecture. Numerous studies have identified panels of miRNAs—such as miR-21, miR-26a, miR-27a, miR-29a/c, miR-122, miR-143, miR-145,

miR-192, miR-223, and others—that can detect early-stage HCC,[7,8] predict overall and disease-free survival, and inform prognosis following systemic therapy[9] Additionally, lncRNA panels have shown diagnostic and prognostic value in HBV-related HCC. However, the translation of lncRNA-based diagnostics into clinical use has been hampered by methodological variability, lack of standardization, and incomplete data on their contribution to HCC.

Extracellular vesicles (EVs), including exosomes, microvesicles, and apoptotic bodies, are lipid bilayer-bound particles released by virtually all mammalian cells. These vesicles carry diverse cargo—including cfDNA, cfRNA, proteins, and lipids—that reflect the physiological or pathological state of their cell of origin. Owing to their ability to mediate intercellular communication and their stability in circulation, EVs have become attractive targets for liquid biopsy. Several studies have proposed EV-derived nucleic acid and proteomic signatures for HCC diagnosis and treatment monitoring.[10] In particular, EV-associated miRNA panels have demonstrated sensitivity and specificity exceeding 90%.[11] Nonetheless, technical challenges remain, including the lack of standardized protocols for EV isolation and the difficulty in enriching for tumor-specific EVs. While liquid biopsies are not yet part of routine clinical care, several platforms have received FDA approval as breakthrough diagnostic tests for HCC detection, including Oncoguard® Liver, HelioLiver™, HCCscreen™, HCCBloodTest, and Guardant360®. However, their widespread clinical implementation is hindered by three major challenges: insufficient validation of clinical utility, lack of intuitive scoring systems, and high inter-assay variability. Harmonizing sample preparation methods and establishing standardized reporting criteria are essential next steps.

In contrast, tissue biopsy remains a cornerstone of diagnosis in certain contexts. It is particularly important in patients with non-cirrhotic livers, where imaging-based diagnosis of HCC is less reliable. Biopsies are also indispensable when intrahepatic cholangiocarcinoma, mixed HCC-cholangiocarcinoma, or metastatic disease is suspected, as histological markers can differentiate HCC from other tumours.

Furthermore, sampling the non-tumorous liver parenchyma can yield the underlying liver disease and provide insight into HCC prognosis.[12] Another key advantage of tissue biopsy is the ability to classify HCC into histological and molecular subtypes. For instance, well-differentiated tumors often harbor CTNNB1 mutations, whereas poorly differentiated tumors frequently exhibit TP53 mutations.[13-15] Although histopathological biomarkers have not yet been widely adopted for guiding treatment selection, tissue biopsy may become a more routine diagnostic procedure in the era of precision medicine. In the future, biomarkers identified from liver biopsy may guide targeted treatment stratification.

Several tissue-based biomarkers—including glypican-3 (GPC3), epithelial cell adhesion molecule (EpCAM), MET, mucin 1 (MUC1), major histocompatibility complex class I (MHC1), and TERT—are currently being investigated in clinical trials as potential therapeutic targets. Efforts are also underway to identify predictive biomarkers for immunotherapy, such as PD-L1 expression, high tumor mutational burden (TMB), microsatellite instability (MSI), and composite gene signatures. These developments highlight the growing importance of tissue-based biomarker analysis in guiding immunotherapy decisions.

In summary, although neither liquid nor tissue biopsy has yet been fully integrated into standard clinical practice for HCC, both hold substantial promise. Ongoing research is addressing critical issues related to their sensitivity, specificity, cost-effectiveness, and complementary roles. Ultimately, the integration of molecular diagnostics—via either tissue or liquid biopsy—represents a major advance in the personalized management of HCC, enabling earlier detection, more accurate risk stratification, and tailored therapeutic approaches.

References

1. Kaseb AO, Sanchez NS, Sen S, Kelley RK, Tan B, Bocobo AG, et al. Molecular Profiling of Hepatocellular Carcinoma Using Circulating Cell-Free DNA. Clin Cancer Res 2019;25:6107-6118.
2. Zhang Y, Yao Y, Xu Y, Li L, Gong Y, Zhang K, et al. Pan-cancer circulating tumor DNA detection in over 10,000 Chinese patients. Nat Commun 2021;12:11.
3. Cheishvili D, Wong C, Karim MM, Kibria MG, Jahan N, Das PC, et al. A high-throughput test enables specific detection of hepatocellular carcinoma. Nat Commun 2023;14:3306.
4. Jiang P, Sun K, Peng W, Cheng SH, Ni M, Yeung PC, et al. Plasma DNA End-Motif Profiling as a Fragmentomic Marker in Cancer, Pregnancy, and Transplantation. Cancer Discov 2020;10:664-673.
5. Sun X, Feng W, Cui P, Ruan R, Ma W, Han Z, et al. Detection and monitoring of HBV-related hepatocellular carcinoma from plasma cfDNA fragmentation profiles. Genomics 2022;114:110502.
6. Zhou Q, Kang G, Jiang P, Qiao R, Lam WKJ, Yu SCY, et al. Epigenetic analysis of cell-free DNA by fragmentomic profiling. Proc Natl Acad Sci U S A 2022;119:e2209852119.
7. Yamamoto Y, Kondo S, Matsuzaki J, Esaki M, Okusaka T, Shimada K, et al. Highly Sensitive Circulating MicroRNA Panel for Accurate Detection of Hepatocellular Carcinoma in Patients With Liver Disease. Hepatol Commun 2020;4:284-297.
8. Lin XJ, Chong Y, Guo ZW, Xie C, Yang XJ, Zhang Q, et al. A serum microRNA classifier for early detection of hepatocellular carcinoma: a multicentre, retrospective, longitudinal biomarker identification study with a nested case-control study. Lancet Oncol 2015;16:804-815.
9. Teufel M, Seidel H, Kochert K, Meinhardt G, Finn RS, Llovet JM, et al. Biomarkers Associated With Response to Regorafenib in Patients With Hepatocellular Carcinoma. Gastroenterology 2019;156:1731-1741.
10. Sun N, Lee YT, Zhang RY, Kao R, Teng PC, Yang Y, et al. Purification of HCC-specific extracellular vesicles on nanosubstrates for early HCC detection by digital scoring. Nat Commun 2020;11:4489.
11. Yang J, Dong W, Zhang H, Zhao H, Zeng Z, Zhang F, et al. Exosomal microRNA panel as a diagnostic biomarker in patients with hepatocellular carcinoma. Front Cell Dev Biol 2022;10:927251.
12. Vogel A, Cervantes A, Chau I, Daniele B, Llovet JM, Meyer T, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29:iv238-iv255.
13. Torbenson MS. Morphologic Subtypes of Hepatocellular Carcinoma. Gastroenterol Clin North Am 2017;46:365-391.
14. Torbenson MS. Hepatocellular carcinoma: making sense of morphological heterogeneity, growth patterns, and subtypes. Hum Pathol 2021;112:86-101.
15. Calderaro J, Ziol M, Paradis V, Zucman-Rossi J. Molecular and histological correlations in liver cancer. J Hepatol 2019;71:616-630.

Sung Hak Lee

The Catholic University of Korea

Self Introduction

Prof. Sung Hak Lee currently works as a professor at the department of hospital pathology at Seoul St. Mary's hospital (2022-present).

He received his Doctor of Medicine from The Catholic University of Korea in 2002. He received his Ph.D. from The Catholic University of Korea in 2013. Dr. Lee completed his residency in pathology at the Catholic Medical Center.

After the program, he was an assistant professor, department of hospital pathology at Seoul St. Mary's hospital (2014-2018). Then he was an associate professor in the same institute (2018-2021). Prior to his professorship, he worked as a visiting scholar at Center for biomedical informatics and biostatistics (CB2), University of Arizona and Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic (2017-2018).

Research Interests

- GI & Hepatobiliary Tract Pathology
- Artificial Intelligence in Computational Pathology
- Bioinformatics Analysis in Molecular Pathology

Representative Publications

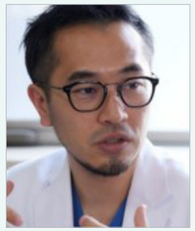
1. Spatial dissection of tumour microenvironments in gastric cancers reveals the immunosuppressive crosstalk between CCL2+ fibroblasts and STAT3-activated macrophages. Gut. 2025 Apr 7;74(5):714-727.
2. Artificial Intelligence Applications in Image-Based Diagnosis of Early Esophageal and Gastric Neoplasms. Gastroenterology. 2025 Mar 3:S0016-5085(25)00471-8.
3. Spatially Distinct Reprogramming of the Tumor Microenvironment Based On Tumor Invasion in Diffuse-Type Gastric Cancers. Clin Cancer Res. 2021 Dec 1;27(23):6529-6542.
4. Deep learning-based prediction of molecular cancer biomarkers from tissue slides: A new tool for precision oncology. Clin Mol Hepatol. 2022 Oct;28(4):754-772.
5. Deep learning captures selective features for discrimination of microsatellite instability from pathologic tissue slides of gastric cancer. Int J Cancer. 2023 Jan 15;152(2):298-307.

KLCA Symposium 2 | DAY 2: May 30 (Fri.) | ROOM 2 [3F]

Artificial Intelligence-Based Pathology as a Biomarker of Sensitivity to Immunotherapy

Sung Hak Lee *The Catholic University of Korea*

Artificial intelligence (AI)-based pathology has emerged as a promising tool to predict immunotherapy response in hepatocellular carcinoma (HCC). Deep learning models applied to histological slides can accurately infer immune and inflammatory gene signatures associated with treatment sensitivity, bypassing the limitations of traditional molecular profiling. Recent studies demonstrated that AI models, including clustering-constrained attention multiple-instance learning (CLAM), effectively predict immune activation status and correlate with clinical outcomes such as progression-free survival in HCC patients treated with atezolizumab–bevacizumab. Moreover, spatial transcriptomics analyses validated the biological relevance of AI-derived predictions. In parallel, AI-driven immunoprofiling has shown potential in predicting nivolumab efficacy. These findings highlight the clinical utility of AI pathology as a rapid, cost-effective, and scalable biomarker platform for patient stratification in immunotherapy. Future directions involve prospective validation and integration of multimodal approaches to enhance precision oncology.



Hideki Iwamoto

Kurume University, Japan

Self Introduction

Education

2005.3 M.D., Kurume University School of Medicine
2011.3 Ph.D., Graduate School of Medicine, Kurume University

Professional Training and Employment

2005.3 Passed the Medical Examination of Japanese National Board
2005.4 Resident, Kurume University Hospital
2007.4 Fellow, Department of Gastroenterology, Division of Medicine, Kurume University School of Medicine
2008.4 Graduate Student, Department of Gastroenterology, Division of Medicine and Senior Fellow, Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine
2012.1 Postdoc Fellow, Department of Microbiology Tumor and Cell biology, Karolinska Institutet, Stockholm, Sweden
2014.5-Present Chief Executive of Iwamoto Internal Medicine Clinic
2015.4-Present Assistant Professor, Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine

Research Interests

- Basic and Clinical Research of Molecular Targeted Agent, Angiogenesis, Immune Oncology,
- Tumor Microenvironment, and Interventional Radiology in Hepatocellular Carcinoma

Representative Publications

1. Iwamoto, H*., H. Suzuki, A. Masuda, T. Sakaue, T. Nakamura, T. Tanaka, M. Sakai, Y. Imamura, H. Yano, T. Torimura, H. Koga, K. Yasuda, M. Tsurusaki, T. Seki and T. Kawaguchi (2024). "A tumor endothelial cell-specific microRNA replacement therapy for hepatocellular carcinoma." iScience 27(2): 108797.
2. Suzuki, H., H. Iwamoto*, T. Seki, T. Nakamura, A. Masuda, T. Sakaue, T. Tanaka, Y. Imamura, T. Niizeki, M. Nakano, et al. "Tumor-derived insulin-like growth factor-binding protein-1 contributes to resistance of hepatocellular carcinoma to tyrosine kinase inhibitors." Cancer Commun (Lond) 43 (2023): 415-34. 10.1002/cac2.12411. https://www.ncbi.nlm.nih.gov/pubmed/36825684
3. Iwamoto, H*., S. Shimose, T. Shirono, T. Niizeki and T. Kawaguchi. "Hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma in the era of chemo-diversity." Clin Mol Hepatol (2023): 10.3350/cmh.2022.0391. https://www.ncbi.nlm.nih.gov/pubmed/36775834.
4. Iwamoto, H*., H. Suzuki, S. Shimose, T. Niizeki, M. Nakano, T. Shirono, S. Okamura, Y. Noda, N. Kamachi, T. Nakamura, et al. "Weekends-off lenvatinib for unresectable hepatocellular carcinoma improves therapeutic response and tolerability toward adverse events." Cancers (Basel) 12 (2020): 10.3390/cancers12041010. https://www.ncbi.nlm.nih.gov/pubmed/32325921.
5. Iwamoto, H., M. Abe, Y. Yang, D. Cui, T. Seki, M. Nakamura, K. Hosaka, S. Lim, J. Wu, X. He, et al. "Cancer lipid metabolism confers antiangiogenic drug resistance." Cell Metab 28 (2018): 104-17.e5. 10.1016/j.cmet.2018.05.005. https://www.ncbi.nlm.nih.gov/pubmed/29861385.

Strategies to Effectively Drive the Cancer-Immunity Cycle: Roles of Each Therapeutic Modality in Hepatocellular Carcinoma

Hideki Iwamoto *Kurume University, Japan*

Background

Combination immunotherapy has become a mainstay in systemic treatment for hepatocellular carcinoma (HCC), leading to a growing focus on the tumor immune microenvironment (TIME). It is critical to drive the cancer-immunity cycle appropriately to maximize immunotherapy outcomes. The impact of various tyrosine kinase inhibitors (TKIs) and locoregional therapies on the TIME remains poorly understood. This presentation aims to clarify how each treatment modulates TIME, enhances the cancer-immunity cycle, and improves therapeutic efficacy.

Methods

1. TIME Modulation by TKIs

TKIs—cabozantinib (Cab), lenvatinib (Len), sorafenib (Sora), regorafenib (Reg), and ramucirumab (Ram)—were administered to syngeneic orthotopic HCC mouse models. TIME markers (CD3, CD4, CD8, CD68) were evaluated by immunohistochemistry.

2. TIME Modulation by the triple therapy (Anti-VEGF, CTLA-4, and PD-L1 antibody)

In syngeneic subcutaneous HCC models, sequential therapies of atezolizumab plus bevacizumab (AB), durvalumab plus tremelimumab (DT) were administered (AB→DT, DT→AB). TIME markers (CD31, CD4, CD8, FOXP3, F4/80, CD11c, and Granzyme B) were analyzed.

3. TIME Modulation by TACE and HAIC

TIME markers (CD8, PD-L1, MHC class I) were assessed in HCC specimens resected after HAIC.

Results

- ***TIME Modulation by TKIs***

All TKIs reduced regulatory T cells (Tregs) and macrophages. Lenvatinib specifically increased cytotoxic T lymphocytes (CTLs) and granzyme B-positive cells. Cabozantinib uniquely enhanced dendritic cell infiltration and increased granzyme B-positive cells.

- ***TIME Modulation by the triple therapy (Anti-VEGF, CTLA-4, and PD-L1 antibody)***

Each sequential therapy (AB→DT, DT→AB) enhanced CTL and Granzyme B-positive cell infiltration, compared with each monotherapy. However, there was no significant difference in each sequence order.

- ***TIME Modulation by TACE and HAIC***

HAIC significantly enhanced the expression of PD-L1, CTL, and MHC class I in tumor tissues. Previous reports suggest that TACE also activates TIME through enhanced tumor antigen expression.

Conclusion

Each TKI and locoregional treatment induced distinct modulations of the tumor immune microenvironment. A thorough understanding of these differential effects may allow for more strategic activation of the cancer-immunity cycle, ultimately enhancing the efficacy of combination immunotherapies.

Jungmin Choi

Korea University

Self Introduction

Dr. Choi is an Assistant Professor in the Department of Biomedical Sciences at Korea University College of Medicine, specializing in human genetics, genomics, and computational biology.

He completed his undergraduate studies in Chemistry at Yonsei University in 2004 and earned his Ph.D. in Molecular Genetics from the University of Maryland, College Park in 2012.

From 2013 to 2019, he honed his expertise through extensive postdoctoral and research associate positions under the mentorship of Dr. Richard P. Lifton, a distinguished figure in human genetics. This included work at Yale University School of Medicine's Department of Genetics and The Rockefeller University's Laboratory of Human Genetics and Genomics before joining Korea University in 2019.

Research Interests

Genetics, Genomics, Computational Biology

Representative Publications

1. Lee J, Kim Y, Lee C, Jeon SS, Seo H, Lee J, Choi J[§], Kang M, Kim E, Shin K. Generation of Prostate Cancer Assembloids Modeling the Patient-specific Tumor Microenvironment. PLoS Genet. 2025 in press.
2. Kim B*, Chun H*, Lee J, Park M, Kwak Y, Kim JM, Kim SG, Ryu JK, Choi J[§], Cho SJ. Predictive biomarkers for metachronous gastric cancer development after endoscopic resection of early gastric cancer. Cancer Med. 2024 Aug;13(16):e70104. doi: 10.1002/cam4.70104. PMID: 39171503; PMCID: PMC11339598.
3. Lee S*, Yoon JG*, Hong J*, Kim T, Kim N, Vandrovcova J, Yau WY, Cho J, Kim S, Kim MJ, Kim SY, Lee ST, Chu K, Lee SK, Kim HJ, Choi J[§], Moon J[§], Chae JH[§]. Prevalence and Jungmin Choi 4 Characterization of NOTCH2NLC GGC Repeat Expansions in Koreans: From a Hospital Cohort Analysis to a Population-Wide Study. Neurol Genet. 2024 May 20;10(3):e200147. doi: 10.1212/NXG.0000000000200147. PMID: 38779172; PMCID: PMC11110025.
4. Bellone S*, Jeong K*, Halle MK, Krakstad C, McNamara B, Greenman M, Mutlu L, Demirkiran C, Hartwich TMP, Yang-Hartwich Y, Zipponi M, Buza N, Hui P, Raspagliesi F, Lopez S, Paolini B, Milione M, Perrone E, Scambia G, Altwerger G, Ravaggi A, Bignotti E, Huang GS, Andikyan V, Clark M, Ratner E, Azodi M, Schwartz PE, Quick CM, Angioli R, Terranova C, Zaidi S, Nandi S, Alexandrov LB, Siegel ER, Choi J[§], Schlessinger J[§], Santin AD[§]. Integrated mutational landscape analysis of poorly differentiated high-grade neuroendocrine carcinoma of the uterine cervix. Proc Natl Acad Sci U S A. 2024 Apr 23;121(17):e2321898121. doi: 10.1073/pnas.2321898121. Epub 2024 Apr 16. PMID: 38625939; PMCID: PMC11046577
5. Miao R, Chun H, Feng X, Gomes AC, Choi J[§], Pereira JP[§]. Competition between hematopoietic stem and progenitor cells controls hematopoietic stem cell compartment size. Nat Commun. 2022 Aug 8;13(1):4611. doi: 10.1038/s41467-022-32228-w. PMID: 35941168; PMCID: PMC9360400.

Mechanisms of Metastasis Revealed through Single-Cell Spatial Transcriptome Analysis in Patients with Liver Metastatic Colorectal Cancer

Jungmin Choi *Korea University*

Colorectal cancer (CRC) liver metastases remain difficult to treat due to substantial intratumoral and intertumoral heterogeneity, driven by diverse cell populations and complex tumor microenvironment interactions. In this study, 23 formalin-fixed paraffin-embedded tissue samples from 11 patients, comprising primary lesions and matched liver metastases (6 synchronous and 5 metachronous), were analyzed using NanoString 6K CosMx SMI. Pathologists selected optimal fields of view at the tumor invasive fronts, and an in-house CosMx SMI pipeline was employed for image processing, cell segmentation, and feature extraction. Following quality control, 105,624 high-quality cells underwent unsupervised clustering, differential gene expression, and cell-to-cell interaction analyses using the Seurat R package, revealing 23 distinct cell clusters, including ten epithelial tumor clusters, three cancer-associated fibroblast (CAF) clusters, two endothelial clusters, five immune cell subtypes (T cell, Monocyte, Macrophage, SPP1+ Macrophage, and Plasma cell), alveolar cells, hepatocytes, and low complexity populations. Notably, liver CAFs exhibited upregulation of 92 genes linked to epithelial-mesenchymal transition (EMT). Enhanced cellular crosstalk between CAFs, T cells, and macrophages was detected specifically in metastatic lesions, characterized by enriched ligand-receptor pairs such as SPP1–ITGA4/ITGB1, LGALS9–P4HB, LGALS9–CD44, and CXCL12–CXCR4. These findings underscore the distinct spatial heterogeneity and intercellular communication networks in CRC liver metastases, providing new insights into liver-specific CAF gene expression and potential therapeutic targets.

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LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

KLCA-JLCA Joint Symposium

Optimizing Bridging Gaps in Pre- and Post-Liver Transplantation Management for Hepatocellular Carcinoma

Chairs:

June Sung Lee (Inje Univ.)
Etsuro Hatano (Kyoto Univ., Japan)

Jongman Kim

Sungkyunkwan University

Self Introduction

Prof. Jongman Kim received his MD from Korea University in 2000 and trained in the Department of Surgery, Korea University Medical Center until 2005. From 2008 to 2011, he worked as a fellow in the Transplantation Division, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine in Seoul, Korea. He studied solid organ transplantation and HCC in those periods.

He completed his Ph.D. (Korea University, 2009), which subject was immunotherapy using a 4-1BB antibody against cancer. As a professor, his career has continued in the Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine until now (2024).

He operated on laparoscopic liver resection in liver malignancy and living liver donors and has studied HCC hepatectomy patients. He has performed many prospective clinical trials, and international multicenter registration studies and thus published many papers. In addition, he has operated on living or deceased donor liver transplantation. His focus projects were minimal invasive surgical techniques, surgical techniques of liver transplantation, ABO-incompatibility, HCC, and immunosuppression in liver transplantation. He performed several clinical trials as principal investigator at this time. He published approximately 430 articles related to liver transplantation and/or HCC in the Journal of Hepatology, Hepatology, Annals of Surgery, British Journal of Surgery, Liver Transplantation, and Transplantation etc.

Research Interests

- Living Donor Liver Transplantation, Surgical Techniques, Post-Transplant Management
- Living Liver Donors, Immunosuppression, Hepatocellular Carcinoma

Representative Publications

1. Jongman Kim, Sang Jin Kim, Boram Park, Kyunga Kim, YoungRok Choi, Geun Hong, Jun Yong Park, Young Seok Han, Nam-Joon Yi, Seung Heui Hong, Soon-Young Kim, Jung-Bun Park, Youngwon Hwang, Dong-Hwan Jung. Outcomes of small size graft in highly urgent living donor liver transplantation: Korean National data. HBSN 2025 (in press).
2. Roberto Ivan Troisi, Mariano Cesare Giglio, Jongman Kim, Dieter Boering, David Cherqui, Go Wakabayashi, Catherine Teh, Mohammed Abu-Hilal, Kwang-Wong Lee, Avi Soin, Jan Lerut, Luca Aldrigetti, Paulo Hermann, Horacio Asbun, Mohammed Rela, Ki Hun Kim, Susumo Eguichi, Ho-Seong Han, Kyung-Suk Suh, Mureo Kasahara, Kim Olthoff, David Geller, Hiroto Egawa, Chung-Ngai Tang. Current status of the diffusion of the minimally invasive approach for donor hepatectomy: a worldwide survey (a joint initiative of the International Laparoscopic Liver Society – ILLS - and the International Living Donor Liver Transplantation Group – ILDLTG). Transplantation 2025 (in press)
3. Sang Jin Kim, Boram Park, Jongman Kim, Kyunga Kim, YoungRok Choi, Geun Hong, Jun Yong Park, Young Seok Han, Nam-Joon Yi, Seung Heui Hong, Soon-Young Kim, Jung-Bun Park, Youngwon Hwang, Dong-Hwan Jung. Outcomes of highly urgent living donor liver transplantation in Korean national data. HBSN 2025 (in press) (Corresponding author).
4. Jinsoo Rhu, Gy-Seong Choi, Jong Man Kim, Choon Hyuck David Kwon, Jae-Won Joh. Risk factors associated with surgical morbidities of laparoscopic living liver donors. Ann Surg 2023; 1;278(1):96-102
5. Helio Tedesco-Silva Junior, Yama Tokat, Jinzhen Cai, Inderjeet Singh, Anudeep Sandhu, Dirk Demuth, Jongman Kim. Epidemiology, Management, and Burden of Cytomegalovirus in Solid Organ Transplant Recipients in Selected Countries Outside of Europe and North America: A Systematic Review. Transplant Infect Dis 2023;25:e14070.

Pre-Transplant Hepatocellular Carcinoma Control: Surgical Resection and Bridging Strategies

Jongman Kim *Sungkyunkwan University*

Introduction

Hepatocellular carcinoma is the most common primary liver malignancy and a leading indication for liver transplantation. While transplantation can eliminate both the tumor and the underlying cirrhosis, patients frequently face long wait times due to organ scarcity. This latency increases the risk of disease progression, leading to dropout from transplant eligibility criteria such as the Milan or UCSF criteria. Pre-transplant tumor control strategies—including surgical resection, ablation, transarterial chemoembolization (TACE), and systemic therapies—aim to reduce dropout and improve post-LT survival. While locoregional therapies are widely used, surgical resection offers unique advantages as a bridge or downstaging tool. Effective pre-transplant control strategies are, therefore, essential to improve transplant outcomes.

Rationale for Pre-transplant HCC Control

Patients on the liver transplant waitlist often face median wait times ranging from several months to over a year. During this period, up to 20% of patients may experience tumor progression beyond transplant criteria. Pre-transplant control aims to maintain eligibility by stabilizing tumor growth or reducing tumor burden (downstaging). In addition to reducing waitlist dropout, such strategies may positively influence post-transplant survival and recurrence rates.

Surgical Resection as a Pre-transplant Strategy

Surgical resection continues to be a potentially curative alternative for patients with single hepatocellular carcinoma and well-compensated liver function (Child-Pugh A). It is especially advantageous for patients with maintained hepatic function and circumscribed neoplasms. The benefits of surgical resection include quick and total tumor excision, precise pathological staging and evaluation of microvascular invasion, and the possibility of functioning as a downstaging method for patients who are marginally eligible for transplant requirements. Nonetheless, the constraints of surgical resection include the risk of post-operative liver decompensation, especially in cirrhotic patients, the possibility of tumor recurrence prior to transplantation, and technical difficulties arising from portal hypertension or multifocal disease.

Bridging Strategies

Bridging therapy encompasses locoregional treatments aimed at controlling tumor progression while awaiting transplantation.

1. Transarterial Chemoembolization (TACE)

TACE is the predominant bridging treatment employed. It is advised for patients with intermediate-stage hepatocellular carcinoma and maintained liver function. TACE induces partial necrosis in the majority of instances and has demonstrated a reduction in dropout rates.

2. Radiofrequency Ablation (RFA)

RFA is suitable for small tumors (<3 cm) and offers complete ablation with minimal invasiveness. Its curative intent and safety profile make it ideal for bridging in selected cases.

3. Microwave Ablation (MWA)

MWA shares similarities with RFA but may achieve more uniform ablation zones. Its use is increasing, especially in tumors >3 cm or adjacent to vessels.

4. Stereotactic Body Radiation Therapy (SBRT)

SBRT administers high-dose radiation with precision. It is especially beneficial for patients who are ineligible for TACE or RFA due to anatomical limitations.

5. Combination Strategies

In certain instances, combinatorial strategies (e.g., TACE + RFA) may improve tumor management and diminish recurrence rates. Customized treatment strategies informed by multidisciplinary tumor boards are crucial.

Conclusion

Pre-transplant management of HCC is essential for preserving transplant eligibility and enhancing outcomes. Surgical resection serves as an effective intermediary to liver transplantation in specific individuals, providing both diagnostic and therapeutic advantages. Multimodal approaches (TACE, ablation, systemic therapy) enhance outcomes. Biomarker-directed strategies and AI-enhanced predictive models may enhance treatment selection. Collaborative decision-making is crucial for mitigating risks and prioritizing transplant candidates.

References

1. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996;334(11):693-699.
2. Yao FY, Ferrell L, Bass NM, Watson JJ, Bacchetti P, Venook A, et al. Liver transplantation for hepatocellular carcinoma: expansion of the tumor size limits does not adversely impact survival. Hepatology. 2001;33(6):1394-1403.
3. Vitale A, Volk ML, Pastorelli D, Lonardi S, Farinati F, Burra P, et al. Use of liver transplantation for hepatocellular carcinoma in the MELD era: the Italian experience. Liver Transpl. 2012;18(1):20-27.
4. Cucchetti A, Cescon M, Pinna AD. Current role of surgery in patients with hepatocellular carcinoma awaiting liver transplantation. Liver Transpl. 2013;19(4):396-405.
5. Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet. 2018;391(10127):1301-1314.
6. Mehta N, Dodge JL, Grab JD, et al. National experience on downstaging of hepatocellular carcinoma before liver transplant: influence of tumor burden, alpha-fetoprotein, and wait time. Hepatology. 2020;71(3):943-954.
7. Kim WR, Lake JR, Smith JM, Skeans MA, Schladt DP, Edwards EB, et al. OPTN/SRTR 2015 Annual Data Report: Liver. Am J Transplant. 2017;17(Suppl 1):174-251.
8. Clavien PA, Lesurtel M, Bossuyt PM, et al. Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report. Lancet Oncol. 2012;13(1):e11-e22.
9. Zhong JH, Ke Y, Gong WF, et al. Hepatic resection associated with good survival for selected patients with intermediate and advanced-stage hepatocellular carcinoma. Ann Surg. 2014;260(2):329-340.
10. Pompili M, Francica G, Ponziani FR, et al. Bridging and downstaging treatments for hepatocellular carcinoma in patients on the waiting list for liver transplantation. World J Gastroenterol. 2013;19(43):7515-7530.
11. Vibert E, Schwartz M, Olthoff KM. Advances in resection and transplantation for hepatocellular carcinoma. J Hepatol. 2020;72(2):262-276.

Tomoharu Yamada

The University of Tokyo, Japan

Self Introduction

Prof. Yamada graduated from the Jikei University School of Medicine, Department of Medicine, in 2010.

He completed his residency at the University of Tokyo Hospital and subsequently undertook fellowship trainingat Mitsui Memorial Hospital.

In 2016, he entered the Graduate School of Medicine at the University of Tokyo, where he conducted research on the development of novel therapies for hepatocellular carcinoma (HCC) and pancreatic cancer using the oncolytic virus G47Δ.

Currently, he serves as the lead physician for systemic therapy for unresectable HCC at the University of Tokyo Hospital. He is also leading translational research using patient-derived samples, such as plasma and peripheral blood lymphocytes, and is conducting a phase 2 clinical trial utilizing butyrate-producing bacteria (https://jrct.mhlw.go.jp/en-latest-detail/jRCTs031220724).

Research Interests

- Analysis of the Tumor Immune Microenvironment Using Human Cancer Tissue Specimens
- Basic Analysis of Clinical Samples for Biomarker Discovery
- Translational Research Using Mouse Models
- Phase 2 Clinical Trials for HCC and Primary Biliary Cirrhosis

Representative Publications

1. Yamada T, Fujiwara N, Kubota N, Matsushita Y, Nakatsuka T, Kurosaki S, Minami T, et al. Lenvatinib recruits cytotoxic GZMK+CD8 T cells in hepatocellular carcinoma. Hepatol Commun 2023;7.
2. Minami T, Sato M, Toyoda H, Yasuda S, Yamada T, Nakatsuka T, Enooku K, et al. Machine learning for individualized prediction of hepatocellular carcinoma development after the eradication of hepatitis C virus with antivirals. J Hepatol 2023.
3. Yamada T, Tateishi R, Iwai M, Tanaka M, Ijichi H, Sano M, Koike K, et al. Overcoming resistance of stroma-rich pancreatic cancer with focal adhesion kinase inhibitor combined with G47Δ and immune checkpoint inhibitors. Mol Ther Oncolytics 2023;28:31-43.
4. Yamada T, Minami T, Tateishi R, Koike K. Limited efficacy of atezolizumab and bevacizumab for hepatocellular carcinoma previously treated with tyrosine kinase inhibitor. Liver Int 2021;41:2233-2234.
5. Yamada T, Tateishi R, Iwai M, Koike K, Todo T. Neoadjuvant Use of Oncolytic Herpes Virus G47Δ Enhances the Antitumor Efficacy of Radiofrequency Ablation. Mol Ther Oncolytics 2020;18:535-545.

Innovative Bridging Therapies for Hepatocellular Carcinoma: From Transarterial Chemoembolization to Immune Checkpoint Inhibitors

Tomoharu Yamada *The University of Tokyo, Japan*

Since the late 1990s, liver transplantation for hepatocellular carcinoma (HCC) has gradually expanded through the extension of transplant criteria.[1] In the 2010s, two key strategies further broadened transplant eligibility: bridging strategy, which aims to prevent progression in listed patients within criteria, and downstaging strategy, which seeks to shrink tumors to bring patients within acceptable transplant criteria.[2,3]

In 2020, atezolizumab plus bevacizumab was approved for unresectable HCC, followed by the introduction of durvalumab plus tremelimumab in 2022, marking the beginning of the immunotherapy era in HCC using immune checkpoint inhibitors (ICIs).[4,5] While locoregional therapies such as transarterial chemoembolization (TACE) and radiofrequency ablation (RFA) have traditionally been used as bridging treatments before liver transplantation, systemic therapies—with their higher response rates—are now being explored as promising new bridging options.[6]

Although ICIs carry the risk of inducing allograft rejection through immune activation, recent retrospective studies suggest that liver transplantation performed 2–3 months after discontinuation of ICI therapy is associated with an allograft rejection rate of less than 20%, indicating that transplantation can be performed relatively safely in selected cases.[7,8]

Based on these findings, the EASL guidelines released in 2025 now include pre-transplant systemic therapy as a treatment option for selected transplant candidates.[9]

In this lecture, I will discuss the emerging role of systemic therapy as a novel bridging approach prior to liver transplantation.

References

1. Yao FY, Ferrell L, Bass NM, Watson JJ, Bacchetti P, Venook A, Ascher NL, et al. Liver transplantation for hepatocellular carcinoma: expansion of the tumor size limits does not adversely impact survival. Hepatology 2001;33:1394-1403.
2. Mehta N, Frenette C, Tabrizian P, Hoteit M, Guy J, Parikh N, Ghaziani TT, et al. Downstaging Outcomes for Hepatocellular Carcinoma: Results From the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT) Consortium. Gastroenterology 2021;161:1502-1512.
3. Lai Q, Sapisochin G, Gorgen A, Vitale A, Halazun KJ, Iesari S, Schaefer B, et al. Evaluation of the Inten-

tion-to-Treat Benefit of Living Donation in Patients With Hepatocellular Carcinoma Awaiting a Liver Transplant. JAMA Surg 2021;156:e213112.
4. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Kudo M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-1905.
5. Abou-Alfa GK, Lau G, Kudo M, Chan SL, Kelley RK, Furuse J, Sukeepaisarnjaroen W, et al. Tremelimumab plus Durvalumab in Unresectable Hepatocellular Carcinoma. NEJM Evidence 2022;1:EVIDoa2100070.
6. Frangakis C, Geschwind JF, Kim D, Chen Y, Koteish A, Hong K, Liapi E, et al. Chemoembolization decreases drop-off risk of hepatocellular carcinoma patients on the liver transplant list. Cardiovasc Intervent Radiol 2011;34:1254-1261.
7. Moeckli B, Wassmer CH, El Hajji S, Kumar R, Rodrigues Ribeiro J, Tabrizian P, Feng H, et al. Determining safe washout period for immune checkpoint inhibitors prior to liver transplantation: An international retrospective cohort study. Hepatology 2025.
8. Rezaee-Zavareh MS, Yeo YH, Wang T, Guo Z, Tabrizian P, Ward SC, Barakat F, et al. Impact of pre-transplant immune checkpoint inhibitor use on post-transplant outcomes in HCC: A systematic review and individual patient data meta-analysis. J Hepatol 2025;82:107-119.
9. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol 2025;82:315-374.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Soon Sun Kim

Ajou University

Self Introduction

Prof. Soon Sun Kim is a Professor at the Department of Gastroenterology, Ajou University School of Medicine. Currently, she serves in this position since March 2025. Previously, she held several roles at the same institution, including Associate Professor (2020-2025), Assistant Professor (2016-2020), Clinical Assistant Professor (2012-2016), and Clinical Fellow (2010-2012). She completed her residency and internship in Internal Medicine at Ajou University Hospital.

She earned her Ph.D. in Medicine from Ajou University School of Medicine in 2013 and holds a Master's degree and Doctor of Medicine from the same institution.

Research Interests

Hepatocellular Carcinoma, Biomarkers, Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Big Data, Microbiome

Representative Publications

1. Kim SS, Lee J, Ahn SB, et al. Clinical Course and Prognosis of Long-Term Survivors of Hepatocellular Carcinoma. Aliment Pharmacol Ther. 2025;61(8):1333-1342.
2. Son JA, Weon JH, Baek GO, Ahn HR, Choi JY, Yoon MG, et al. Circulating small extracellular vesicle-derived splicing factor 3b subunit 4 as a non-invasive diagnostic biomarker of early hepatocellular carcinoma. J Exp Clin Cancer Res. 2023;42:288.
3. Kim SS, Lee JY, Park SJ, Choi HJ. Early detection of hepatocellular carcinoma via liquid biopsy: Panel of small extracellular vesicle-derived long noncoding RNAs identified as markers. Mol Oncol. 2021;15:2715-2731.
4. Ahn HR, Baek GO, Yoon MG, et al. Hypomethylation-mediated upregulation of the WASF2 promoter region correlates with poor clinical outcomes in hepatocellular carcinoma. J Exp Clin Cancer Res. 2022;41(1):158.
5. Kim SS, Cho HJ, Lee JH, Park SY. Serum small extracellular vesicle-derived LINC00853 as a novel diagnostic marker for early hepatocellular carcinoma. Mol Oncol. 2020;14:2646-2659.

Post-Transplant Hepatocellular Carcinoma Recurrence: Predictors, Surveillance, and Novel Interventions

Soon Sun Kim *Ajou University*

Hepatocellular carcinoma (HCC) remains one of the leading indications for liver transplantation (LT), and appropriately selected candidates often achieve excellent long-term outcomes. However, HCC recurrence after LT occurs in 15–20% of recipients, and is associated with markedly poor survival. Notably, over 70% of recurrences occur within the first 2 years, underscoring the need for accurate risk stratification, optimized surveillance, and effective post-LT interventions.

Predictors of Recurrence

Prediction models have evolved from focusing solely on tumor morphology to integrating biomarkers, explant pathology, and molecular signatures. Among serologic markers, AFP-L3 and des-gamma-carboxy prothrombin (DCP) have demonstrated superior prognostic value over AFP alone. In a prospective cohort, Norman et al. (2023) reported that dual positivity (AFP-L3 ≥15% and DCP ≥7.5) was strongly associated with 3-year recurrence-free survival of only 43.7%, compared to 97% in biomarker-negative patients. Their subsequent study (2024) incorporated these biomarkers into the RETREAT scoring system, resulting in an improved AUC of 0.86 for predicting post-LT recurrence. Pretransplant immunotherapy has emerged as a topic of debate. In a 2025 meta-analysis, Yang et al. showed that immune checkpoint inhibitors (ICIs) used prior to LT were associated with 26% risk of acute rejection and 10% recurrence at a median follow-up of ~2 years. Downstaging within Milan criteria and longer ICI-to-LT intervals were protective against rejection. These findings suggest that in select cases, ICIs may be used without significantly compromising post-LT outcomes. Immunosuppression regimens also play a pivotal role. De Simone et al. (2023) demonstrated that mTOR inhibitor–based therapy (everolimus) reduced recurrence risk by more than half compared to tacrolimus (7.7% vs. 16.9%), with a hazard ratio of 0.46 after IPTW adjustment. Early introduction and therapeutic-level exposure were critical to maximizing benefit.

Surveillance Strategies

Standard surveillance recommendations suggest 3–6-month interval imaging with CT or MRI and tumor markers during the first 2 years, with individualized adjustments thereafter. Risk-adapted strategies are increasingly advocated. Burra et al. (2024) recommend intensified imaging and biomarker-based monitoring for patients with high-risk features such as microvascular invasion or Milan-out tumors.

Emerging modalities include circulating tumor DNA (ctDNA), exosomal RNA, and AI-based imaging tools. Although still investigational, these may provide earlier detection of recurrence. The role of PET/CT remains limited but may be considered in selected high-risk patients.

Novel Interventions and Adjuvant Strategies

Despite ongoing efforts, no established adjuvant therapy exists to prevent post-LT recurrence. The SiLVER trial (NCT00355862), a phase III RCT, found no overall survival benefit with sirolimus, though subgroup analysis suggested reduced recurrence in selected patients. Trials exploring sorafenib as adjuvant therapy (e.g., NCT01624285) faced challenges in accrual and tolerability, and were ultimately inconclusive. A retrospective study (Oropeza et al., 2025) noted no survival benefit and frequent toxicity in sorafenib-treated patients. Novel approaches include post-recurrence ICI therapy. Ongoing trials (NCT03966209, NCT04564313) are evaluating PD-1 inhibitors (toripalimab, camrelizumab) for safety and efficacy in post-LT recurrence, with early focus on graft rejection risk and tumor response.

Conclusion

Post-transplant HCC recurrence continues to present a clinical challenge. Integration of serologic biomarkers, pathology, and individualized surveillance strategies offers improved recurrence prediction. While mTOR-based immunosuppression shows promise, effective adjuvant therapies remain elusive. Future directions include prospective biomarker-guided trials and safe deployment of immunotherapy in post-LT settings.

References

1. Norman JS, Li PJ, Kotwani P, Shui AM, Yao F, Mehta N. AFP-L3 and DCP strongly predict early hepatocellular carcinoma recurrence after liver transplantation. J Hepatol 2023;79:1469–1477.
2. Norman JS, Li PJ, Kotwani P, Yao FY, Pham S, Gamez J, et al. Enhancing the prognostic accuracy of the RETREAT score with AFP-L3 and DCP tumor markers. Liver Transpl 2024;30:309–318.
3. Rezaee-Zavareh MS, Yeo YH, Wang T, et al. Impact of pre-transplant immune checkpoint inhibitor use on post-transplant outcomes in HCC: A systematic review and individual patient data meta-analysis. J Hepatol 2025;82:107–119.
4. De Simone P, Ferla F, Gruttadauria S, et al. Everolimus mitigates the risk of hepatocellular carcinoma recurrence after liver transplantation. Cancers (Basel) 2023;15:598.
5. Oropeza A, et al. Sorafenib as adjuvant therapy post–liver transplant: A single-center experience. Transplant Direct 2025;11:e1375.
6. Burra P, et al. Hepatocellular carcinoma recurrence after liver transplantation: Risk factors, targeted surveillance, and management options. Hepatoma Res 2024;10:259–268.
7. Geissler EK, Schnitzbauer AA, Zülke C, Lamby PE, Proneth A, Duvoux C, et al. Sirolimus use in liver transplant recipients with hepatocellular carcinoma: A randomized, multicenter, open-label phase 3 trial. Transplantation 2016;100:116–125.
8. U.S. National Library of Medicine. A study of JS001 (toripalimab) in the treatment of recurrent hepatocellular carcinoma after liver transplantation. ClinicalTrials.gov Identifier: NCT03966209 [Internet]. Available from: https://clinicaltrials.gov/study/NCT03966209
9. U.S. National Library of Medicine. Safety and efficacy study of camrelizumab in patients with recurrent hepatocellular carcinoma after liver transplantation. ClinicalTrials.gov Identifier: NCT04564313 [Internet]. Available from: https://clinicaltrials.gov/study/NCT04564313
10. U.S. National Library of Medicine. Sorafenib as adjuvant therapy following liver transplantation in hepatocellular carcinoma patients with high recurrence risk. ClinicalTrials.gov Identifier: NCT01624285 [Internet]. Available from: https://clinicaltrials.gov/study/NCT01624285

Tomoharu Yoshizumi

Kyushu University, Japa

Self Introduction

Prof. Yoshizumi graduated from Kyushu University Faculty of Medicine, JAPAN in 1992 and started general surgical resident, at Kyushu University Hospital from April, 1992 to March, 1994.

He entered Graduate school of Kyushu University in 1994 and was conferred Ph.D. from Kyushu University in 2000.

He worked as a General Surgical Fellow at Saiseikai Karatsu Hospital, Saga, JAPAN between 1998 and 2000 and at Shin Nakama Hospital, Fukuoka, JAPAN between January, 2002 and March, 2003.

He worked as Research Fellow at Recanati/Transplant Institute, Mount Sinai Hospital, USA from April, 2000 to December, 2001. He experienced many living donor and cadaveric donor transplantation there.

He worked as an Assistant Professor at Department of Surgery and Science, Kyushu University (2003-2006 and 2007-2010) and at Department of Surgery, University of Tokushima (2006-2007).

He worked as an Associate Professor at Department of Surgery and Science, Kyushu University (2010-2022).

He has become Professor at Department of Surgery and Science, Kyushu University since 2022.

He is an expert in liver surgery including minimal invasive surgery and liver transplantation, among hepatobiliary surgery. He is a director of Japan Surgical Society, Japanese Society for Transplantation and Endoscopic Liver Surgery Study Group.

Research Interests

Portal Modulation in Living Donor Liver Transplantation, Liver Transplantation for Hepatocellular Carcinoma

Representative Publications

1. Toshima T., Harada N., Yoshizumi T, et al. What Are Risk Factors for Graft Loss in Patients Who Underwent Simultaneous Splenectomy During Living-donor Liver Transplantation? Transplantation; 108(7): 1593-604, 2024.
2. Akahoshi K., Shindoh J., Yoshizumi T., et al. Oncological Resectability Criteria for Hepatocellular Carcinoma in the Era of Novel Systemic Therapies: The Japan Liver Cancer Association and Japanese Society of Hepato-Biliary-Pancreatic Surgery Expert Consensus Statement 2023. Liver Cancer; 13(6): 0-10, 2024.
3. Toshima T., Rhu J., Yoshizumi T., et al. Aborted living-donor liver transplantation in the real-world setting, lessons from 13 937 cases of Vanguard Multi-center Study of International Living Donor Liver Transplantation Group. Am J Transplant; 24(1): 57-69, 2024.
4. Yoshizumi T., Itoh S., Shimokawa M., et al. Simultaneous splenectomy improves outcomes after adult living donor liver transplantation. J Hepatol; 74(2): 372-79, 2021.
5. Itoh S., Yoshizumi T., Yugawa K., et al. Impact of Immune Response on Outcomes in Hepatocellular Carcinoma: Association With Vascular Formation. Hepatology; 72(6): 1987-99, 2020.

Immunosuppression and Immunotherapy in Post-Liver Transplant Hepatocellular Carcinoma: Striking the Right Balance

Tomoharu Yoshizumi *Kyushu University, Japa*

Due to the establishment of strict preoperative criteria, including the Milan criteria, the prognosis of liver transplantation (LT) for hepatocellular carcinoma (HCC) has improved compared to the past. However, in cases where HCC recurrence occurs after LT, patients are under immunosuppression, making them more susceptible to multiple organ and multiple site recurrences. The recurrence patterns after LT are reported as follows: intrahepatic recurrence in 16% of cases, combined intrahepatic and extrahepatic recurrence in 32%, and extrahepatic recurrence alone in 52%. The median time to HCC recurrence after LT is 17 months, with reported recurrence rates of 5.1% at 1 year, 14.3% at 5 years, and 16.4% at 10 years.[1]

If all recurrent lesions are surgically resectable, the 5-year survival rate after recurrence is 58.2%, and the median survival period after recurrence is 5.95 years. However, in cases where surgical resection is not feasible and only sorafenib was available as a treatment option, the 3-year survival rate was 0%, with a median post-recurrence survival of only 6.8 months.[2]

The treatment of HCC has been undergoing significant changes as new drug regimens, including immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs), become increasingly available.[3] However, ICIs function by activating the immune system, such as cytotoxic T cells, raising concerns about the risk of rejection in LT recipients. For this reason, the AASLD guidelines recommend sorafenib or lenvatinib as the first-line treatment for recurrent HCC after LT, while ICIs are not recommended due to the increased risk of graft loss and mortality.[4] A recent review reported a disease control rate of 25.6% and a progressive disease rate of 46.2% with ICI use after LT. The incidence of rejection was 20.5%, and among those who experienced rejection, 50% resulted in death. Evaluation using biopsy from graft liver indicated that PD-L1-negative cases had a 0% rejection rate, whereas PD-L1-positive cases had a rejection rate of 66.7%.[5,6]

The use of ICIs after LT remains controversial, and no definitive conclusion has been reached regarding their appropriate use.

Reference

1. Tabrizian P. Advances in Understanding the Complexities of Recurrent HCC Following Liver Transplantation. Transplantation, online ahead of print
2. Kurihara T, Yoshizumi T, et al. Predictive Factors for the Resectable Type of Hepatocellular Carcinoma Recurrence After Living Donor Liver Transplant. Transplant Proc 55: 191-6, 2022
3. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma J Hepatol 2025; 82: 315-374.
4. Singal AG, et al. AASLD Practice Guidance on Prevention, Diagnosis, and Treatment of Hepatocellular Carcinoma Hepatology 78: 1922-65, 2023
5. Kahramangil D, et al. Immune checkpoint inhibitors in the posttransplant landscape of HCC: A systematic literature review. Liver Transpl, Online ahead of print.
6. Shi GM, et al, Graft Programmed Death Ligand 1 Expression as a Marker for Transplant Rejection Following Anti-Programmed Death 1 Immunotherapy for Recurrent Liver Tumors. Liver Transpl 27: 444-9, 2021

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

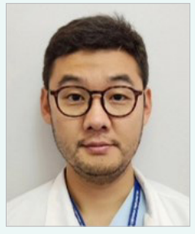
May 29 - 31, 2025 | HICO, Gyeongju, Korea

KAHBPS Symposium 1

Assessment and Management of Uncommon Considerations in Liver Surgery

Chairs:

Chinburen Jigjidsuren (Parliament of Mongolia, Mongolia)
Young Chul Yoon (The Catholic Univ. of Korea)



Unenbat Gurbadam

National Cancer Center, Mongolia

Self Introduction

Prof. Unenbat Gurbadam stands as a one of the leading figures in Mongolian healthcare and renowned by President of Mongolia in 2023, serving as the Chief of the Hepatobiliary and Pancreatic Surgery and Organ Transplantation Department at the National Cancer Center of Mongolia. His expertise lies in the intricate fields of hepatobiliary and pancreatic surgery and organ transplantation, where he has dedicated over 14 years of his career. HPB & Organ Transplant Center has 14 surgeons including urologist, 2 hepatologist and 1 transplant coordinator. Annually performs 950 surgeries and 60 liver transplants and one and only specialized liver, pancreas, gallbladder cancer services.

Research Interests

HPB, Liver Transplantation, Kidney Transplantation, Translational Research, HCC, CCC

Representative Publications

1. Unenbat, G. & Gantuya, Dorj & Chinburen, J.. (2024). The prognostic factors for longterm survival of hcc after liver surgery in Mongolia. HPB. 26. S214. 10.1016/j.hpb.2024.03.410.
2. Surgical outcome of laparoscopic liver resection in developing country, Gurbadam, Unenbat HPB, Volume 21, S392 - S393
3. Choi, Munseok & Wang, Gurbadam, Unenbat & Park, Byoung & Winslow, Emily & Fishbein, Thomas & Kang, Chang. (2023). Impact of adjuvant therapy in patients with invasive intraductal papillary mucinous neoplasms of the pancreas: an international multicenter cohort study. International journal of surgery (London, England). Publish Ahead of Print. 10.1097/JS9.0000000000000537.
4. Dorj, Gereltuya & Baatarkhuu, Oidov & Gantuya, Dorj & Lkhagvaa, Undram & Walsh, Nick & Choijoo, Amarjargal & Gurbadam, Unenbat. (2025). Viral hepatitis elimination in Mongolia. 10.1016/B978-0-443-23629-7.00007-3.
5. Gurbadam, Unenbat (2024). Evaluation of glypican-3 in patients with hepatocellular carcinoma. Molecular and Clinical Oncology. 22. 10.3892/mco.2024.2796.

KAHBPS Symposium 1 | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

High-Grade Morbid Obesity in Liver Surgery

Unenbat Gurbadam *National Cancer Center, Mongolia*

Introduction

High-grade morbid obesity, also known as Class III obesity, is a severe health condition defined by a Body Mass Index (BMI) of 40 kg/m^2 or greater. The prevalence of this condition is increasing globally, posing significant challenges to healthcare systems. Morbid obesity is associated with a range of comorbidities, including cardiovascular disease, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD), which can progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma (HCC).[1] Liver surgery in patients with high-grade morbid obesity presents unique challenges due to these associated conditions, as well as the physiological changes related to obesity itself. This paper aims to explore the complexities of liver surgery in the context of high-grade morbid obesity, examining the impact on surgical outcomes, associated risks, and management strategies.

Impact of High-Grade Morbid Obesity on Liver Physiology and Disease

Obesity has a profound impact on liver physiology, primarily through the development of NAFLD. The excessive accumulation of triglycerides in hepatocytes, a hallmark of NAFLD, is often present in individuals with high-grade morbid obesity. This can progress to NASH, characterized by inflammation and hepatocyte injury, and eventually to fibrosis and cirrhosis, which are significant risk factors for liver dysfunction and complications.[2]

Liver surgery in patients with high-grade morbid obesity presents several challenges:

- **Technical Difficulties:** Increased abdominal wall thickness and visceral fat can make surgical access and visualization more challenging, regardless of the surgical approach (open or laparoscopic). This can lead to longer operative times and increased blood loss.[3]
- **Increased Risk of Complications:** Obese patients have a higher risk of postoperative complications, including wound infections, pneumonia, and venous thromboembolism. The risk of specific liver-related complications, such as bile leaks and post-hepatectomy liver failure (PHLF), may also be elevated, although this remains a subject of ongoing research.[4]
- **Cardiopulmonary Considerations:** Obesity is often associated with cardiopulmonary comorbidities,

such as sleep apnea, hypertension, and heart disease, which can increase the risk of complications during and after surgery.

- **Metabolic Dysfunction:** Patients with high-grade obesity frequently have metabolic syndrome, characterized by insulin resistance, dyslipidemia, and hypertension. These metabolic abnormalities can impair wound healing and increase the risk of infections.
- **Imaging Challenges:** Preoperative imaging can be more challenging in patients with high-grade obesity due to body habitus, which can limit the quality of ultrasound, CT, and MRI scans.

Preoperative Assessment and Management

Careful preoperative assessment is essential for patients with high-grade morbid obesity undergoing liver surgery. This assessment should include:

- **Detailed Medical History and Physical Examination:** Evaluation of comorbidities, including cardiovascular, pulmonary, and metabolic conditions.
- **Laboratory Tests:** Assessment of liver function (e.g., AST, ALT, bilirubin, albumin), coagulation profile, and metabolic parameters.
- **Imaging Studies:** Ultrasound, CT, or MRI to evaluate liver size, anatomy, and the presence of steatosis, fibrosis, or tumors. Advanced imaging techniques may be needed to accurately assess liver disease.
- **Assessment of Liver Function:** Evaluation of functional liver reserve using tests such as the indocyanine green (ICG) clearance test, especially in cases of major liver resection.
- **Multidisciplinary Approach:** Involvement of a multidisciplinary team, including hepatologists, surgeons, anesthesiologists, and nutritionists, to optimize patient management.
- **Weight Optimization:** Preoperative weight loss, if feasible, can improve surgical outcomes.

Surgical Techniques and Outcomes

Both open and laparoscopic liver resection can be performed in obese patients. Laparoscopic surgery, when feasible, may offer advantages such as reduced blood loss, shorter hospital stays, and lower rates of wound complications.[5] However, laparoscopic procedures can be technically challenging in patients with high-grade obesity.

- **Laparoscopic Liver Resection:** Studies have shown that laparoscopic liver resection can be safely performed in obese patients, but may require longer operative times.
- O**pen Liver Resection:** Open surgery remains a standard approach, particularly for complex resections or in patients with significant comorbidities.
- **Bariatric Surgery and Liver Disease:** Bariatric surgery can improve NAFLD and NASH and may be considered in obese patients with liver disease, potentially even prior to liver resection in selected cases.

Conclusion

High-grade morbid obesity presents significant challenges in liver surgery. Careful patient selection, comprehensive preoperative assessment, and a multidisciplinary approach are crucial for optimizing surgical outcomes. While both open and laparoscopic liver resection can be performed in these patients, surgeons must be aware of the increased risk of complications and adapt their techniques accordingly. Further research is needed to refine surgical strategies and improve long-term outcomes in this complex patient population.

References

1. Aminian A, et al. Bariatric Surgery Reduces Liver Complications in Obese Patients with Cirrhosis. Nature Medicine. 2025.
2. Obesity and its influence on liver dysfunction, morbidity and mortality after liver resection. PMC. https://pmc.ncbi.nlm.nih.gov/articles/PMC10598315/
3. Liver resection in obese patients: results of a case–control study - PMC. https://pmc.ncbi.nlm.nih.gov/articles/PMC3044344/
4. Impact of recipient morbid obesity on outcomes after liver transplantation - Frontiers Publishing Partnerships. https://www.frontierspartnerships.org/articles/10.1111/tri.12483/pdf
5. The impact of obesity on laparoscopic liver surgery: a critical reappraisal - Machairas https://ls.amegroups.org/article/view/4335/4938

Haeil Jung

Soonchunhyang University

Self Introduction

Prof. Haeil Jung is a Professor of the Department of Surgery, Soonchunhyang University College of Medicine and he graduated from Chungnam National University College of Medicine with his medical degree in 2005 and completed his internship and residency at the Department of Surgery at Soonchunhyang University Hospital, receiving his diploma in General Surgery in 2020.

Since 2013	He has been taking a lot of board member including below
2006-Present	The Korean Surgical Society
2013-Present	The Korean Society of Surgical Oncology
2013-Present	The Korean Association of Hepatobiliary Pancreatic Surgery
2013-Present	The Korean Society of Endo-Laparoscopic & Robotic Surgery
2015-Present	The Korean Society for Transplantation
2015-Present	The Korean Pancreas Surgery Club
2018-Present	Korean Journal of Clinical Oncology Managing Editor
2025-Present	Annals of Clinical Nutrition and Metabolism, Hepatobiliary Editor

Research Interests

- Immunotherapy on Hepatobiliary Disease
- Fabrication of New Products to Prevent Pancreatic Leakage

Representative Publications

1. Multi-functional dual-layer nanofibrous membrane for prevention of postoperative pancreatic leakage. Shanto PC, Fahad MAA, Jung HI, Park M, Kim H, Bae SH, Lee BT. Biomaterials. 2024 Jun;307:122508. doi: 10.1016/j.biomaterials.2024.122508. Epub 2024 Feb 19
2. Polycaprolactone-gelatin membrane as a sealant biomaterial efficiently prevents postoperative anastomotic leakage with promoting tissue repair. Joo G, Sultana T, Rahaman S, Bae SH, Jung HI, Lee BT. J Biomater Sci Polym Ed. 2021 Aug;32(12):1530-1547. doi: 10.1080/09205063.2021.1917107. Epub 2021 Aug 1.
3. Dual-layer nanofibrous PCL/gelatin membrane as a sealant barrier to prevent postoperative pancreatic leakage. Shanto PC, Tae H, Ali MY, Jahan N, Jung HI, Lee BT. J Biomater Sci Polym Ed. 2025 Feb;36(3):333-350. doi: 10.1080/09205063.2024.2402135. Epub 2024 Sep 18.
4. Prognostic significance of programmed cell death-ligand 1 expression on immune cells and epithelial-mesenchymal transition expression in patients with hepatocellular carcinoma. Jung HI, Ahn H, Oh MH, Yun J, Lee H, Bae SH, Kim YK, Kim SY, Baek MJ, Lee MS. Ann Surg Treat Res. 2023 Nov;105(5):297-309. doi: 10.4174/astr.2023.105.5.297. Epub 2023 Oct 31
5. Impact of longitudinal tumor location on postoperative outcomes in gallbladder cancer: Fundus and body vs. neck and cystic duct, a retrospective multicenter study. Kim KH, Moon JI, Park JW, You Y, Jung HI, Choi H, Hwang SE, Jo S. Ann Hepatobiliary Pancreat Surg. 2024 Nov 30;28(4):474-482. doi: 10.14701/ahbps.24-117. Epub 2024 Aug 20.

Assessment and Management of Severe Cardiovascular Disease in Liver Surgery

Haeil Jung *Soonchunhyang University*

The intersection of cardiovascular disease and liver surgery represents a critical area of concern in surgical practice. Recent studies indicate that patients with liver disease have a nearly doubled risk of cardiovascular complications, necessitating comprehensive preoperative assessment and management strategies. This presentation aims to elucidate the latest advancements in the evaluation of cardiovascular risk in patients undergoing liver surgery, including the implementation of new scoring systems such as the Revised Cardiac Risk Index (RCRI) and the utilization of advanced imaging techniques for non-invasive cardiovascular assessment.

We will discuss the importance of preoperative cardiovascular management, particularly in patients with recent cardiac events, and highlight evolving strategies for the management of anticoagulation and antiplatelet therapy. During surgery, real-time cardiovascular monitoring technologies and their implications for anesthetic management will be emphasized, alongside the latest findings regarding the impact of anesthetic agents on cardiovascular stability.

Postoperative care will focus on newly established protocols aimed at preventing cardiovascular complications, including early recovery programs that have shown promising results. Additionally, case studies will be presented to illustrate the practical application of these strategies and their outcomes.

In conclusion, the integration of updated guidelines and ongoing research is essential for optimizing the management of cardiovascular disease in patients undergoing liver surgery, ultimately improving patient outcomes and reducing the incidence of postoperative complications

References

1. Mangus, R. S., et al. (2020). “Cardiovascular Risks in Patients with Liver Disease: A Review.” Journal of Cardiac Surgery, 35(5), 1205-1213.
2. Fleisher, L. A., et al. (2014). “Acc/Aha 2014 Guideline on Perioperative Cardiovascular Evaluation and Management for Noncardiac Surgery.” Circulation, 130(24), 2215-2245.
3. Venneman, N. G., et al. (2019). “The Impact of Anesthesia on Cardiovascular Outcomes in Patients Undergoing Liver Surgery.” Anesthesia & Analgesia, 129(2), 444-452.
4. Mullen, J. T., et al. (2018). “Management of Anticoagulation in Patients Undergoing Liver Surgery.” Liver Transplantation, 24(12), 1760-1769.

Etsuro Hatano

Kyoto University, Japan

Self Introduction

Prof. Hatano graduated from Kyoto University in 1989. After residency in surgery, he entered Graduate school of Medicine, Kyoto University. He was in charge of microscopical reconstruction of hepatic artery in living related liver transplantation. He was doing research on signal transduction of hepatocyte apoptosis with Prof. David Brenner at University of North Carolina at Chapel Hill, USA. He resumed as a surgeon in 2000.
Since then, to establish multidisciplinary treatment of liver cancer, he joined and conducted several clinical studies. Especially, he experienced many high-level hepatobiliary surgeries for advanced diseases including liver cancer with macrovascular invasion. Recently, he developed the novel medical imaging projection system using projection mapping with indocyanine green fluorescence and applied for fluorescence-guided minimally invasive surgery.

Professional Organization Japan Liver Cancer Association

Chairman, Japan Surgical Society; Director, Instructing doctor, The Japanese Society of Gastroenterological Surgery; Instructing doctor, Japanese Society of Hepato-Biliary-Pancreatic Surgery; Director, Instructing doctor, The Japan Society for Transplantation; Director, Japanese Liver Transplantation Society; Councilor, Japan Society for Endoscopic Surgery; Councilor, Japan Surgical Association; Councilor, Japan Society for Surgical Infection; Councilor, The Japanese Society of Gastroenterology; Director, Instructing doctor, The Japan Society of Hepatology; Director, Instructing doctor, Japan Biliary Association; Director, Instructing doctor, Japan Pancreas Society; Instructing doctor, Japanese Journal of Portal Hypertension; Councilor, Japanese Clinical Oncology Group (Hepatobiliary Pancreatic Oncology Group) ; head of surgery

Research Interests

Multidisciplinary Treatment for Hepatobiliary Cancer, Minimally Invasive Surgery, Fluorescence-Guided Surgery, Color Coded Surgery, Liver Transplantation, Transplant Oncology

Representative Publications

1. Nakamura I, …Hatano E, et al. A classification model for resectability in hepatocellular carcinoma patients. Hepatol Res. 2024 Sep 27. doi: 10.1111/hepr.14108. Online ahead of print. PMID: 39329320
2. Ueno M, …Hatano E, et al. CRAFITY score as a predictive marker for refractoriness to atezolizumab plus bevacizumab therapy in hepatocellular carcinoma: a multicenter retrospective study. J Gastroenterol. 2024 Dec;59(12):1107-1118.
3. Shen YC, …Hatano E, et al. Clinical Outcomes and Histologic Findings of Patients With Hepatocellular Carcinoma With Durable Partial Response or Durable Stable Disease After Receiving Atezolizumab Plus Bevacizumab. J Clin Oncol. 2024 Dec;42(34):4060-4070.
4. Hatano E, Yoh T, Ishii T. Modification of the "new world" terminology: A new comprehensive notation for hepatectomy. J Hepatobiliary Pancreat Sci. 2024 Oct;31(10):689-69
5. Ichida A, Arita J, Hatano E, et al. A Multicenter Phase 2 Trial Evaluating the Efficacy and Safety of Preoperative Lenvatinib Therapy for Patients with Advanced Hepatocellular Carcinoma (LENS-HCC Trial). Liver Cancer. 2023 Nov 28;13(3):322-334.

Elderly Patients over 75 Years

Etsuro Hatano *Kyoto University, Japan*

As Japan enters an ultra-aging society, liver cancer patients are also aging. It has been reported that of the 37,296 liver cancer cases in 2019, 73.3% were aged 70 years or older, and 38.0% were aged 80 years or older. The surgical patients in our department are also aging, and the proportion of patients aged 65 years or older in 2022 was 44.7% of all cases, and 75 years or older was 21.5%. As the number of elderly people increases, the indications for treatment for the elderly have expanded, but elderly people are more frail than non-elderly people and often have comorbid cardiovascular and respiratory diseases, so careful judgment is required when determining whether or not to treat them.

Surgical treatment for liver cancer includes liver resection and liver transplantation. Liver transplantation is an extremely invasive procedure and requires a donor, so age is a factor in the suitability of the treatment. In the case of deceased donor liver transplantation, people up to 65 years old can register, and in the case of living donor liver transplantation, although this varies depending on the facility, Kyoto University's suitability is up to 69 years old. On the other hand, advanced age is not necessarily considered a limiting factor for hepatectomy. In a large-scale cohort study in Japan, hepatectomy in elderly patients with liver cancer had better outcomes in terms of both recurrence-free survival and overall survival compared with percutaneous aspiration therapy and TACE, and although complications and in-hospital deaths after hepatectomy increased with age up to the 70s, there was no difference between those in their 70s and those over 80 years of age. This is thought to be because the indications for resection and the selection of surgical procedures are determined based on the individual conditions of elderly patients. In addition, when comparing cases of initial hepatectomy for liver cancer in our department by age, recurrence-free survival did not change with age, but overall survival tended to decrease with age. Comparing the results from 2007-2018 with those from 1995-2006, overall survival was longer in younger patients, which can be seen as being largely due to improvements in post-recurrence survival rather than recurrence-free survival. This is likely a reflection of the fact that elderly people are more likely to die from other diseases, and that they are less tolerant of post-recurrence treatments, which have become a significant development in recent years.

In treatments other than liver transplantation, elderly people alone do not limit treatment. When treating elderly people, it is first necessary to consider whether or not they are in a state where they can

tolerate the adverse events associated with the treatment. In addition to the overall performance status and hepatic reserve, the decision is made taking into account renal function, bone marrow function, and the presence or absence of other comorbidities. In addition, in elderly patients, it is necessary to consider whether the expected benefits in improving prognosis are commensurate with the risk of adverse events and the associated deterioration in QOL. As patients get older, their expected life expectancy naturally becomes shorter, and even in cases where the tumor has progressed significantly, the life-prolonging benefits that can be expected from treatment are limited. The method of quantitatively evaluating the physical, mental, and social functions of elderly people is called geriatric assessment (GA), and dedicated GA tools have been developed for each domain. JCOG recommends the use of the simple G8, which broadly covers these domains, as a screening tool as a first step. How to incorporate these assessment results into actual treatment selection remains to be determined.

Chan Woo Cho

Yeungnam University

Self Introduction

Education

2006-2010 M.D., Kyungpook National University School of Medicine, Daegu, Korea
2015-2017 Ph.D., Sungkyunkwan University School of Medicine, Seoul, Korea

Professional Experience

2011-2015 Residency, Department of Surgery, Samsung Medical Center, Seoul, Korea
2015-2018 Fellow, Department of Curgery, Samsung Medical center, Seoul, Korea
2018-2024 Assistant Professor, Department of Surgery, Yeungnam University College of Medicine, Daegu, Korea
2024-Present Associate Professor, Department of Surgery, Yeungnam University College of Medicine, Daegu, Korea

Professional Organizations

The Korean Liver Cancer Association (KLCA)
Korean Association of Hepato-Biliary-Pancreatic Surgery (KAHBP)
The Korean Society of Endo-Laparoscopic & Robotic Surgery (KSELS)
The Korean Surgical Society (KSS)
The Korean Society for Transplantation (KST)
Korean Association for the Study of the Liver (KASL)
International Liver Transplant Society (ILTS)
International Laparoscopic Liver Society (ILLS)

KAHBPS Symposium 1 | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

End-Stage Renal Disease

Chan Woo Cho *Yeungnam University*

Renal dysfunction is a significant factor determining outcomes in posthepatectomy liver failure (POHF) and poses an independent risk for surgical mortality following liver surgery. For hepatic resection in patients with end-stage renal disease (ESRD), careful assessment and management strategies are essential for patient selection and meticulous perioperative care.

A study by Barbas et al. found that patients with ESRD did not show increased perioperative mortality (5.0% versus 2.3%; P=0.08), but did have a significantly higher rate of major complication 45.5% versus 28.5; P<0.001) compared to non-ESRD patients.[1] Additionally, another study indicated an elevated risk of postoperative infections and heart-related complications in the uremia-HCC group.[2] Higher risk of complications in ESRD patients undergoing hepatic resection highlights the need for thorough preoperative evaluation and risk stratification including detailed cardiac evaluation, optimization of renal function, and evaluation of infection risk.

The timing of dialysis in relation to surgery is critical. It is advisable to conduct the last preoperative hemodialysis within 24 hours before surgery, resuming hemodialysis on the first or second postoperative day. Furthermore, ESRD patients are susceptible to fluid overload and electrolyte imbalances. One study recommended the use of infusion solutions without potassium while strictly monitoring for overhydration.[3]

In one retrospective study with hepatocellular carcinoma (HCC) patients, the survival outcomes were comparable between uremia - HCC cohort and the HCC cohort, regardless of extent of hepatic resection. For the uremia - HCC cohort, the 1 - , 5 - , and 10 - year overall and disease - free survival rates were 86, 52, and 38 %, as well as 77, 27, and 18 %, respectively.[2]

In conclusion, managing ESRD patients undergoing hepatic resection is complex and requires a multidisciplinary approach involving hepatobiliary surgeons, nephrologists, anesthesiologists, and critical care specialists. With personalized assessments and collaborative care, hepatic resection in selected ESRD patients can be performed with acceptable outcomes, despite the increased risks of complications including POHF.

References

1. A. Barbas, P. Speicher, B. Clary (2014). Hepatic and pancreatic resection in patients with end-stage renal disease: a propensity analysis. HPB
2. C. Yeh, Jaw-Town Lin, L. Jeng, Iakovidis Charalampos, Tzu-Ting Chen, and 5 more (2013). Hepatic Resection for Hepatocellular Carcinoma Patients on Hemodialysis for Uremia: A Nationwide Cohort Study. World Journal of Surgery
3. M. Yamagata, T. Kanematsu, T. Matsumata, T. Nishizaki, T. Utsunomiya (1993). Possibility of hepatic resection in patients on maintenance hemodialysis. Hepato-Gastroenterology

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

KAHBPS Symposium 2

Laparoscopic Liver Resection vs. Robotic Liver Resection

Chairs:

Poowanai Sarkhampee (Sunpasitthiprasong Hospital, Thailand)
Sang Jin Kim (Korea Univ.)

Dai Hoon Han

Yonsei University

Self Introduction

Education

1997-2004	M.D. Chung Ang University College of Medicine, Seoul
2011	Master degree from Yonsei University
2021	Doctor of Medicine from Yonsei University
2024-2025	Internship, Chung Ang University Hospital, Seoul
2005.09	Residency in Surgery, Severance Hospital, Seoul
2012-2013	Fellowship, Hepatobiliary & Pancreas surgery Fellow, Severance Hospital, Seoul

Professional Experience

2014.03-2020.02	Clinical Assistant Professor of Surgery, Yonsei University College of Medicine, Korea
2020.03-2022.02	Clinical Associate Professor of Surgery, Yonsei University College of Medicine, Korea
2022.03-2024.02	Associate Professor of Surgery, Yonsei University College of Medicine, Korea
2024.03-Present	Professor of Surgery, Yonsei University College of Medicine, Korea

Research Interests

- Surgical Treatment of Primary and Metastatic Liver Cancer
- Liver Transplantation of Primary Liver Cancer and End-Stage Liver Disease
- Minimally Invasive Liver Surgery
- In vivo HCC and Liver Disease Modeling Using Organoid
- Surgical Video Analysis Using Artificial Intelligence

Representative Publications

1. Baek S, Ha HS, Han DH, Sung HJ, et al. Chip collection of hepatocellular carcinoma based on O2 heterogeneity from patient tissue. Nat Commun. 2024;15(1):5117
2. Kim NR, Han DH, Choi GH, Lee JG, Joo DJ, Kim MS, et al. Comparison of surgical outcomes and learning curve for robotic versus laparoscopic living donor hepatectomy: A retrospective cohort study. Int J Surg. 2022;108:107000.
3. Lee HS, Han DH, Cho K, Park SB, Kim C, Leem G, et al. Integrative analysis of multiple genomic data from intrahepatic cholangiocarcinoma organoids enables tumor subtyping. Nat Commun. 2023;14(1):237.
4. Hong SS, Han DH, Kim KS, Choi JS, Choi GH. Left-sided Hepatectomy Leads to Less Postoperative Liver Failure and Comparable Overall Survival to Right-sided Hepatectomy in Type II or IV Perihilar Cholangiocarcinoma. Ann Surg Oncol. 2023;30(3):1381-90
5. Park HJ, Han DH, Choi GH, Choi JS. Surgical outcomes of perihilar cholangiocarcinoma based on the learning curve of a single surgeon at a tertiary academic hospital: A retrospective study. Ann Hepatobiliary Pancreat

KAHBPS Symposium 2 | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

Technical Differences in Surgical Approaches

Dai Hoon Han *Yonsei University*

Introduction

Minimally invasive liver resection is now commonly performed through either laparoscopic (LLR) or robotic (RLR) techniques. While LLR has been widely adopted and offers advantages such as reduced blood loss and postoperative pain, it is inherently limited by two-dimensional visualization, restricted instrument motion, and ergonomic challenges. RLR was introduced to address these limitations through technological advancements, including 3D high-definition vision, articulated instruments, and improved ergonomics. This lecture aims to delineate the key technical differences between the two approaches, particularly in operative setup, visualization, instrument handling, bleeding control, liver parenchymal transection, and use of specialized devices.

1. Surgical Workflow and Operative Setup

LLR is typically performed bedside, with the surgeon directly handling long rigid instruments, and a scopist (camera assistant) providing the visual field. In contrast, RLR involves docking robotic arms after trocar insertion, with the surgeon operating from a remote console. This requires a skilled bedside assistant to manage suction, retraction, and introduction of ancillary tools. Although LLR allows immediate response to intraoperative events, such as bleeding, RLR demands undocking before conversion to open surgery, resulting in slight delays. The surgical flow is thus fundamentally different, with RLR emphasizing coordination and preparation.

2. Visualization and Camera Control

A major distinction lies in the quality and control of the visual field. Traditional laparoscopy provides a 2D image that limits depth perception, although recent 3D and 4K systems have mitigated this to some extent. However, these are still dependent on the scopist's skill, making it difficult to consistently maintain an optimal view. RLR offers a surgeon-controlled, stereoscopic 3D view with high magnification, providing greater precision in identifying tissue planes and vascular structures. Notably, while the robotic FireFly ICG system has aided vascular visualization, recent laparoscopic ICG cameras have demonstrated even clearer real-time imaging in some settings.

3. Instrument Dexterity and Surgeon Ergonomics

Laparoscopic instruments are limited to 4–5 degrees of freedom, making fine tasks such as suturing and intracorporeal knot-tying technically demanding. Robotic systems provide 7 degrees of freedom through wristed end-effectors that mimic human hand movements, enabling meticulous dissection in confined spaces. Additionally, RLR offers superior ergonomics: the surgeon operates in a seated position with arm support and reduced physical strain, which is especially advantageous in prolonged or complex resections. On the other hand, LLR often forces the surgeon into uncomfortable positions, contributing to fatigue and less precise instrument control over time.

One significant limitation of RLR remains the absence of tactile (haptic) feedback. While laparoscopic surgeons experience some degree of resistance through instruments, robotic surgery relies solely on visual cues to assess tissue tension. The recently released da Vinci 5 system has attempted to overcome this with integrated force feedback, although its effectiveness still requires clinical validation.

4. Hemostasis and Intraoperative Bleeding Control

Both LLR and RLR aim for minimal blood loss during hepatic transection, utilizing similar principles such as low central venous pressure and the Pringle maneuver. However, RLR provides certain advantages in bleeding control due to stable visualization and precise instrument articulation. Studies have shown reduced intraoperative blood loss and lower conversion rates in RLR compared to LLR. In cases of unexpected hemorrhage, RLR enables faster and more controlled suture placement or vessel clipping. In contrast, LLR may struggle with instrument maneuverability, increasing the likelihood of conversion if bleeding cannot be promptly controlled.

Furthermore, RLR integrates real-time imaging tools (e.g., TilePro with ICG fluorescence), allowing enhanced visualization of vascular anatomy, which supports safer and more strategic transection. Although LLR also utilizes intraoperative ultrasound and ICG, the robotic system offers more seamless visual integration.

5. Liver Parenchymal Transection Techniques and Device Use

In LLR, various transection tools such as ultrasonic shears (Harmonic), bipolar energy devices (LigaSure, Thunderbeat), CUSA, and water-jet dissectors are routinely employed. These allow selective tissue fragmentation and precise exposure of bile ducts and vessels. In RLR, many of these tools are not robotically integrated. Instead, surgeons rely on modified clamp-crush techniques using robotic Maryland forceps or bipolar energy devices like the vessel sealer or robotic Harmonic scalpel. Major vessels are controlled with clips or staplers, sometimes inserted by the bedside assistant due to the lack of robotic-compatible staplers or CUSA.

This difference in instrument availability affects surgical outcomes. While robotic systems offer superior precision and control, the lack of tools like CUSA can limit the surgeon's ability to preserve fine structures, which may increase the risk of bile leakage. Some studies from high-volume centers have reported a slightly higher incidence of bile leaks in RLR for this reason. Close coordination between console surgeon and assistant is thus essential during RLR to optimize safety and effectiveness.

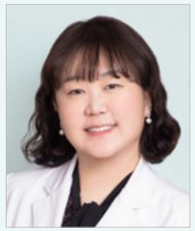
Conclusion

Both laparoscopic and robotic liver resections are effective, minimally invasive techniques that continue to evolve. LLR is cost-efficient and well-supported by a broad range of instruments, though it suffers from limited ergonomics and visualization. RLR, on the other hand, offers significant technical advantages—superior imaging, precision handling, and improved surgeon comfort—but currently lacks full integration of certain critical devices and haptic feedback.

Clinical outcomes are largely comparable in experienced hands, but RLR may provide specific benefits in complex cases, such as reduced blood loss and lower conversion rates. Future improvements in robotic platforms including tactile feedback systems and integrated dissection tools are expected to further close the gap and enhance its role in hepatobiliary surgery. Understanding these differences allows surgeons to better tailor their approach and refine their techniques according to each patient's needs and surgical complexity.

References

1. Giulianotti, P. C., Bianco, F. M., Daskalaki, D., Gonzalez-Ciccarelli, L. F., Kim, J., & Benedetti, E. (2016). Robotic liver surgery: technical aspects and review of the literature. Hepatobiliary Surgery and Nutrition, 5(4), 311–321.
2. Yang, W., & Peng, Y. (2025). Robotic liver surgery: should improving the safety and expanding the indication over laparoscopic liver surgery. Hepatobiliary Surgery and Nutrition, 14(1), 125–127.
3. Landry, J., Jain, A. J., Tzeng, C. W., Newhook, T. E., Ikoma, N., Chun, Y. S., … Tran Cao, H. S. (2025). Robotic hepatic parenchymal transection techniques: A choice between imperfect tools. Annals of Surgical Oncology, 32(2), 438–439.
4. Shimizu, A., Ito, M., & Lefor, A. K. (2022). Laparoscopic and robot-assisted hepatic surgery: an historical review. Journal of Clinical Medicine, 11(12), 3254.
5. Schmelzle, M., Feldbrügge, L., Ortiz Galindo, S. A., Moosburner, S., Kästner, A., Krenzien, F., et al. (2022). Robotic vs. laparoscopic liver surgery: a single-center analysis of 600 consecutive patients in 6 years. Surgical Endoscopy, 36(8), 5854–5862.
6. Ciria, R., Cherqui, D., Geller, D. A., Briceno, J., & Wakabayashi, G. (2016). Comparative short-term benefits of laparoscopic liver resection: 9000 cases and climbing. Annals of Surgery, 263(4), 761–777.
7. Tsung, A., Geller, D. A., & Sukato, D. C. (2014). Robotic versus laparoscopic hepatectomy: a matched comparison. Annals of Surgery, 259(3), 549–555. (One of the earlier comparative studies of RLR vs LLR, demonstrating feasibility and some advantages of RLR)
8. Choi GH, Chong JU, Han DH, Choi JS, Lee WJ. Robotic hepatectomy: the Korean experience and perspective. Hepatobiliary Surg Nutr, 6(4):230-238.



Su Young Hong

Seoul National University

Self Introduction

Prof. Su young Hong is an Assistant Professor in the Division of Hepatobiliary and Pancreatic (HBP) Surgery, Department of Surgery at Seoul National University Hospital, South Korea.

She received Bachelor of Pharmacy (Pharm.D.) from Seoul National University College of Pharmacy in 2011, followed by M.D. degree from Seoul National University College of Medicine in 2015. She went on to earn her Ph.D. in Surgery from the same institution in 2023.

After completing her internship at Seoul National University Hospital in 2016, Dr. Hong undertook residency in General Surgery from 2016 to 2020. She subsequently specialized further through a clinical fellowship in the Hepatobiliary Division until 2022. From 2022 to 2024, she served as a Clinical Professor in the same division. Between 2024 and 2025, she worked as a physician at the Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Korea.

She is actively involved in numerous professional societies, including the Korean Surgical Society, the Korean Association of Hepato Biliary Pancreatic Surgery, the Korean Society for Transplantation, the Korean Liver Transplantation Society, and the International Liver Transplantation Society, among others.

Research Interests

Robotic Liver Resection, Hepatocellular Carcinoma, Biliary and Vascular Complications after Living Donor Liver Transplantation

Representative Publications

1. Hong SY, Kang E, Woo HY, Lee H, Min S, Ha J. Strategies for Monitoring and Supporting Living Donors in Korea: An Expert Position Paper. J Korean Med Sci. 2024 Nov;40(10):e33.
2. Hong SY, Yi NJ, Hong K, Han ES, Suh S, Lee JM, Hong SK, Choi Y, Jin US, Chang H, Lee KW, Suh KS, Minn KW. Redo hepatic artery reconstruction for thrombosis without retransplantation in 1355 adult living donor liver transplantations. Liver Transpl. 2023 Sep 1;29(9):961-969.
3. Jang E, Hong SY, Hong SK, Lee S, Lee JM, Choi Y, Yi NJ, Lee KW, Suh KS. Initial outcome of external biliary drainage in living donor liver transplantation with pure laparoscopic donor hepatectomy. Liver Transpl. 2023 May 1;29(5):531-538.
4. Yoo BM, Hong SY, Hong SK, Ahn YH, Kang HG, Lee S, Suh S, Han ES, Lee JM, Choi Y, Lee KW, Suh KS, Yi NJ. Posttransplant renal replacement therapy is an alarm signal for survival outcomes in pediatric liver transplantation. Pediatr Transplant. 2023 Feb;27(1):e14422.

Challenges and Learning Curve for Beginners

Su Young Hong *Seoul National University*

Minimally invasive liver surgery, including laparoscopic and robotic approaches, has gained increasing popularity due to improved postoperative recovery and comparable oncologic outcomes to open surgery. However, the adoption of these techniques by beginners is hindered by a steep learning curve and procedure-specific technical challenges. Understanding the barriers and specific difficulties faced during the early phase of adoption is essential for optimizing training and ensuring safe implementation. This presentation aims to review key studies on the learning curve and adaptation of laparoscopic and robotic liver resections, and to share personal firsthand experiences with the practical difficulties encountered during the early phase of implementation.

Initial challenges in laparoscopic liver resection include limited visualization, rigid instrumentation, and the ergonomic strain of complex segmental resections. For robotic liver resection, while 3D visualization and articulated instruments mitigate some difficulties, beginners face unique challenges in robotic liver resection.

- **Liver mobilization** is more difficult due to limited retraction capability and lack of tactile feedback.
- **Lack of specialized instruments**, such as right-angle dissectors, can impede dissection and control of vascular structures.
- **Parenchymal dissection** presents an adaptation challenge for beginners who are familiar with the use of CUSA (Cavitron Ultrasonic Surgical Aspirator). In the robotic setting, where CUSA is not available, fine dissection of liver parenchyma must be performed using monopolar or bipolar energy devices, requiring a transition to unfamiliar dissection techniques.
- **High cost** of robotic surgery remains a significant barrier, especially for early-career surgeons. Financial constraints often limit case selection flexibility and restrict opportunities to gain sufficient experience during the early learning phase.

The estimated learning curve for laparoscopic minor resections is approximately 45–60 cases, while robotic resection may require 20–40 cases for minor procedures due to improved ergonomics. Major hepatectomy in either approach significantly extends the learning period.

Robotic liver surgery offers meaningful technical advantages, but early adoption by beginners is hindered by both procedural and systemic challenges. In particular, the absence of familiar tools like CUSA and the need to adapt to new dissection methods represent technical barriers, while high costs restrict case exposure. To ensure safe and effective adoption, institutional support, case selection guidance, and structured mentorship programs are essential.

Kwan Woo Kim

Dong-A University

Self Introduction

Career

1992-1997	Dong-A University College of Medicine, Busan
1999-2003	Asan Medical Center, Seoul Department of Surgery, Intern, Resident
2007-2009	Asan Medical Center, Seoul Division of LT and Hepato-Biliary-Pancrease Surgery, Fellow
2010-2012	Inje University Haeundae Paik Hospital, Busan, Division of Liver Transplantation and Hepato-Biliary-Pancrease Surgery, Assistant professor
2013-Current	Dong-A University College of Medicine, Busan, Chief of organ transplantation center Division of Liver Transplantation and Hepato-Biliary-Pancrease Surgery, Professor

Representative Publications

1. Jang EJ, Kang SH, Kim KW. The method of using robotic Harmonic ACE curved shears for parenchymal transection in robotic hepatectomy. J Minim Invasive Surg. 2024 Jun 15;27(2):114-117. doi: 10.7602/jmis.2024.27.2.114. PMID: 38887003; PMCID: PMC11187608.
2. Shin SY, Jang EJ, Kang SH, Park EH, Kim KW. Advancing treatment for perihilar cholangiocarcinoma: role of hepatopancreaticoduodenectomy in small-volume centers. Front Surg. 2024 May 14;11:1406508. doi: 10.3389/fsurg.2024.1406508. PMID: 38807927; PMCID: PMC11130399.
3. Jang EJ, Kang SH, Kim KW. Exploring the feasibility of robotic liver resection in a limited resource setting. J Robot Surg. 2024 Apr 29;18(1):187. doi: 10.1007/s11701-024-01901-1. PMID: 38683380.
4. Jang, E.J., Kim, K. Comparative analysis of robotic single-site cholecystectomy outcomes between novice and expert surgeons. J Robotic Surg 18, 118 (2024). https://doi-org.libproxy.donga.ac.kr/10.1007/s11701-024-01859-0
5. Jang EJ, Kang SH, Kim KW. Intrahepatic Cholangiocarcinoma in Wilson's Disease: A Case Report. Am J Case Rep. 2024 Jan 27;25:e942372. doi: 10.12659/AJCR.942372. PMID: 38279525; PMCID: PMC10829935.

Clinical Outcomes and Complications: Laparoscopic vs. Robotic Liver Resection

Kwan Woo Kim *Dong-A University*

Minimally invasive liver surgery, including laparoscopic liver resection (LLR) and robotic liver resection (RLR), has become an important approach for treating liver tumors. Both techniques are widely used in experienced centers for a range of procedures, from minor resections to complex major hepatectomies. Recent studies suggest that RLR may offer technical advantages in complex cases due to its enhanced 3D visualization, wristed instruments, and ergonomic comfort.[1,4] Comparative analyses show that RLR is associated with reduced intraoperative blood loss, lower conversion rates, and a similar or slightly lower rate of postoperative complications when compared to LLR, although operative time is generally longer.[1,2]

LLR remains a highly effective and widely adopted technique with a well-established safety profile. It is supported by validated difficulty scoring systems (e.g., Iwate, IMM, Southampton) that help in case selection and surgical planning.[3] Both LLR and RLR demonstrate equivalent oncologic outcomes, including R0 resection rates and long-term survival for hepatocellular carcinoma and colorectal liver metastases.[3,5]

A recent randomized controlled trial confirmed that there is no significant difference in postoperative quality of life, complications, or survival between the two techniques.[5] Although RLR may involve higher costs, its use is expanding globally, especially in high-volume centers with access to robotic platforms.

Ultimately, the choice between RLR and LLR should be individualized, based on patient-specific factors, tumor location and complexity, and surgeon expertise. Both approaches represent safe, effective, and evolving strategies in hepatobiliary surgery.

References

1. Nota CLM et al. Ann Surg. 2024.
2. Chen PD et al. World J Gastroenterol. 2015; 21(27):8441–8449.
3. Wakabayashi G et al. Surg Endosc. 2018.
4. Scuderi V et al. Cancers (Basel). 2022.
5. Soubrane O et al. Lancet Reg Health Eur. 2024.

Kwangho Yang

Pusan National University

Self Introduction

Educational

1996-2002 Pusan National University, School of Medicine

Professional Experience

2003-2007 Resident, Department of Surgery, Pusan National University Hospital

2010-2012 Fellow, Division of HBP and Transplantation Surgery, Department of Surgery, Pusan National University Yangsan Hospital

2012-2017 Assistant Professor, Division of HBP and Transplantation Surgery, Department of Surgery, Pusan National University Yangsan Hospital

2017-Present Associate Professor, Division of HBP and Transplantation Surgery, Department of Surgery, Pusan National University Yangsan Hospital

Research Interests

Liver Transplantation and Outcomes

Representative Publications

1. Yang K, Park Y, Moon K, Ryu J, Chu C. Caudal middle hepatic vein trunk preserved right lobe graft in living donor liver transplantation. Ann Surg Treat Res. 2014 Oct;87(4):185-91.
2. Lee TB, Ko HJ, Shim JR, Choi BH, Ryu JH, Yang K. ABO-Incompatible Living Donor Liver Transplantation with a Simplified Desensitization and Immunosuppression Protocol: A Single-Center Retrospective Study. Exp Clin Transplant. 2021 Jul;19(7):676-685.
3. Yang K, Lee TB, Choi BH, Park YM, Ryu JH, Joo DJ, Chu CW. Development and Applicability of the A-P 200 Criteria for Liver Transplantation for Hepatocellular Carcinoma. Transplant Proc. 2016 Dec;48(10):3317-3322.

KAHBPS Symposium 2 | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

Open Liver Resection as a Good Surgical Approach: Indications and Outcomes

Kwangho Yang *Pusan National University*

Today, minimal invasive liver resection (MILR) has become a widely accepted approach for managing liver tumors. The majority of recent studies indicate that MILR had better short-term surgical outcomes than open liver resection (OLR) and equivalent long-term oncologic outcomes. However, OLR remains indispensable in specific clinical scenarios where minimal invasive techniques may be limited.

1. Posterosuperior Segments

Posterosuperior segments are anatomically deep and located beneath the diaphragm, making laparoscopic access technically demanding and ergonomically challenging. OLR enables better exposure and vascular control, especially in lesions abutting the inferior vena cava or hepatic veins. Nevertheless, in recent years, MILR of the poseterosuperior segments has been increasingly performed due to the development of 3D, flexible scope and surgical instruments.

2. Large or Multiple Tumors

Larger tumors require wider resection margins to ensure oncologic adequacy. Furthermore, en bloc resection or anatomical hepatectomy is often necessary. In such cases, OLR allows precise control of intraoperative bleeding and facilitates safe specimen extraction minimizing risk of tumor rupture or seeding. While it is technically feasible to perform MILR for larger lesions, the data in this regard are lacking, and OLR may be more appropriate. Similarly, OLR may be favored among patients with multifocal malignancy disease, as the benefits of MILR are less established.

3. Major Vessel Invasion

When tumors are adjacent to or encasing major vascular structures such as the portal vein, hepatic artery, or major hepatic veins, OLR provides superior visualization and allows for vascular isolation, clamping, or reconstruction. This is crucial for minimizing intraoperative blood loss and achieving negative surgical margins.

4. Repeat Hepatectomy

In patients with prior liver surgery, severe adhesions increase the risk of bowel or vascular injury during

laparoscopic or robotic dissection. OLR offers better tactile feedback and facilitates safer adhesiolysis, especially in cases involving previous major hepatectomy or bile duct reconstruction.

5. Advanced Liver Cirrhosis

In cirrhotic patients with complications such as splenomegaly, thrombocytopenia, or varices, OLR allows for meticulous hemostasis and intraoperative management of collateral vessels. It also enables parenchyma-sparing techniques that are critical in preserving residual liver function.

In conclusion, despite the rise of minimally invasive techniques, OLR retains critical value in era of minimal invasive surgery. Careful patient selection and understanding of its indications are essential for optimizing surgical outcomes.

References

1. Alvikas J, Lo W, Tohme S, Geller DA. Outcomes and Patient Selection in Laparoscopic vs. Open Liver Resection for HCC and Colorectal Cancer Liver Metastasis. Cancers (Basel). 2023 Feb 12;15(4):1179.
2. Berardi G, Muttillo EM, Colasanti M, et al. Challenging Scenarios and Debated Indications for Laparoscopic Liver Resections for Hepatocellular Carcinoma. Cancers (Basel). 2023 Feb 27;15(5):1493.
3. Jo SJ, Rhu J, Kim JM, et al. Indications for open hepatectomy in the era of laparoscopic liver resection: a high volume single institutional study. J Liver Cancer. 2022 Sep;22(2):146-157.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

KLTS Coordinator Session

Multidisciplinary Approach to Liver Transplantation for Alcohol-Associated Liver Disease

Chairs:

Seung Heui Hong (Samsung Medical Center)
Hae Won Lee (Seoul National Univ.)

Kye-Seong Lee

Incheon Chamsarang Hospital

Self Introduction

Dr. Kye-Seong Lee was graduated from Yonsei University Wonju medical college in 1994. and received diploma of psychiatrist in 1999.

He served as 4th grade ofiicial of Ministry for Health & Welfare of Korean Government from 2009 to 2014.

From 2015 he has worked as Research director and Director of Addiction Treatment and Rehabilitation Center attached at Incheon Chamsarang Hospital.

He has served as a Director of Incheon Gyeyang-gu Addiction management Community Center, and Director of Association of Korean Addiction Treatment and Rehabilitation Community Center(2023-), and elected as next 17th President of Korean Academy of Addiction Psychiatry(2026-2028).

Research Interests

Alcohol, Gambling and Executive Funtion of Prefrontal Lobe

Representative Publications

1. Therapeutic Intervention for Mental Illness and Alcohol/Drug Use-Related Offenders. J Korean Academy of Addiction Psychiatry Vol. 20, No. 1, 3-9, 2016.
2. Deaths of Celebrities and Substance Use: A Qualitative Investigation. J Addiction Prevention 3(2): 6, 1-6, 2015.
3. Standardization of Korean Version of Alcohol, Smoking & Substance Involvement Screening Test . J Korean Academy of Addiction Psychiatry Vol. 18, No. 1, 29-36, 2014.
4. Treatment of Alcohol Use Disorder. j Korean Diabetes Vol13(2), 85-90,2012.
5. Alcohol Dependence : The Chemical Brain Injury, J Korean Academy of Addiction Psychiatry Vol. 12, No. 1, 15-23, 2008.

Alcohol Dependence and Liver Transplantation: The Importance of Mental Health Care

Kye-Seong Lee *Incheon Chamsarang Hospital*

Alcohol dependence is characterized by compulsive alcohol use, which can potentially result in death.

Recognizing alcohol dependence as a chronic, relapsing brain disorder is a crucial starting point for its management.

Binge drinking and prolonged alcohol use can cause irreversible damage to multiple organs, especially the liver and brain.

Similar to other relapsing chronic diseases such as diabetes or hypertension, alcohol dependence has no cure but is managable.

Therefore, long-term management strategies including treatment adherence, medication compliance, and continuity of care, are critical components of effective management.

The treatment of alcohol dependence is most effective when it integrates biological, psychological, and social approaches.

Hae Won Lee

Seoul National University

Self Introduction

Education

2000.02.26	Bachelor, Medical Science, Seoul Nation University
2007.02	Master, Surgery, Seoul Nation University
2011.08	Doctor, Surgery, Seoul Nation University

Professional Experience

2000-2006	Internship/Residency /Fellowship, Seoul National University Hospital
2007	Clinical Instructor, Seoul National University Hospital
2008-2010	Clinical Instructor/Assistant Professor, Konkuk University Hospital
2011-2019	Assistant/Associate Professor, Seoul National University Boramae Medical Center
2017	Visiting Associate Professor, Stanford University Medical Center
2020-Present	Professor, Seoul National University Bundang Hospital

Research Interests

- Liver Transplantation
- Liver Surgery
- Hepatocellular Carcinoma

Representative Publications

1. Lee HW, Song GW, Lee SG, et al. Patient Selection by Tumor Markers in Liver Transplantation for Advanced Hepatocellular Carcinoma. Liver Transpl. 2018;24(9):1243-1251.
2. Lee HW, Lee JM, Yoon JH, et al. A prospective randomized study comparing radiofrequency ablation and hepatic resection for hepatocellular carcinoma. Ann Surg Treat Res. 2018;94(2):74-82.
3. Lee HW, Suh KS. Advancements of liver transplantation for hepatocellular carcinoma in Korea. Jpn J Clin Oncol. 2017:23:47(2):93-100.
4. Lee DH, Lee HW, Ahn YJ, Kim H, Yi NJ, Lee KW, Suh KS. Initiating liver transplantation at a public hospital in Korea. J Korean Soc Transplant 2017;31(4):182-192.
5. Lee HW, Suh KS. Liver transplantation for advanced hepatocellular carcinoma. Clin Mol Hepatol. 2016 Sep;22:309-318.

Liver Transplantation for Alcohol-Associated Liver Disease: A Surgical Perspective and Prognosis

Hae Won Lee *Seoul National University*

Alcohol-associated liver disease (ALD) has emerged as the leading indication for liver transplantation (LT) in the United States, surpassing hepatitis C in recent years. In Korea as well, since the MELD-based allocation era, ALD has been rapidly increasing along with a decrease in hepatitis B as an indication for transplantation. This shift reflects both the success of antiviral therapies and the increasing incidence and recognition of severe ALD, particularly among younger patients and women. From a surgical perspective, the management of ALD presents a unique intersection of clinical, ethical, and logistical challenges.

Several recent cohort studies and registry analyses have documented the rising burden of ALD in transplant centers. According to the United Network for Organ Sharing (UNOS) database, alcohol-associated cirrhosis now accounts for over 40% of adult liver transplant listings. Alarmingly, there has been a notable increase in acute alcohol-associated hepatitis (AH) cases, particularly among individuals under 40. This trend has led to a reassessment of listing criteria, especially in relation to the traditional 6-month abstinence rule. Historically, many programs required a 6-month period of abstinence prior to LT to assess commitment to sobriety and allow for potential hepatic recovery. However, emerging data have challenged the efficacy and ethical basis of this rule. A landmark multicenter study by Mathurin et al. in 2011 demonstrated that selected patients with severe AH, unresponsive to medical therapy, could achieve excellent post-transplant outcomes without meeting the 6-month criterion. Subsequent studies have shown similar results, with 1-year survival rates exceeding 80% and low rates of alcohol relapse in carefully selected patients. Patient selection remains the cornerstone of successful outcomes in ALD transplantation. Contemporary approaches emphasize psychosocial evaluation, incorporating structured assessments of addiction history, support systems, insight into alcohol use disorder, and willingness to engage in long-term recovery. Tools such as the Sustained Alcohol Use Post-LT (SALT) score have been proposed to predict relapse risk, though no single metric reliably forecasts behavior.

In Korea, LT for ALD is rapidly increasing like in the Western countries, there is no systematic management system for ALD patients before and after transplantation. A surgeon's perspective often includes weighing the urgency of liver failure against the uncertainty of long-term sobriety. This balance requires close collaboration with addiction specialists, social workers, and transplant coordinators. When looking

at western experiences, programs adopting early transplantation for ALD have implemented rigorous multidisciplinary review processes, with favorable outcomes when these frameworks are in place. Although it may be difficult to prove statistically, it is not difficult to realize in actual clinical settings that family and social support have a significant impact on the prognosis of ALD transplant patients. Transplant coordinators play a vital role in post-transplant care, especially in supporting adherence to medical regimens and facilitating long-term sobriety. Studies have underscored the importance of continuous engagement with addiction services, structured follow-up, and early identification of relapse behaviors. Long-term outcomes are improved when patients are integrated into multidisciplinary recovery programs and receive ongoing psychosocial support.

From a technical standpoint, transplantation for ALD is not significantly more complex than for other etiologies. However, patients with ALD frequently accompany severe malnutrition, infections, or active systemic inflammation, which may present added intraoperative and postoperative risks. Timely intervention is essential, as prolonged decompensation can exacerbate frailty and impair recovery. The surgical team also should pay attention to managing alcohol-related complications, such as cardiomyopathy or pancreatitis, which may impact operative planning and graft function.

LT for ALD represents a dynamic and evolving area of clinical practice. Recent evidence supports a more individualized approach to candidate selection, moving beyond rigid abstinence periods and focusing on comprehensive, team-based evaluations. From a surgical perspective, timely transplantation can be life-saving and yields excellent outcomes when embedded in a robust framework of pre- and post-transplant support. I believe that not only transplant surgeons but also addiction specialists, transplant coordinators, and social workers are instrumental in guiding patients through this complex journey and ensuring sustained success beyond the operating room.

References

1. Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011;365(19):1790-800.
2. Lee BP, Vittinghoff E, Dodge JL, Cullaro G, Terrault NA. National Trends and Long-term Outcomes of Liver Transplant for Alcohol-Associated Liver Disease in the United States. JAMA Intern Med. 2019;179(3):340-348.
3. Lee BP, Vittinghoff E, Hsu C, et al. Predicting Low Risk for Sustained Alcohol Use After Early Liver Transplant for Acute Alcoholic Hepatitis: The Sustained Alcohol Use Post-Liver Transplant Score. Hepatology. 2019;69(4):1477-1487.
4. Jophlin LL, Singal AK, Bataller R, et al. ACG Clinical Guideline: Alcohol-Associated Liver Disease. Am J Gastroenterol. 2024;119(1):30-54.

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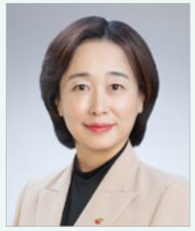

Sunyoung Son

Gangnam Severance Hospital

Self Introduction

Prof. Son is a Transplant Coordinator at the Transplantation Center of Gangnam Severance Hospital and currently serves as President of the Korean Organ Transplant Coordinator Organization. She is also Chair of the Coordinator Committee of the Korean Liver Transplantation Society, an Adjunct Professor at Yonsei University College of Nursing, and a long-standing member of the IRB Committee at Gangnam Severance Hospital.

She earned her PhD in Nursing from Yonsei University Graduate School in 2007, where she completed her dissertation on "The Experiences of Adolescents with Hematologic Malignancies." She also received her M.S. in Nursing in 2002 with a thesis on "Self-Image of Adolescents with Cancer," and obtained her B.S. in Nursing from Yonsei University College of Nursing in 1996.

Since 2010, she has served as a Transplant Coordinator at Gangnam Severance Hospital. Her previous roles include Full-time Instructor at the Red Cross College of Nursing, Transplant Coordinator at Myongji Hospital, Child Hospice Nurse at Yonsei University Medical Center, and Teaching Assistant at both Yonsei University and Red Cross College of Nursing.

She has also been actively involved in academic and professional leadership, including serving on the Board of Education for the Korean Society for Transplantation since 2017.

Research Interests

Patient Education and Self-Care Improvement in Transplantation, Donor Follow-Up and Health Management, Clinical Communication, Curriculum Development and Professional Competency of Transplant Coordinators, Ethical Decision-Making in Clinical Settings

Representative Publications

1. Son, S., Min, D., & Kim, S. (2025). Effectiveness of a simulation programme with lectures about end-of-life care using a standardised patient. BMC Nursing, 24, 371.
2. You, J., Kim, M., Son, S., & Lee, I. (2025). Organ donation and transplantation coordinators' experience and needs for ethics education. Nursing Ethics. (Advance online publication)
3. Kim, S., Son, S., Ju, M. K., Hong, S., Park, J. Y., & Kim, H. S. (2024). Workforce, task performance, and analysis of organ transplant coordinators in Korea: A survey study. Clinical Transplant Research, 38, 222–234.
4. Sim, M. K., Son, S., & Ju, M. K. (2022). Factors influencing the self-management of kidney transplant patients based on self-determination theory: A cross-sectional study. Korean Journal of Transplantation, 36, 37–44.
5. Kim, S., Ju, M. K., Son, S., Jun, S., Lee, S. Y., & Han, C. S. (2020). Development of video-based educational materials for kidney-transplant patients. PLOS ONE, 15(8), e0236750.

Coordination of the Liver Transplant Process and Patient Management for Alcoholic Liver Disease: Evolving Roles of Transplant Coordinators in Korea

Sunyoung Son *Gangnam Severance Hospital*

Alcohol-related liver disease (ALD) has become a leading indication for liver transplantation (LT) in Korea, accounting for 40% of brain-dead donor liver transplants in 2022. Despite this trend, there is no standardized national protocol for managing ALD patients before and after LT, and clinical practices vary widely across centers.

A new turning point was made at the first half of 2024 Korean Society for Liver Transplantation seminar, when the *My Liver Guardian* program, an ideal model for managing alcoholic liver disease (ALD) liver transplant recipients at Chonnam National University Hospital, was introduced. This presentation raised awareness of the Korean Association of Addiction Management Centers and laid the foundation for forming a multidisciplinary team. The Korean Society for Liver Transplantation subsequently formed a multidisciplinary collaboration team including transplant specialists, addiction psychiatrists, coordinators, and social workers, and began efforts to develop a national protocol.

Around the same period, a nationwide survey conducted by the Korean Society for Liver Transplantation revealed significant variability in the pre- and post-transplant management of ALD patients, further reinforcing the urgent need for standardized guidelines. While international practices emphasize the essential role of transplant coordinators in alcohol relapse monitoring and multidisciplinary coordination, this role remains underdeveloped and undervalued in Korea.

Recognizing this gap, we argue that empowering transplant coordinators must become a key agenda item in future policy and clinical development. However, the reality is sobering—many coordinators are already overextended, struggling for professional recognition and fair compensation. Assigning them greater responsibilities without structural support may widen the gap between expectation and capacity.

And yet, we cannot remain still. This presentation calls for collective commitment to change—investing in the coordinators, building collaborative systems, and sharing responsibility to create a more ethical, effective, and sustainable model for ALD liver transplantation in Korea.

Keywords: Alcohol-related liver disease, liver transplantation, transplant coordination, relapse prevention, multidisciplinary collaboration, protocol development, Korea

References

1. Park, H. S. (2024). My Liver Guardian: A multidisciplinary program for managing alcoholic liver disease liver transplant recipients. In Korean Society for Liver Transplantation (Ed.), 2024 First-Half Seminar Abstract Book (pp. 22–23). June 15, 2024, Seoul, Korea.
2. Lee, S. K. (2024). Liver transplantation for alcohol-related liver disease in Korea: The need for patient management guidelines. Annals of Liver Transplantation, 4(2), 40–41. https://doi.org/10.52604/alt.24.0021
3. Choi, H. H., Lee, K. W., et al.(2024). Varied strategies for alcohol-related liver transplants in South Korea. Annals of Liver Transplantation, 4(2), 95–101. https://doi.org/10.52604/alt.24.0013
4. Addolorato, G., Caputo, F., Vassallo, G. A., Stopponi, S., Ricci, E., Rando, M. M., ... & Lattanzi, B. (2023). Integrating an addiction team into the management of patients transplanted for alcohol-associated liver disease reduces the risk of severe relapse. JHEP Reports, 5(8), 100832. https://doi.org/10.1016/j.jhepr.2023.100832

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Eunseon Suh

Hwaseong Community Addiction Management Center

Self Introduction

Dr. Eunseon Suh, who has completed her Ph.D. coursework, is the Director of the Hwaseong Community Addiction Management Center.

She earned her Master's degree in Social Work from Soongsil University in 1996 and began her career in 1997 at Gangnam Mental Health Center and various psycho-social rehabilitation facilities. Since 2014, she has been working at the Hwaseong Community Addiction Management Center.

Since 2023, she has also been serving as the Vice President of the Korean Association of Community Addiction Management Centers.

Research Interests

Development of Integrated Service Model and Programs for Alcohol Use Disorders in Hospital and Community, Ministry of Healthy and Welfare , 2019-2021

Development of Service Model Using Non-Face-to-Face Intervention Technology for High-Risk Drinkers and Alcoholics, Ministry of Healthy and Welfare, 2022-2024

Effectiveness of Psychosocial Interventions for Illicit Drug Users in Inpatient Settings: A Systematic Review, Ministry of Healthy and Welfare, 2024-Present

Representative Publications

1. Self-Recovery Through Building Relationships, Human and Well-Being, 2011

KLTS Coordinator Session | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

Social Support and Rehabilitation for Liver Transplant Patients with Alcoholic Liver Disease

Eunseon Suh *Hwaseong Community Addiction Management Center*

Alcohol use disorder is a chronic and relapsing brain disease that significantly affects treatment outcomes, especially in patients undergoing liver transplantation due to alcoholic liver disease. Despite the necessity of long-term care and rehabilitation, many individuals with addiction are isolated from social support systems due to stigmatization and the behavioral manifestations of addictive thinking.

This presentation explores the challenges in providing continuous care for individuals with alcohol use disorders, with a focus on the psychological and behavioral traits that hinder recovery—such as denial, shame, distorted thinking, and emotional instability. It emphasizes the essential role of community-based addiction management centers and highlights existing support systems in Korea, including mental health centers, rehabilitation facilities, and peer support groups such as Alcoholics Anonymous.

The session will introduce key intervention strategies, including detoxification, craving-reduction medications, cognitive-behavioral therapy, motivational enhancement, and the 12-step program. Based on real-world data, the presentation also discusses the effectiveness of long-term sobriety and the importance of structured support in achieving lasting recovery.

Ultimately, this presentation advocates for integrated hospital-community service models, emphasizing that although addiction is not the fault of the individual, recovery is a responsibility that must be supported by both the person and the community.

References

1. Korean Society of Addiction Psychiatry. (2019). Addiction psychiatry.
2. Ha, J. E. (2014). Why Do We Fall Into Alcohol? One & One Contents Group.
3. Gwangju Dong-gu Addiction Management Integrated Support Center. (2023). Development of a Management Program for Patients Undergoing Liver Transplantation Due to Alcohol-Related Liver Disease.

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DAY 2: May 30 (Fri.)

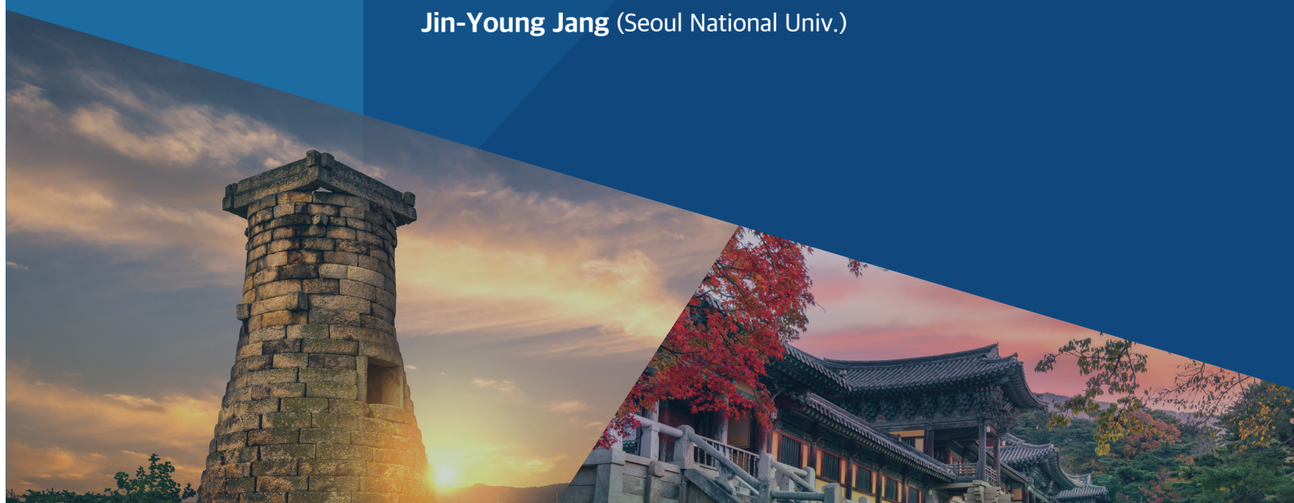
KAHBPS Symposium 3

Recent Updates in Cholangiocarcinoma

Chairs:

In Seok Choi (Konyang Univ.)

Jin-Young Jang (Seoul National Univ.)



Kyeong Deok Kim

Inha University

Self Introduction

Prof. Kyeong Deok Kim is an assistant professor of the Department of Surgery, Inha University Hospital.

He graduated from Soonchunhyang University College of Medicine with his medical degree in 2011 and completed his internship and residency at the Department of Surgery at Soonchunhyang Univertisy Bucheon Hospital. He completed a fellowship in transplantation surgery at Samsung Medical Center.

Since 2022, he has been working at Inha University Hospital.

Representative Publications

1. Kim, K.D., et al., Laparoscopic liver resection as a treatment option for intrahepatic cholangiocarcinoma. Updates Surg., 2024; 76: 869–878.
2. Kim, K.D., et al., Postoperative Outcomes of Distal Pancreatectomy for Retroperitoneal Sarcoma Abutting the Pancreas in the Left Upper Quadrant. Front Oncol 2021. 11
3. Kim, K.D., et al., Cost-effectiveness and long-term outcomes of liver transplantation using hepatitis B core antibody-positive grafts with hepatitis B immunoglobulin prophylaxis in Korea. Clin Mol Hepatol, 2021.27(4):603-615

Minimal Invasive Surgery for Intrahepatic Cholangiocarcinoma

Kyeong Deok Kim *Inha University*

Intrahepatic cholangiocarcinoma (iCCA) is a rare but increasingly prevalent malignancy with poor prognosis and limited treatment options. Surgical resection remains the only potentially curative modality. While open liver resection (OLR) has been the standard approach, the role of minimally invasive surgery (MIS)—including laparoscopic and robotic techniques—has been actively explored in recent years.

Several retrospective studies have reported that MIS for iCCA, when performed in selected patients, is associated with comparable oncologic outcomes to OLR, including overall survival and recurrence-free survival. Moreover, MIS has demonstrated potential advantages in terms of reduced blood loss, shorter hospital stay, and lower postoperative morbidity. Despite these benefits, concerns remain regarding technical feasibility, particularly in cases requiring major hepatectomy or lymph node dissection.

This presentation will provide an overview of the current evidence and clinical considerations for MIS in the treatment of iCCA. Key aspects include patient selection, operative technique, and perioperative outcomes, as well as the evolving role of MIS in complex liver resections. By examining both laparoscopic and robotic approaches, this session aims to clarify the indications and limitations of MIS and to outline future directions for its safe and effective integration into iCCA surgical management.

Poowanai Sarkhampee

Sunpasitthiprasong Hospital, Thailand

Self Introduction

Career

2007	MD, Second-Class Honor, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
2014	Resident in General Surgery, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Thailand
2017	Fellowship of Hepato-Pancreato-Biliary and Transplantation Unit, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Thailand
2017-Present	Hepato-Pancreato-Biliary Surgeon, Department of surgery, Sunpasitthiprasong Hospital, Ubon Ratchathani, Thailand

Research Interests

Cholangiocarcinoma, Especially Perihilar Cholangiocarcinoma and Intrahepatic Cholangiocarcinoma

Representative Publications

1. Sarkhampee P, Ouransatien W, Chansitthichok S, Lertsawatvicha N, Wattanarath P. The Impact of Resection Margin Status According to Lymph Node Metastasis on the Survival Outcome of Perihilar Cholangiocarcinoma. The American Journal of Surgery 2025;242:116236.
2. Sarkhampee P, Ouransatien W, Lertsawatvicha N, Chansitthichock S, Wattanarath P. The impact of Positive Resection Margin in Perihilar Cholangiocarcinoma, Ductal Margin vs Radial Margin. Langenbecks Arch Surg 2024;409:359.
3. Sarkhampee P, Ouransatien W, Lertsawatvicha N, Chansitthichock S, Wattanarath P. Resectability and Survival Outcome In Real World Practice of 720 Cholangiocarcinoma Patients: Intrahepatic, Perihilar and Distal Cholangiocarcinoma. World J Surg Oncol 2024;22:314.
4. Sarkhampee P, Junrungsee S, Tantraworasin A, Sirichindakul P, Ouransatien W, Chansitthichok S, Lertsawatvicha N, Wattanarath P. Survival Outcomes of Surgical Resection in Perihilar Cholangiocarcinoma in Endemic Area of O. Viverrini, Northeast Thailand. Asian J Surg. 2024 Mar 21:S1015-9584(24)00522-0. doi: 10.1016/j.asjsur.2024.03.116. Epub ahead of print. PMID: 38519311.
5. Sarkhampee P, Ouransatien W, Chansitthichok S, Lertsawatvicha N, Wattanarath P. The Impact Of Post-Hepatectomy Liver Failure on Long-Term Survival After Liver Resection for Perihilar Cholangiocarcinoma. HPB (Oxford). 2024 Jun;26(6):808-817. doi: 10.1016/j.hpb.2024.02.016. Epub 2024 Feb 28. PMID: 38467530.

Extent of Lymph Node Dissection in Intrahepatic Cholangiocarcinoma

Poowanai Sarkhampee *Sunpasitthiprasong Hospital, Thailand*

Importance of LNM in Prognosis of iCCA.

Lymph node metastasis (LNM) is a crucial prognostic factor in intrahepatic cholangiocarcinoma (iCCA). Studies report that LNM is found in 25–60% of patients undergoing surgery, and its presence significantly reduces overall survival (OS) and disease-free survival (DFS).[1-3] The median OS for patients with LNM is reported between 15–20 months, compared to 40–50 months for node-negative patients.[3-5]

Effects of LND on Survival Outcomes of iCCA.

The impact of lymph node dissection (LND) on survival remains controversial. While some studies suggest that LND provides survival benefits through accurate staging and potential removal of micrometastasis,[1,3,5,6] others indicate no significant improvement in OS or DFS compared to patients who did not undergo LND.[4,7] A recent meta-analysis demonstrated that while LND may not directly improve survival, it is critical for guiding adjuvant therapy, particularly in patients with LNM.[8-10]

Extent of LND in iCCA

According to LNM status: LND plays a crucial role in staging and prognosis determination in iCCA patients with LNM, but its survival benefit remains controversial.[8,9] Some studies suggest that its direct impact on OS is limited, particularly in patients with extensive nodal involvement (N2, ≥3 positive nodes).[9,10] However, patients with limited nodal disease (N1, 1–2 positive nodes) may benefit from LND.[3,4,11] In LNM-negative (LNM—) patients, while some studies suggest that adequate LND (≥6 nodes examined) improves OS, others indicate no significant OS advantage and increased postoperative morbidity.[12-14] Predictive models suggest that patients with small, solitary tumors and low CA19-9 levels may not benefit from LND, supporting a selective approach rather than routine dissection.[15]

Regional vs. Extended: Regional LND typically involves dissection of the hepatoduodenal ligament and common hepatic artery, while extended LND includes nodes from the celiac trunk, para-aortic, and peripancreatic regions.[6,16,17] Studies suggest that regional LND is sufficient for accurate staging and may improve survival in selected patients, particularly those with limited lymph node metastasis.[6,16,17]

According to tumor location: The lymphatic drainage patterns differ between central (hilar) and periph-

eral tumors. Central tumors have a higher rate of LNM (~45%), necessitating at least regional LND up to the common hepatic artery and peripancreatic nodes.[18] In contrast, peripheral tumors have a lower risk of LNM (~25%), and LND beyond the hepatoduodenal ligament may not be necessary, as metastasis to distant nodes (e.g., celiac) is uncommon.[6,16]

Conclusion

LND in iCCA is essential for accurate staging, but its survival benefits remain debated. Patients with limited lymph node metastasis (N1) may benefit from LND, while those with extensive metastasis (N2) show no significant survival advantage. In LNM-negative patients, routine LND is controversial, and a selective approach based on tumor characteristics and risk factors is recommended. Overall, regional LND (stations 8, 12) is often sufficient, while extended LND beyond these regions does not improve survival and increases morbidity.

References

1. Zhu J, Liu C, Li H, Ren H, Cai Y, Lan T, et al. Adequate lymph node dissection is essential for accurate nodal staging in intrahepatic cholangiocarcinoma: A population-based study. Cancer Med 2023;12:8184-98.
2. Zhang R, Tan Y, Liu M, Wang L. Lymph node metastasis of intrahepatic cholangiocarcinoma: the present and prospect of detection and dissection. Eur J Gastroenterol Hepatol 2024;36:1359-69.
3. Zhang XF, Xue F, Dong DH, Weiss M, Popescu I, Marques HP, et al. Number and Station of Lymph Node Metastasis After Curative-intent Resection of Intrahepatic Cholangiocarcinoma Impact Prognosis. Ann Surg 2021;274:e1187-e95.
4. Yoshino J, Nara S, Yokoyama M, Ban D, Mizui T, Miyata A, et al. Prognostic impact of lymph node dissection in intrahepatic cholangiocarcinoma: a propensity score analysis. Langenbecks Arch Surg 2024;410:3.
5. Yang F, Wu C, Bo Z, Xu J, Yi B, Li J, et al. The clinical value of regional lymphadenectomy for intrahepatic cholangiocarcinoma. Asian J Surg 2022;45:376-80.
6. Umeda Y, Mitsuhashi T, Kojima T, Satoh D, Sui K, Endo Y, et al. Impact of lymph node dissection on clinical outcomes of intrahepatic cholangiocarcinoma: Inverse probability of treatment weighting with survival analysis. Journal of Hepato-Biliary-Pancreatic Sciences 2022;29:217-29.
7. Kizy S, Altman AM, Marmor S, Wirth K, Ching Hui JY, Tuttle TM, et al. Surgical resection of lymph node positive intrahepatic cholangiocarcinoma may not improve survival. HPB (Oxford) 2019;21:235-41.
8. Yeow M, Fong KY, Zhao JJ, Tan AYH, Koh YX, Kam JH, et al. Value of lymph node dissection in intrahepatic cholangiocarcinoma: a systematic review and meta-analysis. HPB (Oxford) 2024;26:161-70.
9. Ishii T, Iwaki K, Nakakura A, Yoh T, Uchida Y, Hatano E. Is routine lymph node dissection recommended for liver resection of intrahepatic cholangiocarcinoma? A systematic review and meta-analysis. HPB (Oxford) 2024;26:731-40.
10. Atif M, Borakati A, Mavroeidis VK. Role of routine lymph node dissection alongside resection of intrahepatic cholangiocarcinoma: Systematic review and meta-analysis. World J Gastrointest Oncol 2023;15:2017-32.
11. Huang S, Song JL, Li B, Yi PS, Yang J. Should lymphadenectomy performed routinely in patients with primary intrahepatic cholangiocarcinoma undergoing curative hepatectomy? A retrospective cohort study with propensity-score matching analysis. BMC Surg 2023;23:364.
12. Yoh T, Cauchy F, Le Roy B, Seo S, Taura K, Hobeika C, et al. Prognostic value of lymphadenectomy for long-term outcomes in node-negative intrahepatic cholangiocarcinoma: A multicenter study. Surgery 2019;166:975-82.
13. Sposito C, Ratti F, Cucchetti A, Ardito F, Ruzzenente A, Di Sandro S, et al. Survival benefit of adequate lymphadenectomy in patients undergoing liver resection for clinically node-negative intrahepatic cholangiocarcinoma. J Hepatol 2023;78:356-63.
14. Sha M, Cao J, Qin CL, Zhang J, Fan C, Li Z, et al. Impact of Lymph Node Dissection for Patients With Clinically Node-Negative Intrahepatic Cholangiocarcinoma: A Multicenter Cohort Study. World J Oncol 2024;15:579-91.
15. Miura Y, Ashida R, Ohgi K, Yamada M, Kato Y, Otsuka S, et al. Predictive score for identifying intrahepatic cholangiocarcinoma patients without lymph node metastasis: a basis for omitting lymph node dissection. HPB (Oxford) 2024;26:800-7.
16. Wang J, Shu M, Peng H, Li S, Li D, Shen J, et al. The influence of the extent of lymph node metastasis on the prognosis for patients with intrahepatic cholangiocarcinoma. Ann Surg Treat Res 2023;104:258-68.
17. Kim SH, Han DH, Choi GH, Choi JS, Kim KS. Extent of Lymph Node Dissection for Accurate Staging in Intrahepatic Cholangiocarcinoma. J Gastrointest Surg 2022;26:70-6.
18. Endo Y, Moazzam Z, Lima HA, Alaimo L, Munir MM, Shaikh CF, et al. The impact of tumor location on the value of lymphadenectomy for intrahepatic cholangiocarcinoma. HPB (Oxford) 2023;25:650-8.

Sang Hwa Song

Chonnam National University

Self Introduction

2011-2015	Chonnam National University Graduate School of Medicine
2015-2016	Chonnam National University Hospital Intern
2016-2020	Chonnam National University Hospital General Surgery Resident
2020-2021	Chonnam National University Hospital HPBS Clinical Fellow
2021-2022	Hwasun Chonnam National University Hospital HPBS Clinical Practice Professor
2022-Present	Hwasun Chonnam National University Hospital HPBS Clinical Assistant Professor

KAHBPS Symposium 3 | DAY 2: May 30 (Fri.) | ROOM 3 [2F]

Surgical Approach to Hilar Cholangiocarcinoma

Sang Hwa Song *Chonnam National University*

Background: Hilar cholangiocarcinoma (HCCA) presents unique surgical challenges due to its anatomical complexity, late presentation, and tendency for perineural and vascular invasion. Achieving R0 resection is crucial for improving long-term survival, but complete surgical removal often necessitates extensive procedures, including liver and vascular resection.

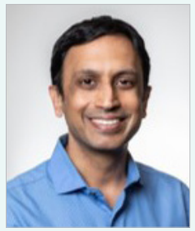
Objective: This presentation outlines a stepwise management plan for HCCA, including preoperative evaluation, strategies for improving resectability, surgical technique selection, and consideration of alternative therapies such as liver transplantation.

Methods: Comprehensive preoperative evaluation includes multimodal imaging (CT, MRI/MRCP, FDG-PET), biliary drainage (ERCP vs. PTBD), and assessment of future liver remnant (FLR). Techniques such as portal vein embolization (PVE) and PVE/HVE are considered to enhance FLR. Lymphadenectomy and intraoperative margin assessment via frozen section are emphasized for staging and achieving oncologic clearance. The presentation further reviews evidence from extended lymphadenectomy trials (e.g., Relay-HC) and vascular reconstruction strategies to maximize curability.

Results: Data indicate that R0 resection significantly improves 5-year survival, especially with >5mm tumor-free margins. Extended lymphadenectomy may benefit select patients without M1 disease. While minimally invasive surgery (MIS) has shown feasibility with comparable oncologic outcomes, it is recommended only in experienced high-volume centers. Liver transplantation (LT) has emerged as a promising treatment for unresectable, early-stage HCCA in selected patients, particularly those meeting strict criteria (e.g., Mayo Protocol), although surgical resection remains the standard for resectable disease.

Conclusion: R0 resection remains the cornerstone of curative-intent surgery for HCCA. Surgical outcomes can be optimized through careful preoperative planning, selective vascular resection, and appropriate use of MIS or LT in highly selected cases. Continued research through multicenter prospective trials is essential to refine surgical strategies and expand treatment options for this challenging malignancy.

Keywords: Hilar cholangiocarcinoma, R0 resection, lymphadenectomy, vascular reconstruction, minimally invasive surgery, liver transplantation, portal vein embolization



Amit Singal

UT Southwestern Medical Center, USA

Self Introduction

Prof. Singal is a Professor of Medicine at UT Southwestern Medical Center and serves as Chief of Hepatology and Director of the Liver Tumor Program. His research focuses on prevention, screening and treatment of HCC, including evaluation of interventions to improve early cancer detection and reduce HCC-related mortality. He has over 400 peer-reviewed original publications and has been awarded the Willis Maddrey Distinguished Chair in Liver Disease and Blue Faery Award for Excellence in Liver Cancer Research.

Research Interests

Liver Cancer, Screening and Early Detection, Health Services Research

Representative Publications

1. Singal AG, Quirk L, Boike J, Chernyak V, Feng Z, Guimarqo G, Kanwal F, Ioannou G, Manes S, Marrero J, Mehta N, Pillai A, Shaheen N, Shaukat A, Sirlin C, Verna E, Wani S, Woods A, Yang JD, Parikh ND. Value of HCC surveillance in a landscape of emerging surveillance options: Perspectives of a multi-stakeholder modified Delphi panel. Hepatology 2025
2. Singal AG, Narasimman M, Daher D, Yekkaluri S, Liu Y, Lee M, Cerda V, Khan A, Seif El Dahan K, Kramer J, Gopal P, Murphy C, Hernaez R. Effectiveness of mailed outreach and patient navigation to promote HCC screening process completion: A multi-center pragmatic randomized clinical trial. Gut 2024; 73(12): 2037-2044.
3. Singal AG, Zhang E, Narasimman M, Rich NE, Waljee AK, Hoshida Y, Yang JD, Reig M, Cabibbo G, Nahon P, Parikh ND, Marrero JA. HCC Surveillance Improves Early Detection, Curative Treatment Receipt, and Survival in Patients with Cirrhosis: A Systematic Review and Meta-Analysis. J Hepatology 2022; 77(1): 128-139
4. Wolf E, Rich NE, Marrero JA, Parikh ND, Singal AG. Use of hepatocellular carcinoma surveillance in patients with cirrhosis: A systematic review and meta-analysis. Hepatology 2021; 73(2): 713-25.
5. Tzartzeva K, Obi J, Rich NE, Parikh ND, Marrero JA, Yopp A, Waljee A, Singal AG. Surveillance imaging and alpha fetoprotein for early detection of hepatocellular carcinoma in patients with cirrhosis: A meta-analysis. Gastroenterology 2018; 154(6): 1706-18.e1

Role of Liver Transplantation in the Treatment of Intrahepatic Cholangiocarcinoma

Amit Singal *UT Southwestern Medical Center, USA*

Cholangiocarcinoma (CCA) is the second most common type of primary liver cancer. It has an increasing incidence, primarily driven by increases in intrahepatic cholangiocarcinoma (iCCA). CCA is typically considered to be more aggressive than HCC, with a poor overall survival. This poor prognosis has historically been driven by the high proportion of patients presenting with large tumor burden, at which time curative therapies are not possible. Previously, treatment options were largely restricted to surgical resection or chemotherapy, but there have been increasing data for the roles of locoregional therapy and liver transplantation LT).

Much like hepatocellular carcinoma (HCC), early reports demonstrated poor outcomes for LT in patients with iCCA, with high rates of recurrence and a 5-year survival of only ~30%. These data led to many considering iCCA as a contraindication to LT. A paradigm shift began after retrospective studies of incidentally discovered iCCA on explants identify a subgroup of patients with acceptable post-LT outcomes. Specifically, patients with iCCA ≤2 cm incidentally found on explant had a 5-year survival of 65%, compared to 61% for those with tumors (that were not poorly differentiated) between 2-3 cm, and 42% for those with larger tumors. These results were confirmed in a meta-analysis, including 18 studies among 355 patients. Patients with very early stage iCCA had better 3- and 5-year OS than those with larger tumors. Cirrhosis was associated with recurrence-free survival (RFS) but not OS in meta-regression, but limited data precluded subgroup analysis by cirrhosis status. There were also limited data on neoadjuvant therapy or disease stability prior to LT.

A subsequent multi-center retrospective cohort study of patients with iCCA or cHCC-CCA ≤5 cm that were found incidentally reported 5-year overall survival of 67%. Results appeared to be similar between patients who had CCA ≤2 cm compared to those with larger tumors ≤5 cm. There have also been data from Houston Methodist in the USA showing that patients with larger iCCA could achieve acceptable outcomes using a strict protocol including careful patient selection excluding extrahepatic disease and use of neoadjuvant chemotherapy requiring stability for at least 6 months. Patients in the most recent report had large tumor burden including median 2 tumors on imaging and median total tumor size 10.4 cm (range 2.5 – 19.9 cm). There were 6% well differentiated tumors, 56% moderately differentiated tumors, and 33% poorly differentiated tumors. Overall, 3- and 5-year OS were 71% and 57%, respective-

ly, with RFS at 3 years of 52%.

Overall, these data have created a movement away from size-number algorithms to ones that consider tumor biology, similar to what we have observed in HCC. Prior studies have shown the predictive ability of risk stratification models to identify patients at low vs. high risk of recurrence, although these largely preceded current selection criteria. If newer models were derived and validated, these models could help with optimal patient selection. Further, our understanding of genetic alterations and ctDNA, as well as their prognostic significance, has improved, so these could be incorporated into patient selection and treatment algorithms.

The ILTS-ILCA Consensus document on the role of liver transplantation for patients with primary liver cancer, including CCA, was recently published. Statements for iCCA included the following:

References

1. Moderate-strength recommendation for LT in cirrhosis patients with iCCA ≤3 cm without extrahepatic metastases, after a period of stability.
2. Weak recommendation for LT in patients without cirrhosis who have unresectable liver-confined iCCA who have stability of at least 6 months of neoadjuvant therapy (under investigational protocol)
3. Weak recommendation for use of neoadjuvant therapies for 6 months or greater prior to LT to help identify those with favorable tumor biology.

Overall, these decisions are complex and likely require multidisciplinary input for optimal management of patients with iCCA being considered for LT.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

KASL Special Interest Group 2.
The KASL Abdominal Ultrasound Study Group

Recent Progress in Clinical Application of Ultrasound

Chairs:

Soon Koo Baik (Yonsei Univ. Wonju)
Sang Gyune Kim (Soonchunhyang Univ.)

Moon Hyung Lee

Kyung Hee University

Self Introduction

Prof. Moonhyung Lee is an Assistant Professor in the Department of Gastroenterology and Hepatology at Kyung Hee University Hospital at Gangdong, Seoul, Korea.

She earned medical degree from Kyung Hee University College of Medicine.

Research Interests

Prof. Moonhyung Lee's clinical and research interests include hepatocellular carcinoma, portal hypertension, metabolic dysfunction-associated steatotic liver disease (MASLD) and big-data analysis using common data models.

Representative Publications

1. Lee M, Kim M, Cha JM. Risk of Lower Gastrointestinal Bleeding in NSAID and Proton Pump Inhibitor Users Compared with NSAID-Only Users: A Common Data Model Analysis. Gut and Liver. Published online January 3, 2025. https://doi.org/10.5009/gnl240247
2. Lee M, Myung SK, Lee SH, Chang Y. Smoking and Risk of Fatty Liver Disease: A Meta-Analysis of Cohort Studies. Gastroenterology Insights. 2025;16(1):1. https://doi.org/10.3390/gastroent16010001
3. Lee M, Cha JM. Real-World Bleeding Risk of Anticoagulant and NSAID Combotherapy versus Anticoagulant Monotherapy. Gut and Liver. Published online May 10, 2024. https://doi.org/10.5009/gnl230541
4. Lee M, Shin HP. Efficacy of Transarterial Chemoembolization (TACE) for Early-Stage Hepatocellular Carcinoma. Medicina. 2023;59(12):2174. https://doi.org/10.3390/medicina59122174

Comparison of Liver Fibrosis Assessment Using VCTE versus SWE

Moon Hyung Lee *Kyung Hee University*

Background: Non-invasive assessment of liver fibrosis is crucial for the management of chronic liver diseases, including MASLD, chronic hepatitis B and C, and autoimmune hepatitis. Two widely used modalities—Vibration-Controlled Transient Elastography (VCTE) and Shear Wave Elastography (SWE)—have become mainstays in fibrosis staging. However, each has distinct technical principles, operational limitations, and diagnostic performance characteristics.

Objectives: This lecture aims to compare the clinical utility of VCTE and SWE in liver fibrosis assessment, highlighting their comparative strengths, limitations, and applications in different clinical contexts.

Discussion: VCTE (FibroScan®) measures liver stiffness based on low-frequency elastic shear waves generated by a mechanical vibrator. It is operator-independent, rapid, and reproducible, but has limitations in patients with high BMI, ascites, or narrow intercostal spaces. In contrast, SWE, integrated into conventional ultrasound machines, utilizes acoustic radiation force to generate shear waves and provides real-time 2D mapping. SWE offers improved anatomical guidance and is advantageous in obese patients and those with heterogeneous liver parenchyma.

Multiple studies have shown that both techniques have high diagnostic accuracy for significant fibrosis (≥F2), with AUROCs generally exceeding 0.85. However, SWE may outperform VCTE in certain subgroups, especially in MASLD and autoimmune hepatitis. The lecture will present data from comparative studies, real-world applications, and recommendations from international guidelines.

Conclusion: While both VCTE and SWE are valuable tools in non-invasive fibrosis staging, the choice of modality should be tailored based on patient characteristics, disease etiology, and institutional resources. A complementary approach may maximize diagnostic yield and guide optimal clinical decisions.

Keywords: liver fibrosis, VCTE, SWE, MASLD, non-invasive assessment, elastography

References

1. Castera L. Noninvasive methods to assess liver disease in patients with hepatitis B or C. Gastroenterology. 2012;142(6):1293–1302.e4.
2. Yoneda M, et al. Comparative evaluation of VCTE and SWE in MASLD patients. Hepatol Int. 2020;14(4):566–574.
3. Barr RG, et al. Elastography assessment of liver fibrosis: Society of Radiologists in Ultrasound consensus conference statement. Radiology. 2015;276(3):845–861.

Heejoon Jang

Seoul National University

Self Introduction

Prof. Heejoon Jang is an assistant professor at the Department of Internal Medicine, Seoul Metropolitan Government (SMG)-Seoul National University (SNU) Boramae Medical Center.

He is certified as an abdominal ultrasonography specialist and holds qualification as an abdominal ultrasound teaching specialist.

Research Interests

- Viral Hepatitis
- Hepatocellular Carcinoma
- Metabolic Dysfunction-Associated Steatotic Liver Disease

Representative Publications

1. Jang H, et al. Aspirin use and risk of hepatocellular carcinoma in patients with chronic hepatitis B with or without cirrhosis. Hepatology. 2022 Aug;76(2):492-501.
2. Jang H, et al. Impact of HBeAg on Hepatocellular Carcinoma Risk During Oral Antiviral Treatment in Patients with Chronic Hepatitis B. Clin Gastroenterol Hepatol. 2022 Jun;20(6):1343-1353.e16.
3. Jang H, et al. Outcomes of Various Classes of Oral Antidiabetic Drugs on Nonalcoholic Fatty Liver Disease. JAMA Intern Med. 2024;184(4):375-383.
4. Jang H, et al. Efficacy of Antiviral Prophylaxis up to 6 or 12 Months from Completion of Rituximab in Resolved Hepatitis B Patients: A Multicenter, Randomized Study. J Korean Med Sci. 2023 Jul 17;38(28)

The Role of Ultrasound in the Diagnosis and Assessment of MASLD

Heejoon Jang *Seoul National University*

Background

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), represents a significant global health burden affecting approximately 25-30% of the world's population. MASLD is defined as steatotic liver disease in patients with one or more cardiometabolic risk factors in the absence of harmful alcohol intake. The spectrum encompasses simple steatosis, metabolic dysfunction-associated steatohepatitis (MASH, previously NASH), fibrosis, cirrhosis, and MASH-related hepatocellular carcinoma.

While liver biopsy remains the gold standard for diagnosis and staging, its invasiveness, cost, and sampling variability limit widespread clinical application. Consequently, non-invasive approaches have gained prominence, with ultrasound establishing itself as a cornerstone imaging modality in MASLD management due to its accessibility, safety, and cost-effectiveness.

Conventional Ultrasound Techniques

Conventional B-mode ultrasound has been widely employed as an initial screening method for detecting hepatic steatosis. This technique relies on subjective assessment of liver echogenicity relative to adjacent structures, primarily the kidney cortex. Several ultrasound parameters are routinely evaluated, including (1) parenchymal brightness/echogenicity, (2) deep beam attenuation, (3) vessel visualization, and (4) liver-to-kidney contrast. Meta-analyses demonstrate that conventional ultrasound exhibits good diagnostic accuracy for detecting moderate to severe hepatic steatosis (≥20-30% fat infiltration), with pooled sensitivity of 84.8% (95% CI: 79.5-88.9) and specificity of 93.6% (95% CI: 87.2-97.0). Among the various ultrasound parameters, liver-to-kidney contrast demonstrates the highest sensitivity (98%), followed by vessel wall brightness (81%) and deep beam attenuation (59%), while specificity remains consistently high (93-95%) across all parameters.

Despite these strengths, conventional ultrasound has significant limitations. Its diagnostic performance decreases substantially for mild steatosis (<20% hepatocytes), potentially leading to underdiagnosis in early disease stages when interventions might be most effective. Additionally, ultrasound has poor accuracy in diagnosing microvesicular fat (sensitivity 43%, specificity 73%) and cannot reliably distinguish

between simple steatosis and steatohepatitis, which requires assessment of inflammatory changes not visible on conventional ultrasound.

Quantitative Ultrasound Techniques

To overcome these limitations, several quantitative ultrasound techniques have emerged, offering more objective assessment of hepatic steatosis:

Controlled Attenuation Parameter (CAP) measures ultrasound beam attenuation through liver tissue using A-mode ultrasound integrated with vibration-controlled transient elastography (VCTE, FibroScan®). CAP values range from 100-400 dB/m, with higher values indicating greater steatosis. In a comprehensive meta-analysis of 61 studies involving 10,537 patients with NAFLD, Cao et al. reported that the mean CAP cutoff values for detecting hepatic steatosis based on liver biopsy were 268.5 dB/m for grade S1 (mild steatosis), 288.0 dB/m for grade S2 (moderate steatosis), and 313.1 dB/m for grade S3 (severe steatosis). Importantly, CAP thresholds were significantly higher among individuals with obesity (BMI ≥30 kg/m^2), with mean increases of 30.7 dB/m for S1, 28.2 dB/m for S2, and 27.9 dB/m for S3 compared to those with BMI <30 kg/m^2. These findings underscore the influence of body habitus on CAP measurements and suggest that BMI-adjusted thresholds may enhance diagnostic accuracy. While prior guidelines proposed fixed thresholds for steatosis grading, the substantial inter-individual variability observed in CAP performance highlights the importance of population- and BMI-specific reference values in clinical practice.

Attenuation Imaging (ATI) enables real-time visualization of signal attenuation in hepatic steatosis using a calculated attenuation coefficient. The ATI values increase with increasing levels of steatosis. Shear Wave Elastography (SWE) uses acoustic radiation force impulses to induce shear waves in liver tissue, measuring their speed as a correlate of tissue stiffness. Though primarily developed to assess liver fibrosis, SWE has shown utility in steatosis detection. SWE's effectiveness improves as steatosis progresses to fibrosis and inflammation, as lipid accumulation initially affects tissue viscosity rather than elasticity. Shear Wave Dispersion (SWD) quantifies changes in viscoelasticity of liver parenchyma, which increases with lipid accumulation and inflammation. In some studies, SWD has proven more effective than Attenuation Imaging (ATI) and SWE for hepatic steatosis detection, with higher sensitivity and specificity. This advantage relates to SWD's ability to detect viscoelasticity changes that precede the elasticity changes measured by SWE.

Ultrasound-derived fat fraction (UDFF) provides a simple and accurate imaging biomarker for assessing hepatic steatosis and monitoring changes in hepatic fat content over time. Hepatorenal sonographic index based on liver/kidney cortex echogenicity ratio shows excellent results with AUROCs exceeding 0.90 for all steatosis grades in preliminary studies. Hamaguchi score, which evaluates four ultrasound findings (hepatorenal echo contrast, bright liver, deep attenuation, and vessel blurring), provides a structured approach to grading steatosis.

Comparative Assessment of Imaging Modalities

Magnetic resonance imaging-based proton density fat fraction (MRI-PDFF) is considered the gold standard for non-invasive fat quantification in the liver. For detecting steatosis grade ≥S1, MRI-PDFF substantially outperforms CAP (AUC 0.99 vs. 0.77). For grading hepatic steatosis, MRI-PDFF shows superior performance across all steatosis grades compared to CAP (AUC 0.96, 0.90, 0.79 vs. 0.88, 0.73, 0.70 for grades ≥S1, ≥S2, and S3, respectively).

Limited studies comparing ultrasound with computed tomography (CT) and other imaging techniques without histology found that ultrasound had an overall sensitivity of 93.6% and specificity of 80.1%. When compared against histology as the reference standard, ultrasound demonstrated slightly better overall accuracy for detecting fatty liver than other techniques.

Despite MRI-PDFF's superior diagnostic performance, its high cost and limited accessibility restrict its routine clinical use, particularly for screening purposes. Conversely, ultrasound's relatively low cost, safety profile, and wide accessibility make it well-suited for initial screening in clinical and population settings.

Current Guidelines and Recommendations

Guidelines from major professional organizations present divergent approaches to ultrasound use in MASLD. The American Association for the Study of Liver Diseases (AASLD) does not recommend conventional ultrasound for diagnosing MASLD, citing its limited sensitivity and subjective quantification of steatosis. For monitoring treatment response, AASLD notes that improvements in ALT levels or reduction in fat by imaging techniques can serve as histological markers of improvement.

In contrast, the European Association for the Study of the Liver (EASL) and the Asian Pacific Association for the Study of the Liver (APASL) still recommend ultrasound as the preferred first-line diagnostic procedure for MASLD. These organizations recognize MRI as the gold standard for quantifying liver fat but do not recommend it for routine clinical practice due to its high cost.

Conclusion

Ultrasound remains a valuable tool in the diagnosis and assessment of MASLD, particularly for initial screening due to its wide availability, safety, and cost-effectiveness. While conventional B-mode ultrasound demonstrates good diagnostic accuracy for moderate to severe hepatic steatosis, its limitations in detecting mild steatosis and distinguishing between simple steatosis and steatohepatitis highlight the need for more advanced techniques.

Quantitative ultrasound methods such as CAP, ATI, SWE, and SWD offer promising improvements in diagnostic accuracy, enabling more objective assessment of hepatic steatosis. The integration of these techniques with clinical parameters and emerging technologies presents a compelling path forward for enhancing the early detection and monitoring of MASLD, potentially allowing for earlier interventions and improved patient outcomes in this increasingly prevalent condition.

Jun Sik Yoon

Inje University

Self Introduction

Prof. Jun Sik Yoon is a Professor in the Department of Internal Medicine at Inje University College of Medicine. He currently serves as the associate professor at Busan Paik Hospital.

He graduated from Hanyang University College of Medicine with his medical degree in 2008 and completed his internship and residency at the Department of Internal Medicine at Hanyang University Hospital.

Since 2019, he has been working as a professor at Busan Paik Hospital. The academic societies currently participated in are as follows:
The Korean Liver Cancer Association
The Korean Association of Clinical Ultrasound
The Busan-Ulsan-Gyeongnam Liver Association
Convergence Liver Cancer Study Group

Research Interests

Liver Cancer, MASLD

Representative Publications

1. Kim et al. Risk of cardiovascular disease with high-dose versus low-dose use of non-steroidal anti-inflammatory drugs in ankylosing spondylitis. Ann Rheum Dis. 2024 Jul 15;83(8):1028-1033.
2. Yoon et al. High-dose proton pump inhibitor treatment is associated with a higher mortality in cirrhotic patients: A multicentre study. Aliment Pharmacol Ther. 2024 Apr;59(8):973-983.
3. Yoon et al. Impact of HBeAg on Hepatocellular Carcinoma Risk During Oral Antiviral Treatment in Patients With Chronic Hepatitis B. Clin Gastroenterol Hepatol. 2022 Jun;20(6):1343-1353.e16.
4. Yoon et al. Toward a complete cure for chronic hepatitis B: Novel therapeutic targets for hepatitis B virus. Clin Mol Hepatol. 2022 Jan;28(1):17-30.
5. Yoon et al. Empirical Treatment With Carbapenem vs Third-generation Cephalosporin for Treatment of Spontaneous Bacterial Peritonitis. Clin Gastroenterol Hepatol. 2021 May;19(5):976-986.e5.

KASL Special Interest Group 2. | DAY 2: May 30 (Fri.) | ROOM 4 [2F]

Outcome Prediction Using Ultrasound in Chronic Liver Diseases

Jun Sik Yoon *Inje University*

Chronic liver diseases (CLD), including non-alcoholic fatty liver disease, viral hepatitis, and cirrhosis, represent a significant global health burden, contributing to substantial morbidity and mortality. Accurate prediction of clinical outcomes, such as fibrosis progression, portal hypertension, and hepatocellular carcinoma (HCC), is critical for optimizing patient management. Ultrasound-based techniques, including B-mode imaging, Doppler ultrasound, and elastography, have emerged as non-invasive, cost-effective tools for assessing liver pathology and predicting disease outcomes. This presentation explores the role of ultrasound in outcome prediction for CLD, focusing on its ability to evaluate liver stiffness, detect portal hypertension, and identify early HCC. Advanced techniques, such as shear wave elastography and artificial intelligence (AI)-enhanced ultrasound, have improved diagnostic accuracy, with studies reporting up to 90% sensitivity for detecting advanced fibrosis (F3-F4). However, limitations such as operator dependency and reduced efficacy in obese patients persist. We also discuss future directions, including AI integration and portable ultrasound devices, which promise enhanced precision and accessibility. By leveraging these advancements, ultrasound can significantly improve prognostic assessments in CLD, ultimately enhancing patient outcomes.

Keywords: Chronic Liver Disease, Ultrasound, Outcome Prediction, Elastography, Artificial Intelligence

References

1. Barr RG, et al. Elastography Assessment of Liver Fibrosis: Society of Radiologists in Ultrasound Consensus Conference Statement. Radiology. 2020;296(3):263-274.
2. Ferraioli G, et al. Ultrasound-based liver elastography: Recent advances and future perspectives. World J Gastroenterol. 2023;29(15):2165-2180.
3. Dietrich CF, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part I. Ultraschall Med. 2021;42(5):e15-e31.

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Hepatology Associates 1

Updates in Clinical Hepatology

Chairs:

Jaeseok Hwang (Keimyung Univ.)
Hee Bok Chae (Chungbuk National Univ.)

Hyeon Ji Jang

University of Ulsan

Self Introduction

Hyeon Ji Jang has been serving as a senior fellow in the Department of Radiology at Asan Medical Center since March, 2024.

She completed her residency in Radiology at Chungnam National University Hospital from March 2016 to Feb. 2020. From July 2020 to February 2022, Hyeon Ji Jang worked as a radiologist at Sejong Chungnam National University Hospital. Then, Hyeon Ji Jang completed a fellowship in the Department of Radiology at Asan Medical Center from March 2022 to February 2024.

Research Interests

Hyeon Ji Jang's research focuses on advanced imaging evaluation of liver and pancreatic diseases, with particular emphasis on oncologic imaging. Her work centers on identifying imaging biomarkers and prognostic indicators that can aid in early diagnosis, treatment planning, and risk stratification.

Representative Publications

1. Jang HJ, Choi SH, Wee S, Choi SJ, Byun JH, Won HJ, Shin YM, Sirlin CB. CT- and MRI-based Factors Associated with Rapid Growth in Early-Stage Hepatocellular Carcinoma. Radiology. 2024 Dec;313(3):e240961. doi: 10.1148/radiol.240961.
2. Ji Jang H, Soo Lee S, Baek S, Jeong B, Wook Kim D, Hee Kim J, Jung Kim H, Ho Byun J, Lee W, Cheol Kim S. Prognostic implication of extra-pancreatic organ invasion in resectable pancreas ductal adenocarcinoma in the pancreas tail. Eur J Radiol. 2024 Dec;181:111715. doi: 10.1016/j.ejrad.2024.111715. Epub 2024 Sep 2.
3. Oh NE, Choi SH, Kim S, Lee H, Jang HJ, Byun JH, Won HJ, Shin YM. Suboptimal performance of LI-RADS v2018 on gadoxetic acid-enhanced MRI for detecting hepatocellular carcinoma in liver transplant candidates. Eur Radiol. 2024 Jan;34(1):465-474. doi: 10.1007/s00330-023-10014-6. Epub 2023 Aug 3.
4. Jang HJ, Choi SH, Choi SJ, Choi WM, Byun JH, Won HJ, Shin YM. LI-RADS version 2018 for hepatocellular carcinoma < 1.0 cm on gadoxetate disodium-enhanced magnetic resonance imaging. Eur Radiol. 2023 Aug;33(8):5792-5800. doi: 10.1007/s00330-023-09554-8. Epub 2023 Apr 5.
5. Jang HJ, Min JH, Lee JE, Shin KS, Kim KH, Choi SY. Assessment of liver fibrosis with gadoxetic acid-enhanced MRI: comparisons with transient elastography, ElastPQ, and serologic fibrosis markers. Abdom Radiol (NY). 2019 Aug;44(8):2769-2780. doi: 10.1007/s00261-019-02041-z.

Percutaneous Liver Biopsy: When to Decide to Perform and How to Minimize Risk

Hyeon Ji Jang *University of Ulsan*

Ultrasound-guided percutaneous core needle biopsy is a widely used diagnostic technique for obtaining tissue samples from abdominal organs. It offers several advantages over CT or MRI guidance, such as real-time needle visualization, shorter procedure times, portability, lack of ionizing radiation, and lower costs.

The indications for US-guided biopsy include confirming and staging malignancies, differentiating benign from malignant lesions, and diagnosing diffuse parenchymal diseases.

Absolute contraindications include uncooperative patients, severe coagulopathy, infection near the biopsy site, and extrahepatic biliary obstruction. **Relative contraindications** involve ascites, morbid obesity, vascular lesions, amyloidosis, and hydatid disease. Patients who cannot cooperate during the procedure, especially in breath-holding, are at increased risk of liver laceration and bleeding. In such cases, transvenous or laparoscopic approaches under sedation may be safer. The presence of ascites complicates percutaneous access and may necessitate therapeutic paracentesis beforehand or alternate routes. Lesions that are highly vascular, such as hemangiomas, should generally not be biopsied due to the bleeding risk. For suspected malignancies, there is a small but real concern for tumor seeding along the needle track, although recent studies suggest this risk is lower with coaxial techniques and careful planning. Hydatid cysts pose a risk of anaphylaxis and are considered an absolute contraindication to biopsy.

Pre-procedural preparation involves fasting, coagulation testing, and planning a safe biopsy route using cross-sectional imaging. The choice of biopsy needle, including its gauge and automation type, impacts tissue adequacy and safety. Typically, 18-gauge automated needles are used, and coaxial or non-coaxial techniques may be selected based on operator preference.

Real-time needle visualization is essential and can be optimized through correct alignment, echogenic needles, and Doppler imaging. Operators should avoid critical structures and aim for orthogonal entry into organs. In small or mobile lesions, graded compression or a pump maneuver may enhance needle visibility and control.

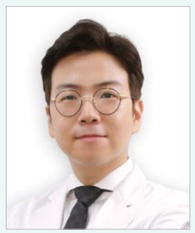
Complications following liver biopsy are uncommon but can range from minor discomfort to

life-threatening events. Pain is the most frequent complication, often localized to the right upper quadrant or referred to the shoulder. It is usually self-limited and managed conservatively with analgesics such as acetaminophen, while avoiding NSAIDs due to bleeding risk. **Bleeding** is the most serious complication and typically presents within the first few hours post-procedure. Management includes close hemodynamic monitoring during the immediate post-biopsy period, serial hemoglobin checks, and urgent imaging (e.g., non-contrast CT) if hypotension, significant pain, or hemoperitoneum is suspected. Minor bleeding may resolve spontaneously, while major hemorrhage might require blood transfusion, angiographic embolization, or surgical intervention. Tumor seeding along the needle track is rare but remains a concern in hepatocellular carcinoma, particularly in liver transplant candidates. To reduce this risk, a coaxial technique and limiting the number of needle passes are recommended.

Infectious complications, though rare, should be promptly addressed with antibiotics if signs of fever, chills, or localized infection appear. Damage to adjacent organs, such as the gallbladder or lung (in intercostal approaches), necessitates clinical and imaging evaluation followed by appropriate surgical or medical treatment. Hemobilia, pseudoaneurysm, or arteriovenous fistulas, though very rare, may require specialized interventional radiology treatment. After the biopsy, patients are usually observed for 2–4 hours in a recovery area where vital signs are monitored. Those who develop significant abdominal pain, tachycardia, or a drop in blood pressure should be evaluated promptly for bleeding or organ injury. When severe coagulopathy or ascites are present, a **transjugular liver biopsy** may be preferred from the outset, as it offers a safer alternative with lower bleeding risks by containing any potential hemorrhage within the venous system. Overall, prompt recognition, careful monitoring, and readiness for escalation of care are key to safely managing liver biopsy complications.

References

1. Kim JW, Shin SS. Ultrasound-Guided Percutaneous Core Needle Biopsy of Abdominal Viscera: Tips to Ensure Safe and Effective Biopsy. Korean J Radiol. 2017 Mar-Apr;18(2):309-322. doi: 10.3348/kjr.2017.18.2.309. Epub 2017 Feb 7.
2. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. Hepatology. 2009 Mar;49(3):1017-44. doi: 10.1002/hep.22742
3. Behrens G, Ferral H. Transjugular liver biopsy. Semin Intervent Radiol. 2012 Jun;29(2):111-7. doi: 10.1055/s-0032-1312572. PMID: 23729981



Jae Hyun Yoon

Chonnam National University

Self Introduction

Prof. Jae Hyun Yoon is a Professor of the Department of Gastroenterology and Hepatology, Chonnam National University Hospital, College of Medicine and is currently holding a position as assistant professor since 2020.

He graduated from Chonnam National University College of Medicine with his medical degree in 2011 and completed his Doctor's degree in same institute at 2023.

He has been taking a number of roles, including member of committee of publication, committee of education in Korean Association for the Study of the liver (KASL), and member of committee of academy in Korean Liver Cancer Association (KLCA).

Research Interests

Viral Hepatitis, Hepatocellular Carcinoma, Alcoholic Hepatitis, Cirrhosis, Microbiome

Representative Publications

1. Albumin-Bilirubin Grade as a Valuable Predictor of Recurrence and Prognosis in Patients with Hepatocellular Carcinoma Following Radiofrequency Ablation. (Cancers, 2024.12.)
2. Stage dependent microbial dynamics in hepatocellular carcinoma and adjacent normal liver tissues (Sci Rep 2024.10.)
3. Management of early-stage hepatocellular carcinoma: challenges and strategies for optimal outcomes (Journal of liver cancer, 2023. 09.)
4. Prognosis of Patients with Chronic Hepatitis C Genotype 1b Infection Treated Using Daclatasvir/Asunaprevir after Sustained Virologic Response: A 6-Year Multicenter Prospective Observational Study (Meidicina(Kaunas, 2023.08.)
5. Altered Frequency, Activation, and Clinical Relevance of Circulating Innate and Innate-Like Lymphocytes in Patients With Alcoholic Liver Cirrhosis (Immune network, 2023.04.)
6. Early extrahepatic recurrence as a pivotal factor for survival after hepatocellular carcinoma resection: A 15-year observational study (World J of gastroenterology, 2022.09.)
7. Etiology and clinical characteristics of acute viral hepatitis in South Korea during 2020-2021: a prospective multicenter study (Sci Rep, 2023.08.)

Management of Hospitalized Patients with Alcohol Withdrawal Syndrome

Jae Hyun Yoon *Chonnam National University*

Alcohol Withdrawal Syndrome (AWS) remains a common and potentially serious complication among hospitalized patients with chronic alcohol use. When coexisting liver disease is present, particularly in cases of cirrhosis, the clinical course of AWS often becomes more unpredictable and difficult to manage. The usual physiological stress of alcohol cessation is compounded by altered drug metabolism, baseline cognitive impairment, and increased susceptibility to complications. These factors demand a more tailored and cautious approach.

This review examines the management of AWS in the context of liver dysfunction, with particular attention to diagnostic challenges, therapeutic adjustments, and supportive care considerations. While the neurobiology of AWS, centered on disrupted balance between inhibitory GABA and excitatory glutamate signaling, is well established, its clinical expression may be atypical in patients with hepatic encephalopathy. Differentiating between early withdrawal and encephalopathy can be subtle, and misclassification may lead to either under-treatment or overt sedation, both of which carry significant risk.

Although tools like the CIWA-Ar scale are used for symptom-guided therapy, their applicability in patients with advanced liver disease is limited. In practice, some clinicians adopt fixed-dose or hybrid protocols to reduce variability and avoid misinterpretation of symptoms in encephalopathic or hypoactive patients. Benzodiazepines continue to be the mainstay of treatment, but agent selection and dosing must be guided by hepatic metabolism. Drugs such as lorazepam and oxazepam, which undergo minimal hepatic transformation, are generally preferred. The potential role of adjunctive medications like phenobarbital or dexmedetomidine is increasingly discussed, though high-quality data specific to cirrhotic populations remain sparse.

Although supportive care is often underestimated, is essential. This includes early thiamine administration, correction of electrolyte disturbances, nutritional support, and careful fluid management. Patients with underlying liver disease are more prone to complications such as Wernicke's encephalopathy, aspiration, or renal injury during withdrawal, further highlighting the importance of multidisciplinary coordination.

Emerging literature suggests the need for AWS protocols specifically adapted for patients with hepatic impairment. Until such tools are standardized, clinicians must rely on clinical judgment, careful monitor-

ing, and an individualized approach. A better understanding of how liver disease modifies the course of AWS is crucial for improving outcomes in this high-risk population.

References

1. Day E, Daly C. Clinical management of the alcohol withdrawal syndrome. Addiction. 2022;117(3):804–814. doi:10.1111/add.15647
2. Bahji A, Crockford D, El-Guebaly N. Neurobiology and Symptomatology of Post-Acute Alcohol Withdrawal: A Mixed-Studies Systematic Review. Journal of Studies on Alcohol and Drugs. 2022;83(4):461–469. doi:10.15288/jsad.2022.83.461
3. Sechi GP, Sechi MM. Challenges in Prediction and Diagnosis of Alcohol Withdrawal Syndrome and Wernicke Encephalopathy. JAMA Internal Medicine. 2020;180(12):1716. doi:10.1001/jamainternmed.2020.3558

Heechul Nam

The Catholic University of Korea

Self Introduction

Prof. Heechul Nam is an Assistant professor of the Department of Internal Medicine, The Catholic University of Korea.

He graduated from Catholic University College of Medicine with his medical degree in 2009 and completed his internship and residency at the Department of Internal Medicine at Catholic University, receiving his diploma in Internal Medicine in 2024.

He currently as editorial board member of the Journal of Liver Cancer.

Research Interests

HBV, HCC

Representative Publications

1. Nam H, Sung PS, Lee SW, Song DS, Kwon JH, Jang JW, et al. Incorporating ALBI Grade with Geriatric Nutritional Risk Index Enhances Hepatocellular Carcinoma Risk Stratification. Liver Cancer 2024:1-18.
2. Nam H, Lee J, Han JW, Lee SK, Yang H, Lee HL, et al. Analysis of Immune-Related Adverse Events of Atezolizumab and Bevacizumab in Patients with Hepatocellular Carcinoma: A Multicentre Cohort Study. Liver Cancer 2024;13:413-425.
3. Nam H, Lee SW, Kwon JH, Lee HL, Yoo SH, Kim HY, et al. Prediction of Hepatocellular Carcinoma by On-Therapy Response of Noninvasive Fibrosis Markers in Chronic Hepatitis B. Am J Gastroenterol 2021;116:1657-1666
4. Nam H, Lim JH, Kim TW, Kim EN, Oum SJ, Bae SH, et al. Extracellular Superoxide Dismutase Attenuates Hepatic Oxidative Stress in Nonalcoholic Fatty Liver Disease through the Adenosine Monophosphate-Activated Protein Kinase Activation. Antioxidants (Basel) 2023;12.
5. Nam H, Yang H, Chun HS, Lee HA, Nam JY, Jang JW, et al. Impact of Low Skeletal Muscle Mass on Long-Term Outcomes in Hepatocellular Carcinoma Treated with Trans-Arterial Radioembolization: A Retrospective Multi-Center Study. Cancers (Basel) 2023;15.

Hepatology Associates 1 | DAY 2: May 30 (Fri.) | ROOM 4 [2F]

Inpatient Care for Gastrointestinal Bleeding in Patients with Liver Cirrhosis

Heechul Nam *The Catholic University of Korea*

1. Initial Assessment and Stabilization

1.1 Early Evaluation

- Assess for signs of GI bleeding (hematemesis, melena, hematochezia) and check vital signs.
- Secure large-bore intravenous access and start fluid resuscitation.
- Obtain laboratory tests: CBC, PT/INR, liver function, renal function, and blood type/cross-match.
- Calculate Child-Pugh and MELD scores to assess liver disease severity.

1.2 Hemodynamic Stabilization

- The primary goal is to maintain adequate tissue perfusion and prevent shock.
- Use isotonic fluids for initial resuscitation.
- Apply a restrictive transfusion strategy: target hemoglobin 7–9 g/dL.
- Avoid over-transfusion, as it may increase portal pressure and risk of rebleeding.

2. Pharmacologic Therapy

2.1 Vasoactive Agents

- Start vasoactive drugs as soon as variceal bleeding is suspected, even before endoscopy.
- Terlipressin, somatostatin, or octreotide are recommended options.
- These agents reduce portal hypertension and improve bleeding control.
- Continue therapy for 2–5 days after hemostasis.

2.2 Prophylactic Antibiotics

- All cirrhotic patients with GI bleeding should receive prophylactic antibiotics.
  - Ceftriaxone 2g IV daily for 5–7 days is preferred.
  - Antibiotic prophylaxis reduces bacterial infections, rebleeding, and mortality.

3. Endoscopic Diagnosis and Treatment

3.1 Timing of Endoscopy

- Perform endoscopy within 12–24 hours after stabilization.
- Early endoscopy is crucial for diagnosis and treatment.

3.2 Endoscopic Findings
- Active variceal bleeding: spurting or oozing from varices, presence of blood clots or white nipple sign.
- If blood is present in the stomach without another source, suspect variceal bleeding.

3.3 Endoscopic Therapy
- Esophageal variceal ligation (EVL) is the first-line treatment for esophageal variceal bleeding.
- For gastric varices, endoscopic variceal obturation (EVO) using cyanoacrylate is preferred.
- For non-variceal bleeding, standard endoscopic hemostasis (clips, thermal coagulation, injection) is applied.

4. Rescue Therapy for Treatment Failure

4.1 Indications
- Failure of endoscopic and pharmacologic therapy to control bleeding.
- Early rebleeding within 48–72 hours.
- Massive bleeding precluding endoscopy.

4.2 Rescue Options
- Transjugular intrahepatic portosystemic shunt (TIPS) is the main rescue therapy for uncontrolled variceal bleeding.
- For gastric varices, consider balloon-occluded retrograde transvenous obliteration (BRTO) or plug-assisted retrograde transvenous obliteration (PARTO).
- Surgical shunt or devascularization is reserved for selected cases.

5. Prevention of Rebleeding

5.1 Esophageal Varices
- Combine non-selective beta-blockers (propranolol, carvedilol) with EVL.
- Adjust beta-blocker dose to achieve resting heart rate of 55–60 bpm.

5.2 Gastric Varices
- EVO, PARTO, or TIPS may be used for secondary prophylaxis.
- Beta-blockers can be added if tolerated.

5.3 Non-variceal Bleeding
- Maintain proton pump inhibitor (PPI) therapy for peptic ulcer disease.
- Eradicate Helicobacter pylori if present.

6. Special Considerations

6.1 Anticoagulant/Antiplatelet Use
- Assess bleeding versus thrombosis risk individually.

- Restart anticoagulation after bleeding is controlled, if indicated.

6.2 Management of Complications
- Monitor and treat hepatic encephalopathy (lactulose, correct precipitating factors).
- Manage ascites with albumin and diuretics as needed.
- Prevent and monitor for acute kidney injury.

7. Summary and Conclusion
- GI bleeding in cirrhotic patients requires rapid assessment and a multidisciplinary approach.
- Early stabilization, prompt pharmacologic therapy, and timely endoscopy are essential.
- Apply guideline-based protocols for optimal outcomes.
- Prevent rebleeding and monitor for complications during hospitalization and follow-up.

References (Guideline Recommendations)

1. KASL Clinical Practice Guideline for Liver Cirrhosis: Varices (2019)
2. Baveno VII Consensus Workshop (2022)
3. AASLD Practice Guidance: Management of Varices and Variceal Hemorrhage (2021)
4. EASL Clinical Practice Guidelines: Management of Decompensated Cirrhosis (2018)

Jae Seung Lee

Yonsei University

Self Introduction

Prof. Jae Seung Lee is a hepatologist from South Korea. He earned his medical degree and PhD from Yonsei University College of Medicine. He completed his residency in Internal Medicine at Severance Hospital, and after completing a two-year fellowship, he has been serving as a clinical assistant professor since 2020. His research encompasses a wide range of topics in hepatology, with a particular focus on developing predictive models for hepatocellular carcinoma (HCC) in patients with chronic hepatitis B and metabolic dysfunction-associated steatotic liver disease (MASLD), as well as evaluating the diagnostic accuracy of non-invasive fibrosis measures.

His numerous publications focus on the treatment and prognosis of patients with liver-related diseases. Additionally, he explores experimental topics such as the mechanisms of drug resistance in HCC using HCC organoids. He is an active member of the Korean Association for the Study of the Liver and the Korean Liver Cancer Association.

Research Interests

Hepatitis B, Hepatitis C, Steatotic Liver Disease, Cirrhosis, Hepatocellular Carcinoma

Representative Publications

1. Lee JS, Jung CY, Lee JI, Ahn SH, Kim BS, Kim SU. Comparison of decline in renal function between patients with chronic hepatitis B with or without antiviral therapy. Aliment Pharmacol Ther. 2023 Jul;58(1):99-109.
2. Lee JS, Lee HW, Kim BK, Park JY, Kim DY, Ahn SH, Jang JY, Park SY, Lee HW, Lee CK, Kim SU. Comparison of FibroScan-Aspartate Aminotransferase (FAST) Score and Other Non-invasive Surrogates in Predicting High-Risk Non-alcoholic Steatohepatitis Criteria. Front Med (Lausanne). 2022 Apr 14;9:869190.
3. Lee JS, Lee HW, Lim TS, Min IK, Lee HW, Kim SU, Park JY, Kim DY, Ahn SH, Kim BK. External Validation of the FSAC Model Using On-Therapy Changes in Noninvasive Fibrosis Markers in Patients with Chronic Hepatitis B: A Multicenter Study. Cancers (Basel). 2022 Jan 29;14(3):711.
4. Lee JS, Sinn DH, Park SY, Shin HJ, Lee HW, Kim BK, Park JY, Kim DY, Ahn SH, Oh JH, Lee JI, Kim SU. Liver Stiffness-Based Risk Prediction Model for Hepatocellular Carcinoma in Patients with Nonalcoholic Fatty Liver Disease. Cancers (Basel). 2021 Sep 11;13(18):4567.
5. Baatarkhuu O, Lee JS (Co-primary), Amarsanaa J, Kim DY, Ahn SH, Naranzul N, Enkhtuya D, Choijamts N, Batbayar P, Otgonbayar R, Saruul BU, Gantuul C, Gegeebadrakh B, Tuvshinbayar N, Badamsuren D, Ulzmaa G, Otgonbold J, Han KH. Efficacy and safety of ledipasvir/sofosbuvir in 5,028 Mongolian patients infected with genotype 1 hepatitis C virus: A multicenter study. Clin Mol Hepatol. 2021 Jan;27(1):125-135.

Precipitating Factors and Management of Hepatic Encephalopathy

Jae Seung Lee *Yonsei University*

Hepatic encephalopathy (HE) is one of the most serious complications of cirrhosis, presenting a broad range of symptoms, from mild cognitive impairments to severe coma. It is primarily caused by the buildup of toxins such as ammonia, which the damaged liver cannot effectively filter out. HE is observed in approximately 10–14% of individuals at the time of cirrhosis diagnosis. Furthermore, a systematic review and meta-analysis underscore that up to 40% of cirrhotic patients may develop HE. Even after HE episodes resolve, cognitive deficits often persist despite medical treatment, with full recovery sometimes elusive even after liver transplantation.

The metabolism of ammonia in the brain relies on two critical enzymes: glutamine synthetase, which detoxifies ammonia by converting it into glutamine, and glutaminase, which breaks down glutamine to release ammonia. Therefore, treatment strategies for HE typically focus on either inhibiting glutaminase to reduce ammonia synthesis or enhancing glutamine synthetase activity to improve ammonia detoxification. However, in patients with liver dysfunction or cirrhosis, this detoxification process is compromised, leading to the buildup of ammonia in the bloodstream and, ultimately, in the brain. This hyperammonemia is a major contributor to the neurotoxicity observed in HE.

Various factors can predispose individuals to HE. Classical precipitants include infection, gastrointestinal bleeding, dehydration, electrolyte disturbances, constipation, and alcohol intake. In addition, new precipitants have been suggested, such as muscle alterations (sarcopenia and myosteatosis) and spontaneous or procedure-induced portosystemic shunts (e.g., transjugular intrahepatic portosystemic shunt). Therefore, the management of HE is based on identifying and correcting the precipitants, as well as on empirical treatment aimed at reducing blood ammonia levels.

Among pharmacological treatments for overt HE, the most commonly used and evidence-based therapies include nonabsorbable disaccharides (e.g., lactulose) and the minimally absorbed oral antibiotic rifaximin. Other therapies that may benefit patients with HE include probiotics, fecal microbiota transplantation, urea cycle modulators such as L-ornithine L-aspartate (LOLA) and zinc, albumin, polyethylene glycol, branched-chain amino acids, newer antibiotics such as nitazoxanide, and agents targeting neurotransmitter systems or neuroinflammation such as L-carnitine or flumazenil. These have high potential for clinical application, although further studies are needed. Ultimately, patients with uncon-

trolled liver failure and HE have a markedly poor prognosis, necessitating consideration of liver transplantation.

Despite current advancements, our understanding of HE remains incomplete, and existing treatment options continue to have limitations. Nevertheless, progress in HE management is ongoing, although more clinical trials are needed to establish the efficacy of emerging therapies.

References

1. Torre A, Córdova-Gallardo J, Martínez-Sánchez FD. Hepatic encephalopathy: risk identification and prophylaxis approaches. Metab Brain Dis 2025;40:138.
2. López-Franco Ó, Morin JP, Cortés-Sol A, Molina-Jiménez T, Del Moral DI, Flores-Muñoz M, et al. Cognitive Impairment After Resolution of Hepatic Encephalopathy: A Systematic Review and Meta-Analysis. Front Neurosci 2021;15:579263.
3. Bellafante D, Gioia S, Faccioli J, Riggio O, Ridola L, Nardelli S. Old and New Precipitants in Hepatic Encephalopathy: A New Look at a Field in Continuous Evolution. J Clin Med 2023;12.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

Data Science Camp 1

Statistics in Hepatology

Chairs:

Jin-Wook Kim (Seoul National Univ.)
Chang Wook Kim (The Catholic Univ. of Korea)

Woojoo Lee

Seoul National University

Self Introduction

Prof. Woojoo Lee is a professor of graduate School of Public Health, Seoul National University.

He received his degree in Physics from Seoul National University in 2003 and completed his Ph.D. in Statistics at the same university.

He subsequently worked as a postdoctoral researcher at the Karolinska Institute in Sweden.

Research Interests

Prof. Lee focuses on research in causal inference and the development of epidemiological methods, and actively collaborates with researchers in the fields of medicine and epidemiology.

Representative Publications

1. Sensitivity analysis for unmeasured confounding in estimating the difference in restricted mean survival time. S Lee, JH Park, W Lee. Statistical Methods in Medical Research 33 (11-12), 1979-1992
2. Reparametrized Firth's Logistic Regressions for Dose - Finding Study With the Biased - Coin Design. H Kim, S Jung, Y Pawitan, W Lee. Pharmaceutical Statistics 23 (6), 1117-1127
3. Outcomes of various classes of oral antidiabetic drugs on nonalcoholic fatty liver disease. H Jang, Y Kim, DH Lee, SK Joo, BK Koo, S Lim, W Lee, W Kim. JAMA internal medicine 184 (4), 375-383

Data Science Camp 1 | DAY 2: May 30 (Fri.) | ROOM 4 [2F]

Advanced Survival Analysis

Woojoo Lee *Seoul National University*

This lecture provides a structured overview of survival analysis, beginning with fundamental concepts such as censoring and the hazard function. It then introduces more advanced topics, including time-varying treatments and competing risks.

Particular attention is given to methodological pitfalls that commonly arise in survival analysis, along with practical guidance on how to identify and address these issues in applied research.

Sehee Kim

University of Ulsan

Self Introduction

Prof. Sehee Kim is a Research Associate Professor in the Department of Clinical Epidemiology and Biostatistics at the University Ulsan College of Medicine and Asan Medical Center.

She received her PhD in Biostatistics from the University of North Carolina and subsequently worked as a research fellow at the Harvard School of Public Health from 2010 to 2012. From 2012 to 2020, she served as a professor of Biostatistics at the University of Michigan, before joining the Asan Medical Center in 2020.

Research Interests

Prof. Kim's research focused on developing statistical methods for joint modeling of longitudinal and time-to-events data and complicated time-to-event outcomes (including recurrent events, left-truncated data, cure-rate models, and competing risks analyses, etc). She also works on risk score development and evaluation.

Through collaborative research, she seeks to advance biological and public health science by bridging the gap between researchers, statistical methodologies, and the effective communication of results.

Representative Publications

1. Chung SW, Kim YJ, Lim J, Choi J, Lee D, Shim JH, Kim KM, Lim YS, Lee HC, Kim S*, Choi WM*. (2025). Risk of Extrahepatic Malignancies in Patients With Autoimmune Hepatitis: A Nationwide Cohort Study. Am J Gastroenterology, in-press. (* Co-corresponding author)
2. Lim J, Kim YJ, Kim S*, Choi J*. (2025). Risk of hepatocellular carcinoma in Asian patients with primary biliary cholangitis: A nationwide and hospital cohort study. JHEP Rep., 7(2):1-11. (* Co-corresponding author)
3. Lee JH*, Kim S*, Oh Y. (2023). A prediction scoring model for the effect of withdrawal or addition of inhaled corticosteroids in patients with Chronic Obstructive Pulmonary Disease. International J of Chronic Obstructive Pulmonary Disease, 18:113-127. (* Co-first author)
4. Hartman N#, Kim S, He K, Kalbfleisch JD. (2023). Concordance indices with left-truncated and right-censored data. Biometrics, 79(3):1624-1634. (# Student under my supervision)
5. Hartman N#, Kim S, He K, Kalbfleisch JD. (2023). Pitfalls of the concordance index for survival outcomes. Statistics in Medicine, 42(13):2179-2190. (# Student under my supervision)
6. Kim S, Schaubel DE, McCullough KP. (2018). A C-index for recurrent event data: Application to hospitalizations among dialysis patients. Biometrics, 74(2):734-743.

Development and Evaluation of Clinical Prediction Models

Sehee Kim *University of Ulsan*

Clinical prediction models are pivotal tools in modern medicine, aiding in decision-making, risk stratification, and personalized care. This seminar will outline the comprehensive process of developing and evaluating such models using medical data. It begins with defining the clinical question and identifying the primary outcome. Data collection and preparation, emphasizing data quality and data processing, are critical initial steps. Variable selection involves identifying relevant predictors through clinical knowledge and exploratory analyses, followed by feature engineering to transform raw data into meaningful features.

Model development includes choosing appropriate statistical or machine learning techniques, such as logistic regression, Cox regression, or random forests, and validating the model through training and cross-validation. Model evaluation employs performance metrics such as sensitivity and specificity, ROC-AUC or C-index for model discrimination, and calibration plots. We will also discuss ways of addressing overfitting issues using cross-validation and regularization techniques.

Model interpretation focuses on understanding predictor effects through raw regression coefficients, odds ratios, or hazard ratios and feature importance. Validation and calibration are crucial, involving internal techniques like bootstrapping and external validation on independent datasets to ensure generalizability.

Case studies illustrate practical applications of these models: one on fibrosis-4 (FIB-4) predicting fibrosis progression in patients with HIV/HCV, and another on predicting hepatocellular carcinoma (HCC) risk in patients with non-alcoholic fatty liver disease (NAFLD)-cirrhosis (as an example of decision curves analysis).

Challenges in data quality, model complexity, and clinical integration are acknowledged, with future directions pointing towards incorporating genomics and real-time data processing.

In conclusion, the structured development of clinical prediction models holds significant promise for enhancing patient care through informed, data-driven decision-making. This seminar will serve as a guide for clinicians to understand and apply predictive analytics in their practice, fostering collaboration between clinicians and data scientists for improved healthcare outcomes.

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Hepatology Associates 2

Essential Elements for a Successful Clinical Trial

Chairs:

Young Seok Kim (Soonchunhyang Univ.)
Byung-Cheol Song (Jeju National Univ.)

Minjong Lee

Ewha Womans University

Self Introduction

Prof. Minjong Lee is an Associate Professor of the Division of Gastroenterology and Hepatology in the Department of Internal Medicine, Ewha Womans University College of Medicine.

He graduated from Seoul National University College of Medicine with his medical degree in 2005 and Ph.D. in 2016 and completed his internship, residency, and fellowship at the Department of Internal Medicine at Seoul National University Hospital.

Since 2016, he has participated in the publication committee of the Korean Association of the Study of the Liver (2017-2023) and currently, in the research committee of the Korean Association of the Study of the Liver and the publication committee of the Korean Association of Gastroenterology (2024-).

Research Interests

Chronic Hepatitis B, Hepatocellular Carcinoma, MASLD

Representative Publications

1. PAGE-B incorporating moderate HBV DNA levels predicts risk of HCC among patients entering into HBeAg-positive chronic hepatitis B. Journal of Hepatology. 2024; 80(1):20-30.
2. Identification of patients with favorable prognosis after resection in intermediate-stage-hepatocellular carcinoma. International Journal of Surgery. 2024; 110(2):1008-1018.
3. Risk Stratification for Sarcopenic Obesity in Subjects With Nonalcoholic Fatty Liver Disease. Clinical Gastroenterology and Hepatology. 2023; 21(9):2298-2307.e18.
4. Association of Physical Activity With Risk of Liver Fibrosis, Sarcopenia, and Cardiovascular Disease in Nonalcoholic Fatty Liver Disease. Clinical Gastroenterology and Hepatology. 2023; 21(2):358-369.e12.
5. Modified PAGE-B score predicts the risk of hepatocellular carcinoma in Asians with chronic hepatitis B on antiviral therapy. Journal of Hepatology. 2018; 69(5):1066-1073

Differences between Sponsor-Initiated Trials and Investigator-Initiated Trials

Minjong Lee *Ewha Womans University*

Clinical research can be broadly divided into two main categories: sponsor-initiated trials (SITs) and investigator-initiated trials (IITs). Each category is characterized by distinct differences in funding mechanisms, research objectives, levels of control, regulatory requirements, data ownership, and publication freedom. A clear understanding of these differences is essential for researchers, sponsors, regulatory agencies, and healthcare providers.

Sponsor-initiated trials (SITs) are clinical studies that are initiated and financially supported by pharmaceutical companies, biotechnology firms, or medical device manufacturers. The primary goal of SITs is often to secure regulatory approval, enter new markets, or expand existing product labels. These studies are frequently conducted across multiple international sites to produce robust and generalizable data for submission to regulatory authorities. In contrast, investigator-initiated trials (IITs) are conceptualized and managed by independent clinicians, researchers, or academic institutions. The main objective of IITs is to generate new scientific knowledge, address unmet clinical needs, or explore novel uses of already approved therapeutic agents or devices. These trials are usually driven by clinical observations or academic interest, rather than commercial considerations.

The funding structure and degree of control also differ significantly between SITs and IITs. SITs are fully sponsored by the industry, giving the sponsor considerable influence over the design of the study, amendments to the trial protocol, data management strategies, and statistical analysis. Sponsors typically engage contract research organizations (CROs) to conduct trial operations, ensure compliance, and monitor quality. On the other hand, IITs are funded through diverse sources such as government agencies, academic research grants, non-profit foundations, or occasional support from industry. In IITs, investigators generally retain substantial control over the design, execution, and analysis of the trial. However, limited funding can constrain the scale or duration of the study, affecting its overall impact.

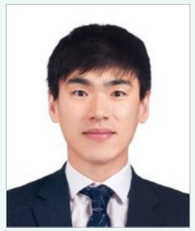
Regulatory compliance also varies between these two trial types. SITs are subjected to intense regulatory scrutiny and are required to follow strict international guidelines, including Good Clinical Practice (GCP), and national regulations such as those issued by the FDA or EMA. These trials must maintain safety monitoring and reporting practices due to the regulatory significance of the data produced. Although IITs are also required to comply with ethical and regulatory standards, they often have slightly

more flexibility in modifying the study protocol. Regulatory oversight is generally less burdensome in IITs, although investigators remain directly responsible for ensuring compliance with all applicable standards. This can pose challenges, especially for researchers or institutions with limited experience in clinical trial management.

Ownership of data and rights to publication represent another important distinction. In SITs, the data are typically owned by the sponsor, who may influence when and how the results are published. This control can lead to potential publication bias or delays in disseminating findings. In contrast, IITs grant investigators full or substantial ownership of the data, thereby allowing them greater freedom to publish their findings in a timely and transparent manner. This independence reduces the risk of publication bias and supports open scientific communication.

Each trial type has its own advantages and limitations. SITs benefit from substantial resources, which enable the execution of large-scale, multi-center studies. However, they often focus on commercially promising products, which may result in the underrepresentation of research that is important clinically but not financially attractive. Meanwhile, IITs, though often constrained by budgetary and logistical limitations, are well-positioned to explore innovative hypotheses and clinically important research questions that industry sponsors may overlook. These trials frequently pave the way for advances in personalized medicine and novel therapeutic strategies.

In conclusion, recognizing the fundamental differences between sponsor-initiated and investigator-initiated trials helps illuminate their complementary contributions to the advancement of medical science. While SITs are crucial for the development and approval of new therapies, IITs play a vital role in fostering scientific exploration and addressing patient-centered clinical questions. A well-balanced research environment that supports both trial types is essential for generating robust evidence and driving innovation in healthcare.



Seungwon Jeung

Korea Health Information Service

Self Introduction

Mr. Seungwon Jeung is a manager at the Korea Health Information & Service, where I am responsible for managing data utilization policies and planning data-related businesses and R&D projects.

He holds a master's degree in Pharmacy from Chung-Ang University.

He serves as a pseudonymization expert at the Personal Information Protection Commission and as the head of the Standardization Committee for the Brain-Computer Interface (BCI) Mind Care Forum.

Research Interests

- Institutional Healthcare Data Review Board
- Pseudonymization

Representative Publications

1. Healthdata guideline(보건의료데이터 활용 가이드라인) 2020, 2021, 2022, 2024

Hepatology Associates 2 | DAY 2: May 30 (Fri.) | ROOM 4 [2F]

Human Subjects Protection and Data Review Board

Seungwon Jeung *Korea Health Information Service*

With the quantitative increase in clinical trials (research) in South Korea, there is a growing social demand to strengthen the protection of the safety and rights of clinical trial participants.

The Ministry of Health and Welfare, the Ministry of Food and Drug Safety, and other regulatory bodies overseeing clinical trials are pursuing institutional improvements through legal amendments (such as the Pharmaceutical Affairs Act) to protect the safety and rights of patients participating in clinical trials.

- **Activation of the Human Research Protection Program (HRPP)**
- **Establishment and operation of a support center for protecting the rights and interests of clinical trial participants**
- **Designation and operation of a public-centered 'Central Institutional Review Board (Central IRB)'**
- **Conducting DRB reviews within medical institutions for the use and provision of clinical trial participants' medical records (in compliance with the Personal Information Protection Act)**

From the perspective of protecting research subjects' rights and information security, the necessity of a Data Review Board (DRB) in medical institutions conducting clinical trials (research) has been increasingly emphasized.

This necessity arises from two major aspects: legal and regulatory perspectives and the changing paradigm of clinical trials.

From a legal and regulatory perspective, the need for DRB review is growing for medical institutions conducting clinical trials to ensure the protection of clinical trial participants' information.

- **(With consent):** According to Article 18 of the Personal Information Protection Act, when providing medical records held by a medical institution to researchers, the institution must request necessary measures to ensure the security of personal information. The recipient of the request must also take the necessary measures to ensure the security of personal information.
- **(Without consent):** According to Article 28-2 of the Personal Information Protection Act, when a medical institution provides medical records for use in clinical trials or research, the data must be pseudonymized, considering the purpose of use, the retained data, and the processing environment.

Additionally, post-management measures must be considered in the decision-making process.

From a paradigm shift perspective, clinical trials can be classified into various categories, but they are largely divided into randomized controlled trials (RCTs) and real-world data (RWD)-based clinical trials.

The necessity of utilizing RWD is emerging, and its application is possible in almost all stages of the product lifecycle management of pharmaceuticals and medical products. RWD utilizes accumulated medical records within healthcare institutions and is typically subject to DRB review before being utilized. Notable examples of RWD-based clinical trial applications include Amgen's Blincyto and *Novartis' Zolgensma*.

The number of DRB operations in medical institutions is rapidly increasing. Among 47 advanced general hospitals in Korea, 94% (44 institutions) have established and are operating DRB review committees. In addition, among the 43 medical institutions participating in the Korea Health Information Service's Medical Data-Centric Hospital initiative, the number of DRB reviews has been growing at an annual average rate of 91%.

The DRB review has been institutionally recommended and operated by the Ministry of Health and Welfare since the amendment of the Personal Information Protection Act in 2020, which introduced a special provision for pseudonymization. However, conflicts with other regulations such as the Medical Service Act and the Bioethics and Safety Act, as well as the existence of regulatory gray areas, have caused confusion in the field of clinical trials (research). Therefore, the Ministry of Health and Welfare aims to eliminate such confusion by enacting a special law on the utilization of healthcare data, ensuring the protection of clinical trial (research) participants' rights and promoting its safe and active use.

Dae Won Jun

Hanyang University

Self Introduction

Prof. Dae Won Jun graduated from Hanyang University and is currently working at Hanyang University.

Research Interests

MASLD

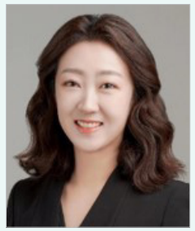
Representative Publications

	Title	Journal	Year	Role	IF
1	Diagnostic Performance of Noninvasive Tests in Patients with MetALD in a Health Check-up Cohort	Journal of Hepatology	2024	Corresponding	IF: 25.0
2	Do we need a new cut-off for FIB-4 in the metabolic dysfunction-associated fatty liver disease era?	Journal of Hepatology	2021	Corresponding	IF: 25.0
3	Diabetes is the strongest risk factor of hepatic fibrosis in lean patients with non-alcoholic fatty liver disease.	GUT	2021	Corresponding	IF: 23.0
4	Prevalence, distribution and hepatic fibrosis burden of the different subtypes of steatotic liver disease in primary care settings	Hepatology	2024	Corresponding	IF: 17.3
5	Is lifestyle modification effective for individuals with high fibrosis-4 index without an additional 2nd tier test?	Hepatology	2023	Corresponding	IF: 17.3
6	KASL clinical practice guidelines for noninvasive tests to assess liver fibrosis in chronic liver disease	Clinical and Molecular Hepatology	2024	Corresponding	IF: 14.0
7	Prevalence of clinically significant liver fibrosis in the general population: A systematic review and meta-analysis	Clinical and Molecular Hepatology	2024	Corresponding	IF: 14.0
8	Diagnostic Performance of the Fibrosis-4 Index and Nonalcoholic Fatty Liver Disease Fibrosis Score in Lean Adults with Nonalcoholic Fatty Liver Disease	JAMA network open	2023	Corresponding	IF: 13.8
9	Sex Differences in Treatment Response to Nucleos(t)ide Therapy in Chronic Hepatitis B: A Multicenter Longitudinal Study	Clinical Gastroenterology and Hepatology	2023	Corresponding	IF: 12.6
10	No Difference of Hepatocellular Carcinoma incidence in Chronic Hepatitis B Infection Treated with Entecavir vs Tenofovir	Clinical Gastroenterology and Hepatology	2020	Corresponding	IF: 12.6

Collection and Management of Patient-Derived Samples in Clinical Trials

Dae Won Jun *Hanyang University*

The management of clinical specimens is crucial for ensuring the integrity and reliability of data in clinical trials. This presentation discusses the best practices for the collection, storage, and processing of patient-derived samples, particularly in investigator-initiated trials (IIT). Proper specimen handling is essential for maintaining the quality of biological samples, such as blood, serum, plasma, liver tissue, and stool, which are widely used in molecular and clinical research. Specimens should be stored at ultra-low temperatures, with -80° C being the ideal condition for long-term preservation. Freezing and thawing cycles can lead to protein denaturation and RNA degradation, hence aliquoting samples is recommended. The use of cryotubes is necessary for preserving samples, as regular E-tubes are not designed for storage at temperatures below -20° C. Specific attention is needed to prevent contamination from RNases and DNases. Each specimen should be assigned a unique identifier according to a pre-established coding system (e.g., institution code, specimen type, visit number). Detailed records should be kept, including the exact location of each sample within the storage facility to facilitate easy retrieval. Samples should be stored in labeled containers, and project information should be clearly indicated on the storage boxes. Blood samples are typically processed into whole blood, serum, plasma, and peripheral blood mononuclear cells for various analyses, including biochemistry, DNA analysis, and immune profiling. Serum is separated by allowing blood to clot at room temperature and centrifuging, while plasma is processed with anticoagulants like EDTA or heparin. For DNA and RNA analysis, it is critical to avoid contamination, and special care must be taken when using anticoagulated blood. Liver tissue samples are fixed using neutral buffered formalin or paraformaldehyde for subsequent histological analysis, including H&E staining and immunofluorescence. For molecular analysis, samples are quickly frozen in OCT compound for single-cell RNA sequencing and spatial transcriptomics. For non-blood samples such as stool, saliva, urine, and environmental samples, special containers and precautions are required to prevent contamination and ensure sample integrity. DNA from microbiota in stool is preserved using specialized tubes such as OMNIgene·GUT kits. Saliva samples require fasting before collection, and urine is typically collected over a 24-hour period and refrigerated. Special attention must be paid to the use of certified containers to avoid contamination from environmental toxins (e.g., bisphenol A, phthalates). For certain assays, such as cell-free DNA testing and LPS (endotoxin) assays, special endotoxin-free certified materials are required.



Elisabet Kim

Asan Medical Center

Self Introduction

Ms. Elisabeth Kim is the Unit Manager of the Academic Research Office (ARO) at the Asan Medical Center Clinical Trial Center. She graduated from Hanyang University with a degree in Nursing and holds a master's degree as an Oncology Nurse Specialist.

Since 2017, she has gained extensive experience in early phase oncology clinical trials as a Clinical Research Coordinator Manager.

In 2024, she began serving as both Project Manager and Unit Manager in the Academic Research Office.

She is also currently serving as Director of Planning at the Korea Association of Clinical Research Coordinators (KACRC). (한국코디네이터회 기획부장 활동 중)

Keywords for Investigator-Initiated Trials (IIT): What Academia Needs to Know

Elisabet Kim *Asan Medical Center*

Investigator-Initiated Trials (IITs) represent a valuable yet often underrecognized component of clinical research. They offer academic investigators opportunities to explore novel scientific hypotheses, address unmet clinical needs, and generate evidence beyond the scope of industry-sponsored research. Such trials frequently lead to new insights into alternative uses of existing therapies, thereby contributing to the broader understanding of drug safety and efficacy, and ultimately improving patient outcomes and public health.[1]

In Korea, IITs are defined under the Regulation on Approval of Clinical Trial Plans for Drugs as clinical studies conducted independently by investigators without external sponsorship. These may involve unapproved drugs or approved drugs used beyond their currently authorized indications.[2] Successfully conducting IITs within academic institutions requires navigating a complex regulatory environment while ensuring scientific rigor. Key success factors include a clearly defined research hypothesis, adequate funding, a thorough understanding of relevant regulations and ethical standards, and collaboration with experienced clinical trial partners. As academia increasingly takes a proactive role in clinical development, institutional support systems and investigator training are becoming ever more critical.

This presentation will highlight key concepts and practical considerations for initiating and managing IITs within hospitals and academic settings, focusing on Korea's regulatory framework and lessons learned from real-world experience.[3]

References

1. Choudhury, K. (2013). Investigator initiated clinical trials (IITs) – A hidden gem. Perspectives in Clinical Research, 4(1), 6–7. https://doi.org/10.4103/2229-3485.103591
2. Ministry of Food and Drug Safety. Regulation on Approval of Clinical Trial Plans for Pharmaceuticals (의약품 임상시험계획 승인에 관한 규정).
3. Kim, K. H., Lee, J., Choi, Y., et al. (2021). A study to evaluate the efficacy and safety of rifaximin in Korean patients with hepatic encephalopathy: A multicenter, investigator-initiated trial. Clinical and Molecular Hepatology, 27(1), 103–113. https://doi.org/10.3350/cmh.2020.0024

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

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THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
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May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

Translational Hepatology

Promising Cutting-Edge Translational Liver Study

Chairs:

Youngmi Jung (Pusan National Univ.)
Ja Hyun Koo (Seoul National Univ.)

Min Kyu Yum

KAIST

Self Introduction

Prof. Min Kyu Yum is an Assistant Professor at the Graduate School of Medical Science and Engineering at KAIST, Republic of Korea. He received his Ph.D. in Biological Science from Seoul National University in 2017 after completing his bachelor's degree in Biology at Korea University in 2011.
He conducted postdoctoral research initially at Seoul National University and subsequently at the WT-MRC Stem Cell Institute and Gurdon Institute, University of Cambridge, UK, from 2017 to 2022.

Research Interests

His current research program aims to elucidate fundamental cellular and molecular mechanisms underlying stem cell dynamics, clonal evolution, and cell fate determination in normal tissue maintenance and cancer progression. Leveraging innovative genetic engineering technologies, advanced mouse models, single-cell genomics, and mathematical modelling, his team investigates how mutant cells divert from normal developmental trajectories during tumorigenesis and metastasis.

Representative Publications

1. Yum MK*, Han S, Fink J, Wu SH, Dabrowska C, Trendafilova T, Mustata R, Chatzeli L, Azzarelli R, Lee E, England F, Kim JK, Philpott A, Lee JH, Koo BK and Simons BD. (2021) Tracing oncogene-driven paracrine remodeling of the intestinal stem cell niche. Nature 594, 442-447
2. Han S, Fink J, Jörg DJ, Lee E, Yum MK, Chatzeli L, Merker SR, Josserand S, Trendafilova T, Andersson-Rolf A, Dabrowska C, Kim H, Naumann R, Lee JH, Sasaki N, Mort RL, Basak O, Clevers Hans, Stange DE, Philpott A, Kim JK, Simons BD and Koo BK. (2019) Defining the Identity and Dynamics of Adult Gastric Isthmus Stem Cells. Cell Stem Cell 25, 342-356
3. Kim JH, Han GC, Seo JY, Park I, Park W, Jeong HW, Lee SH, Bae SH, Seong J, Yum MK, Hann SH, Kwon YG, Seo DG, Choi MH and Kong YY. (2016) Sex hormones establish a reserve pool of adult muscle stem cells. Nature Cell Biology 18, 930-940.
4. Yum MK*, Kang JS, Lee AE, Jo YW, Seo JY, Kim HA, Kim YY, Seong J, Lee EB, Kim JH, Han JM, Kim S and Kong YY. (2016) AIMP2 Controls Intestinal Stem Cell Compartments and Tumorigenesis by Modulating Wnt/ β -Catenin Signaling. Cancer Research 76, 4559-4568.

Tracing Cellular Dynamics during Intestinal Tumorigenesis and Metastasis

Min Kyu Yum *KAIST*

Interactions between tumour cells and the surrounding microenvironment contribute to tumour progression, metastasis and recurrence. Although mosaic analyses in Drosophila have advanced our understanding of such cellular interactions during tumour initiation, parallel approaches have remained challenging to engineer in mammalian systems. Here, we present an oncogene-associated, multicolour reporter mouse model, the Red2Onco system, that allows differential tracing of mutant and wild-type cells in the same tissue. Applied to the small intestine, we show that oncogene-expressing mutant crypts alter the cellular organization of neighbouring wild-type crypts, driving accelerated clonal drift. Crypts expressing oncogenic KRAS or PI3K secrete BMP ligands that suppress local stem cell activity, while induced changes in PDGFRlo CD81+ stromal cells by crypts with oncogenic PI3K alter the Wnt signalling environment. Together, these results show how oncogene-driven paracrine remodelling creates a niche environment that is detrimental to the maintenance of wild-type tissue, promoting field transformation dominated by oncogenic clones. To further extend the research programme towards analysing clonal behaviours during tumour progression and metastasis, we establish robust frameworks including advanced spatial transcriptomics and live imaging with the cell cycle reporting system.

Hyunsoo Rho

Ewha Womans University

Self Introduction

Prof. Hyunsoo Rho is an assistant professor at Ewha Womans University, College of Pharmacy.

He received his Bachelor of Pharmacy degree from Chung-Ang University, College of Pharmacy in 2010, and earned his Master's degree in Pharmacology from Seoul National University, College of Pharmacy in 2014. He subsequently obtained his Ph.D. in Biochemistry and Molecular Genetics from the University of Illinois at Chicago in 2023. Following this, he served as a research assistant professor at Jeonbuk National University, School of Pharmacy until February 2025. Since March of this year, he has been working as an assistant professor of Pharmacology at Ewha Womans University, College of Pharmacy.

Research Interests

Fibrosis, Hepatocellular Carcinoma, Cancer Metabolism, Epigenetics

Representative Publications

1. Jang EJ, Kang SH, Kim KW. The method of using robotic Harmonic ACE curved shears for parenchymal transection in robotic hepatectomy. J Minim Invasive Surg. 2024 Jun 15;27(2):114-117. doi: 10.7602/jmis.2024.27.2.114. PMID: 38887003; PMCID: PMC11187608.
2. Shin SY, Jang EJ, Kang SH, Park EH, Kim KW. Advancing treatment for perihilar cholangiocarcinoma: role of hepatopancreaticoduodenectomy in small-volume centers. Front Surg. 2024 May 14;11:1406508. doi: 10.3389/fsurg.2024.1406508. PMID: 38807927; PMCID: PMC11130399.
3. Jang EJ, Kang SH, Kim KW. Exploring the feasibility of robotic liver resection in a limited resource setting. J Robot Surg. 2024 Apr 29;18(1):187. doi: 10.1007/s11701-024-01901-1. PMID: 38683380.
4. Jang, E.J., Kim, K. Comparative analysis of robotic single-site cholecystectomy outcomes between novice and expert surgeons. J Robotic Surg 18, 118 (2024). https://doi-org.libproxy.donga.ac.kr/10.1007/s11701-024-01859-0
5. Jang EJ, Kang SH, Kim KW. Intrahepatic Cholangiocarcinoma in Wilson's Disease: A Case Report. Am J Case Rep. 2024 Jan 27;25:e942372. doi: 10.12659/AJCR.942372. PMID: 38279525; PMCID: PMC10829935.

Histone Lactylation: A Novel Epigenetic Mark in Liver Fibrosis

Hyunsoo Rho *Ewha Womans University*

Highly glycolytic proliferating cells such as cancer cells induce hexokinase 2 (HK2) expression, which accelerates glucose utilization and results in promoting lactate production1. Previously, lactate was considered as a metabolic waste that is excreted from cells2. However, we found that HK2 producing lactate regulates gene expression via histone lactylation3. To understand whether targeting HK2 mediated gene regulation via histone lactylation can be a therapeutic strategy, we investigated hepatic stellate cells (HSCs) that are known to undergo metabolic reprogramming by inducing HK2 expression during liver damage4. In liver injury, HSCs are activated and become the main source of liver fibrogenic cells, and prolonged activation of these cells develops liver fibrosis, cirrhosis, and liver cancer5. Using RNA-seq and CUT&Tag chromatin profiling, we found that induction of HK2 expression in activated HSCs is required for induced gene expression by histone lactylation but not histone acetylation. Inhibiting histone lactylation by Hk2 deletion or pharmacological inhibition of lactate production diminishes HSC activation, whereas exogenous lactate but not acetate supplementation rescues the activation phenotype. Thus, lactate produced by activated HSCs determines the HSC fate via histone lactylation. We found that histone acetylation competes with histone lactylation, which could explain why class I HDAC (histone deacetylase) inhibitors impede HSC activation. Finally, HSC-specific or systemic deletion of HK2 inhibits HSC activation and liver fibrosis in vivo. Therefore, we provide evidence that HK2 may be an effective therapeutic target for liver fibrosis.

References

1. Hay N. (2016). Reprogramming glucose metabolism in cancer: can it be exploited for cancer therapy? Nat. Rev. Cancer 16, 635–649.
2. Rabinowitz JD and Enerback S. (2020). Lactate: the ugly duckling of energy metabolism. Nat. Metab. 2, 566–571.
3. Rho H, Terry AR, Chronis C, Hay N. (2023). Hexokinase 2-mediated gene expression via histone lactylation is required for hepatic stellate cell activation and liver fibrosis. Cell Metab. 35, 1406–1423.
4. Chen Y, Choi SS, Michelotti GA, Chan IS, Swiderska-Syn M, Karaca GF, Xie G, Moylan CA, Garibaldi F, Premont R, Suliman HB, Piantadosi CA, Diehl AM. (2012). Hedgehog controls hepatic stellate cell fate by regulating metabolism. Gastroenterology. 143, 1319–1329.
5. Mederacke I, Hsu CC, Troeger JS, Huebener P, Mu X, Dapito DH, Pradere JP, Schwabe RF. (2013). Fate tracing reveals hepatic stellate cells as dominant contributors to liver fibrosis independent of its aetiology. Nat. Commun. 4, 2823.

Ju Youn Kim

Hanyang University

Self Introduction

Education

1996-2000	Bachelor in Science Hanyang University, Seoul, South Korea
2001-2003	Master in Science Yonsei University College of Medicine, Seoul, South Korea
2005-2012	Doctor of Philosophy Boston University School of Medicine, Boston, MA
2013-2017	Post-Doctoral Fellow University of California San Diego, San Diego, CA
2018-2020	Assistant Project Scientist University of California San Diego, San Diego, CA
2021-2023.02	Staff Research Associate III University of California San Diego, San Diego, CA
2023.03-Present	Associate Professor Hanyang University, ERICA, Ansan, South Korea

Representative Publications

1. Peng Zhang, Junlai Liu, Allen Lee, Irene Tsaur, Masafumi Ohira, Vivian Duong, Nicolas Vo, Kosuke Watari, Hua Su, Ju Youn Kim, Li Gu, Mandy Zhu, Shabnam Shalapour, Mojgan Hosseini, Gautam Bandyopadhyay, Suling Zeng, Cristina Llorente, Haoqi Nina Zhao, Santosh Lamichhane, Siddharth Morhan, Pieter C Dorrestein, Jerrold M. Olefsky, Bernd Schnabl, Pejman Soroosh, Michael Karin. IL-22 resolves MASLD via enterocyte STAT3 restoration of diet-perturbed intestinal homeostasis. Cell Metabolism (2024), Oct;36:2341-2354.
2. Michael Karin, Ju Youn Kim. MASH as an emerging cause of hepatocellular carcinoma: current knowledge and future perspectives. Molecular Oncology (2024), June;1-8 *Corresponding Author
3. Ju Youn Kim, Lily Q. Wang, Valentina C. Sladky, Tae Gyu Oh, Junlai Liu, Kaitlyn Trinh, Felix Eichin, Michael Downes, Mojgan Hosseini, Etienne D. Jacotot, Ronald M. Evans, Andreas Villunger, Michael Karin. PIDDosome-SCAP cross-talk controls fructose diet-dependent transition from simple steatosis to steatohepatitis. Cell Metabolism (2022), Aug; 34:1548-1560. *Co-corresponding & Lead Author 4. Elodie Bosc, Julie Anastasie, Feryel Soualmia, Pascale Coric, Ju Youn Kim, Lily Q. Wang, Gullen Lacin, Kaitao Zhao, Ronak Patel, Eric Duplus, Philippe Tixador, Andrew Sproul, Bernard Brugg, Michelle Reboud-Ravaux, Michael Shelanski, Serge Bouaziz, Michael Karin, Chahrazade El Amri, and Etienne Jacotot. Genuine Selective Caspase-2 Inhibition with new Irreversible Small Peptidomimetics. Cell Death and Disease (2022), Nov; 13:1~14.
5. Ju Youn Kim, Feng He, Michael Karin. From Liver Fat to Cancer:Perils of the Western Diet. Cancers (2021), Mar;13 (5): 1-19.

Casp2: The New Hepatic Lipid Regulator

Ju Youn Kim *Hanyang University*

Obesity is pandemic, affecting approximately 40% population across the world, and its associated complications are prevalent. Of these, Metabolic dysfunction-associated steatohepatitis (MASH) is becoming the most serious liver complication that causes a heavy social burden and demands high medical costs. Epidemiology indicates that a change in lifestyle and dietary patterns significantly affects the incidence of obesity. Indeed, consumption of western diet (WD), of which the ingredients contain a high portion of processed meat, saturated fats, and refined sweeteners, is steeply increasing and closely correlated with the prevalence of obesity and metabolic syndrome (MS)[1]. However, the pathogenic mechanism linking obesogenic diet to NASH is far from clear.

Sterol regulated element binding protein (SREBP) is the master regulator of hepatic lipid synthesis: SREBP1c mainly regulates triglyceride synthesis and SREBP2 synthesizes cholesterol[2]. Sterol deficiency triggers SCAP-mediated SREBP activation[3], whereas hypernutrition together with ER-stress activates SREBP1/2 via caspase-2 (Casp2), the most conserved cysteine protease, promoting lipid synthesis in response to ER stress by leading non-canonical activation and secretion of site-1 protease (S1P). Hence, we proposed serum S1P as an early detection marker and inhibition of Casp2 as a therapeutic approach for patients with NASH (Kim et al., *Cell* 2018). However, whether these pathways interact and how they are selectively activated by different dietary cues is unknown. In recent study, we revealed regulatory crosstalk between the two pathways that controls the transition from hepatosteatosis to steatohepatitis. Hepatic ER-stress elicited by NASH-inducing diets activates IRE1 and induces expression of the PIDDosome subunits caspase-2, RAIDD and PIDD1, along with INSIG2, an inhibitor of SCAP-dependent SREBP activation. PIDDosome assembly activates caspase-2 and sustains IRE1 activation. PIDDosome ablation or IRE1 inhibition blunt steatohepatitis and diminish INSIG2 expression. Conversely, while inhibiting simple steatosis, SCAP ablation amplifies IRE1 and PIDDosome activation and liver damage in NASH-diet fed animals, effects linked to ER disruption and preventable by IRE1 inhibition. Thus, the PIDDosome and SCAP pathways antagonistically modulate nutrient-induced hepatic ER-stress to control non-linear transition from simple steatosis to hepatitis, a key step in NASH pathogenesis (Kim, et al., *Cell Metabolism* 2022)

In this presentation, we introduce the new role of Casp2/PIDDosome in regulation of hepatic choles-

terol biosynthesis and its effect on MASH progression. In addition, we introduce a new technique that mimics liver in a dish, a liver spheroid.

References

1. Brown M.S. and Goldstein J.L. Cell. 1997
2. Horton J.D., Goldstein J.L., and Brown M.S. J. Clin. Invest. 2002
3. Sakai, J., et al., Cell 1996
4. Kim J.Y. et al., Cell 2018
5. Kim J.Y. et al., Cell Metabolism 2022

Keon Wook Kang

Seoul National University

Self Introduction

Prof. Keon Wook Kang is a Professor of the College of Pharmacy, Seoul National University and is currently serving as the Dean of the College of Pharmacy at Seoul National University. He entered the College of Pharmacy at Seoul National University as an undergraduate in 1989, earning his master's degree from the same institution in 1995, and his Ph.D. in Pharmacology in 1999.

Afterward, he worked as a postdoctoral researcher at the New Drug Development Research Center at Seoul National University and at the University of California, Irvine, in the United States. In 2003, he was appointed as a full-time faculty member at College of Pharmacy, Chosun University. In September 2011, he was appointed as an associate professor at College of Pharmacy, Seoul National University, and since 2017, he has served as the Associate Dean for Students and the Associate Dean for Academic Affairs at the same institution. Since 2020, he has also been serving as the Deputy Director of the Office of Admissions, Seoul National University. In terms of academic society activities, he is currently the Senior Vice President of the Korean Society of Toxicology and has previously served as the Chair of the Academic Affairs Committee of the Korean Pharmaceutical Society.

Research Interests

Identification of Novel Target(s) for the Treatment of MASLD and Development of Small Molecule Inhibitors, Combination Therapy against Intractable Cancer

Representative Publications

1. Choi et al., Prevention of radiotherapy-induced pro-tumorigenic microenvironment by SFK inhibitors. Theranostics 15:875-893 (2025)
2. Yoo & Kim et al., Laser-responsive erastin-loaded chondroitin sulfate nanomedicine targeting CD44 and system xc- in liver cancer: A non-ferroptotic approach. J Control Release 375:574-588 (2024)
3. Park et al., TYRO3 blockade enhances anti-PD-1 therapy response by modulating expression of CCN1 in tumor microenvironment. J Immunother Cancer 11:e006084 (2023)
4. Kim et al., CD44 is involved in liver regeneration through enhanced uptake of extracellular cystine. Clin Transl Med 12:e873 (2022)
5. Park et al., Circulating Small Extracellular Vesicles Activate TYRO3 to Drive Cancer Metastasis and Chemoresistance. Cancer Res 81:3539-3553 (2021)

Translational Hepatology | DAY 2: May 30 (Fri.) | ROOM 6 [1F]

Identification of Novel Targets for the Treatment of MASLD

Keon Wook Kang *Seoul National University*

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a condition characterized by excessive fat accumulation within the liver, unrelated to significant alcohol consumption. It is associated with metabolic syndrome, including obesity, diabetes, hypertension, and hyperlipidemia, and has a global prevalence of approximately 30%.[1] Hepatic fibrosis is characterized by impaired cell-to-cell interactions within the liver tissue due to abnormal deposition of proteins like collagen and elastin. Therapeutic strategies have been developed based on the activity of matrix metalloproteinases (MMPs), which play a role in the degradation of the extracellular matrix.[2] In this study, we investigated the therapeutic potential of novel targets identified using the MASLD-specific eQTL approach. Among the targets derived from eQTL analysis based on bulk RNA sequencing and single-cell RNA sequencing, we specifically highlight Gene-X. Protein-X is a secreted protein that is a member of the MMP-like family. It contains a protease domain with zinc-dependent proteinase activity, similar to MMPs, but unlike MMPs, it possesses an ancillary domain with thrombospondin motifs, enabling it to bind more effectively to proteoglycans. Thus, these structural differences allow Protein-X to more selectively degrade chondroitin sulfate proteoglycans, including versican and aggrecan, contributing directly to the generation of matrikines. In particular, versican, the major substrate of Protein-X, is upregulated under inflammatory conditions and serves as a chemoattractant for lymphoid and myeloid cells, promoting the production of inflammatory cytokines. Versikine, generated by the cleavage of versican, converts bone marrow-derived macrophages (M0) to an inflammatory macrophages (M1), leading to the expression of proinflammatory cytokines.[3]

We conducted the following studies to elucidate the role of Gene-X in MASLD and hepatic fibrosis, with the aim of proposing it as a novel therapeutic target for hepatic fibrosis 1) A correlation study of Gene-X in human samples and mouse MASLD models, 2) Investigation of the role of Gene-X in mouse MASH or fibrosis models, 3) Research into the mechanisms by which Gene-X promotes fibrosis, and 4) Discovery of Protein-X inhibitor and evaluation of its pharmacological activities in mouse hepatic fibrosis model.

We first revealed an increased expression of Gene-X in the liver tissues of human MASLD patients and the fibrotic MASH model in mice. The most significant increase was observed in hepatic stellate cells (HSCs) among non-parenchymal cells under the context of fibrosis. Diet- or chemical- induced liver

fibrosis in Gene-X knockout mice resulted in an improvement in fibrosis markers, accompanied by a significant reduction in the recruitment of myeloid-derived immune cells. Furthermore, we demonstrated that TNFα secreted during MASLD progression accelerates the expression and secretion of Gene-X in HSCs and hepatocytes. We found that Protein-X increased the secretion of versikine from HSCs, and the generated versikine contributed to the recruitment of macrophages and their differentiation into the M1 phenotype, thus accelerating hepatitis and involvement in fibrogenesis. We also found that secreted Protein-X directly induced Col1A1 in HSCs by activating STAT3. These findings propose Protein-X as a novel therapeutic target for the inhibition of MASLD and hepatic fibrosis.

References

1. Sepanlou, S. G. et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Gastroenterology & Hepatology 5, 245-266 (2020).
2. Wynn, T. A. Cellular and molecular mechanisms of fibrosis. The Journal of Pathology 214, 199-210 (2008).
3. Wight, T. N. Provisional matrix: A role for versican and hyaluronan. Matrix Biology 60-61, 38-56 (2017).

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Health Insurance and Policy Forum

Chairs:

In Hee Kim (Jeonbuk National Univ.)
Hyun Woong Lee (Yonsei Univ.)

Panelists:

Yunsuk Kim (Korea Disease Control and Prevention Agency)

Eileen L. Yoon

Hanyang University

Self Introduction

Prof. Eileen Yoon is an Associate Professor of the Department of Internal Medicine, Hanyang University College of Medicine.

Prof. Yoon graduated from Korea University College of Medicine with her medical degree in 2006 and completed her residency at the Department of Internal Medicine at Korean University Hospital, receiving his diploma in Gastroenterology in 2013.

Since 2014, Prof. Yoon has been taking a number of roles, including members of Insurance Committee of the Korean Association of the Study of the Liver (2020- Present) and Korean association of Gastroenterology (2022- Present), and currently as Director of Insurance Committee of the Korean Liver Cancer Association (2024- Present).

Research Interests

Metabolic-associated fatty liver disease, Alcohol-related liver disease, Liver cirrhosis

Representative Publications

1. Lee CM, Yoon EL, Kim M, et al. Prevalence, distribution, and hepatic fibrosis burden of the different subtypes of steatotic liver disease in primary care settings. Hepatology. 2024;79(6):1393-400. Epub 20231101.
2. Park H, Kim M, Kim HL, et al. Diagnostic performances of Fibrosis-4 index and nonalcoholic fatty liver disease fibrosis score in metabolic dysfunction-associated steatotic liver disease in Asian primary care clinics. Hepatol Res. 2024. Epub 20240504.
3. Park H, Yoon EL, Chung GE, et al. Genetic and Metabolic Characteristics of Lean Nonalcoholic Fatty Liver Disease in a Korean Health Examinee Cohort. Gut Liver. 2024;18(2):316-27. Epub 20230810.
4. Park H, Yoon EL, Kim M, et al. Comparative evaluation of non-invasive tests for risk stratification for cause specific mortality in at-risk population of hepatic fibrosis. Sci Rep. 2024;14(1):7189. Epub 20240326.
5. Park H, Yoon EL, Kim M, et al. Cost-effectiveness study of FIB-4 followed by transient elastography screening strategy for advanced hepatic fibrosis in a NAFLD at-risk population. Liver Int. 2024;44(4):944-54. Epub 20240130.

Current Status and Unmet Need of Reimbursement of Systemic Chemotherapy for Hepatocellular Carcinoma

Eileen L. Yoon *Hanyang University*

For clinicians, the most critical aspect of determining a treatment for a patient diagnosed with HCC is selecting the most suitable and appropriate course of action, considering the patient's condition and the current stage of the disease. However, in actual clinical practice, numerous other factors must be taken into consideration. These include the unpredictability of the reimbursement outcome and the potential for financial constraints, which may result in the treatment not being covered by insurance. Consequently, clinicians may find themselves in a defensive position, opting for a financially secure outcome rather than providing the most effective treatment for the patient.

The most recent international guidelines for HCC uniformly recommend the incorporation of a PD-1 or PD-L1 inhibitor, such as atezolizumab plus bevacizumab or durvalumab plus tremelimumab, as the initial treatment modality for patients with advanced HCC.

A review of the current state of systemic anti-cancer therapy in Korea reveals four major challenges. The initial observation is that the reimbursement criteria for first-line immunotherapy are exceedingly stringent. Patients with Stage III, Child Pugh A, ECOG 0-1 must demonstrate that they are "surgically or locally inoperable" to be eligible for reimbursement. However, in the treatment of HCC, there are few stages that are not able to be treated with local treatment. Local treatment, such as embolization, can be considered as an alternative option if other treatment is not eligible. Consequently, it is imperative to redefine the term "impossible to treat with local therapy" to "inappropriate for local therapy". Secondly, the ability of a multidisciplinary team to make treatment decisions that are grounded in clinical expertise is paramount for patients with TACE-refractory hepatocellular carcinoma (HCC). Nevertheless, a divergence of opinion persists among clinicians and reviewers in the Health Insurance Review & Assessment service. It is imperative to acknowledge and honor the treatment decisions made by clinicians in the context of multidisciplinary care. Thirdly, the reimbursement period for first-line immunotherapy is currently limited to two years. While the accumulation of clinical evidence is underway, the reimbursement status for patients with HCC who are well-controlled with immunotherapy for a period exceeding two years should be considered for reimbursement until the sound evidence is more clearly defined. Fourthly, the financial implications of second-line systemic anti-cancer drugs are substantial. There is an urgent need to improve the reimbursement of sorafenib, lenvatinib, carbozantinib, and ramucirumab as second-line therapies.

Procedural Standards for Health Insurance Coverage and Criteria for Oncology Drug Reimbursement

Mi Young Kang *Health Insurance Review & Assessment Service*

Young Joon Park

Korea Disease Control and Prevention Agency

학력

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2006.03-2008.02 가톨릭대학교 의학대학원 예방의학 석사 졸업

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- 역학조사분석담당관
- 인수공통감염병관리과
- 결핵정책과

2025.03-현재 감염병관리과

Introduction of National Hepatitis C Screening and Post-Screening Management Plan

Young Joon Park *Korea Disease Control and Prevention Agency*

Won-Ho Kim

Korea National Institute of Health

Self Introduction

Dr. Won-Ho Kim is a director of the Department of Chronic Disease Convergence Research, Korea National Institute of Health and is currently serving as the Deputy director for the promotion of the establishment of the National institute of Aging along with the National Institute of Cardiovascular disease simultaneously.

After graduating from Chung-Ang University, Dr. Kim received four years of training as a postdoctoral fellowship at the National Institutes of Health (NIH) in the United States from 2000 to 2004. Since 2005, Dr. Kim joined the National Institute of Health in Korea (Korea NIH) as a Deputy Director. He served as the head of the Cardiovascular Disease Research Division and he is currently working as the Director of the Chronic Disease Convergence Research Department.

Research Interests

Dr. Kim's main research areas is to identify and develop the techniques and targets for the prevention, diagnosis, and intervention of NAFLD, diabetes and diabetic complications including CVD and CKD. He has published many excellent papers in journals such as J of Hepatology, Hepatology, Diabetes, Translational Research, and Hearts based on the inter-regulation of the liver-pancreas, liver-heart, DM-CKD and NAFLD-induced diabetes and cardiometabolic diseases. He has published about 120 papers to date.

Representative Publications

1. Lee SH, Cho S, Lee J, and Won-Ho Kim. Methionine sulfoxide reductase B2 protects against cardiac complications in diabetes mellitus. Diabetology & Metabolic Syndrome (2024) 16:149.
2. Lee SH, Cho S, Lee J, and Won-Ho Kim. Identification of potential drug targets for antiplatelet therapy specifically targeting platelets of old individuals through proteomic analysis. Biomedicines (2023) 11:2944.
3. Lee D, Kim J, Cha D, Hwang G-S, Won-Ho Kim. Association between local acidosis induced by renal LDHA and renal fibrosis and mitochondrial abnormalities in patients with diabetic kidney disease. Translational Research (2022) 249:88-109.
4. Park JH, Koo BK, Kim W, and Won-Ho Kim. Histological severity of non-alcoholic fatty liver disease is associated with 10-year risk for atherosclerotic cardiovascular disease. Hepatology International (2021) 15(5):1148-1159.
5. Lee SH, Du J, Hwa J, and Won-Ho Kim. Parkin coordinates platelet stress response in diabetes mellitus: big role in a small cell. International J of Molecular Sciences 2020, 21:5869.
6. Kim JY, Park KJ, Hwang J, Gao B, Kim W, and Won-Ho Kim. Activating Transcription Factor 3 is a target molecule linking hepatic steatosis to impaired glucose homeostasis. J of Hepatol (2017) 67(2):349-359.

Disease Burden of MASLD and Management of High-Risk Groups in Korea

Won-Ho Kim *Korea National Institute of Health*

Background: In 2023, the American and European liver associations have endorsed new nomenclature of steatotic liver disese (SLD) instead of fatty liver disease (FLD) and definition of metabolic dysfunction-associated steatotic liver disease (MASLD), aiming to better reflect the disease pathophysiology, reduce stigma, and enhance clinical management. In 2024, South Korea also officially adopted MASLD as the new nomenclature for NAFLD during The Liver Week conference. MASLD is defined as the presence of hepatic steatosis along with at least one of five cardiometabolic risk factors that correspond to the components of metabolic syndrome.

Prevalence and Burden: MASLD is the most common liver disorder in the world; over 90% of obese, 60% of diabetic, and up to 20% of normal-weight people develop MASLD. MASLD affects about 20 to 25% of people in Europe. In the United States, estimates suggest that 30% to 40% of adults have MASLD, and about 3% to 12% of adults have MASH. The annual economic burden was about US$103 billion in the United States in 2016. In South Korea, the estimated prevalence is also 30-40%, and this rate is expected to rise due to increasing obesity and diabetes cases. MASLD-related complications, including cirrhosis, hepatocellular carcinoma, and cardiovascular diseases, impose a substantial economic burden, with healthcare costs reaching billions annually.

Policy Recommendations for Prevention and Management: To effectively prevent and manage MASLD, a national strategy is required. The following policies are proposed: 1) Early Screening Program for High-Risk Populations: Implement liver ultrasound and non-invasive fibrosis tests for individuals with obesity, diabetes, or metabolic syndrome during routine health check-ups. 2) Lifestyle Modification Programs: Strengthen public health campaigns on nutrition, physical activity, and alcohol consumption reduction. 3) Enhanced Primary Care Integration: Support continuous monitoring and management of MASLD patients in primary healthcare settings. 4) Research and Data Collection: Establish a national MASLD registry for epidemiological studies. 5) Public Awareness and Education: Launch nationwide campaigns to raise awareness of MASLD risks and prevention measures.

Conclusion: MASLD has emerged as a major global health issue, necessitating early detection and systematic management. National preventive policies must be implemented to reduce MASLD prevalence and associated disease burden effectively.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
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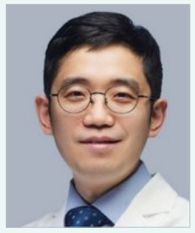
DAY 2: May 30 (Fri.)

KASL Special Interest Group 3.
The KASL Autoimmune and Rare Liver Disease Study Group

Exploring Autoimmune and Rare Liver Diseases

Chairs:

Kyung-Ah Kim (Inje Univ.)
Atsushi Tanaka (Teikyo Univ., Japan)



Soon Kyu Lee

The Catholic University of Korea

Self Introduction

Prof. Soon Kyu Lee is an associate professor in the Division of Gastroenterology and Hepatology at the Catholic University of Korea. He is actively conducting both basic and clinical research related to hepatocellular carcinoma, transplantation, autoimmune liver disease, hepatitis virus infection, and alcoholic liver disease.

He graduated from the Catholic University of Korea, College of Medicine with his medical degree in 2011 and completed his internship and residency at the Department of Internal Medicine at The Catholic University of Korea, receiving his Ph.D. in Internal Medicine in 2022.

He has demonstrated a strong commitment to both basic and clinical research and has received several prestigious honors, including the Young Investigator Award at the Asia-Pacific Primary Liver Cancer Expert (APPLE) Meeting 2023 and recognition as one of the Top 50 Outstanding Achievements (2023) in the Ministry of Education's Academic and Research Support Program, for which he was awarded by the Deputy Prime Minister and Minister of Education of Korea.

Research Interests

Autoimmune Liver Disease, Liver Transplantation, Hepatocellular Carcinoma, Gut Microbiome, Hepatitis Virus Infection, and Alcoholic Liver Disease

Representative Publications

1. Optimal tacrolimus levels for reducing CKD risk and the impact of intrapatient variability on CKD and ESRD development following liver transplantation, Clinical and Molecular Hepatology (2025) 31:131-146
2. Expansion of effector regulatory T cells in steroid-responders of severe alcohol-associated hepatitis, Liver Transplantation (2024) DOI: 10.1097/LVT.0000000000000378
3. An Early Increase in IL-10 and TNF-α Levels Following Atezolizumab Plus Bevacizumab Treatment Predicts Survival in Advanced Hepatocellular Carcinoma Patients: A Prospective Cohort Study, Cancers (2024), Oct 21;16(20):3543
4. A decrease in functional microbiomes represented as Faecalibacterium affects immune homeostasis in long-term stable liver transplant patients, Gut microbes (2022), 14:1, 2102885
5. Immune-mediated liver injury represented as overlap syndrome after SARS-CoV-2 vaccination, Journal of Hepatology (2022), 77:1207-1230

Challenges in the Diagnosis and Treatment of Autoimmune Hepatitis

Soon Kyu Lee *The Catholic University of Korea*

Autoimmune hepatitis (AIH) is an inflammatory liver disease caused by autoimmune mechanisms, with an incidence rate of 1.07 per 100,000 population in Korea.[1] It shows a female predominance among adults and has the highest prevalence in the 60–69-year age group in Korea.[1,2] Clinically, most patients present with chronic hepatitis, and approximately 30% have cirrhosis at the time of diagnosis. AIH can also manifest as acute hepatitis, acute severe AIH (AS-AIH), or even acute liver failure (AIH-ALF). For diagnosis, liver biopsy is recommended in patients with positive autoantibodies (ANA, AMA, anti-LKM1, or anti-SLA) and/or elevated serum IgG levels.[3,4] Typical histopathological features of AIH include interface hepatitis, lymphoplasmacytic portal inflammation, hepatocyte rosettes, emperipolesis, and varying degrees of fibrosis.[5] In addition to histological findings, diagnosis is supported using either the simplified or revised original diagnostic criteria.[1]

In the diagnosis of AIH, distinguishing it from drug-induced autoimmune-like hepatitis (DI-ALH) can be particularly challenging. Several medications—such as nitrofurantoin, minocycline, alpha-methyldopa, and hydralazine—are known to trigger features resembling DI-ALH.[6] To differentiate AIH from DI-ALH, the Roussel Uclaf Causality Assessment Method (RUCAM) score, along with the simplified or revised original diagnostic criteria, may be applied.[5,6] Although liver biopsy plays a critical role in the diagnostic workup, it may not definitively distinguish between the two, as both conditions can present with overlapping histologic features such as interface hepatitis. Given this overlap, when liver biopsy findings suggest "probable" or "possible" AIH, immunosuppressive therapy may be initiated in patients with ongoing liver injury. Following clinical and biochemical resolution, an attempt to withdraw immunosuppressive therapy can aid in differentiating AIH from DI-ALH, as relapse is common in true AIH.[6]

Meanwhile, acute presentations of AIH—including acute AIH, acute severe AIH (AS-AIH), and AIH-associated acute liver failure (AIH-ALF)—must also be considered, as they account for approximately 10–40% of all AIH cases.[7] In acute AIH, serum IgG levels and autoantibody titers may be normal or only mildly elevated.[8] AS-AIH is defined by the presence of jaundice, a prothrombin time-international normalized ratio (PT-INR) ≥1.5, absence of hepatic encephalopathy, and no history of pre-existing liver disease. AIH-ALF is characterized by jaundice, PT-INR ≥1.5, the development of hepatic encephalopathy within 26 weeks of symptom onset, and no prior liver disease.[9] In addition to typical histological

features of AIH, AS-AIH and AIH-ALF may present with central perivenulitis, centrilobular hemorrhagic necrosis, portal lymphoplasmacytic infiltration, and minimal or absent fibrosis/cirrhosis.. For AS-AIH, early evaluation of treatment response—typically within 3–7 days of initiating corticosteroid therapy—is recommended. The SURFASA score, which incorporates day 0 INR, day 3 INR, and day 3 bilirubin levels, may assist in predicting treatment response.[8,10] In patients with AS-AIH who do not improve, or in cases of AIH-ALF with high MELD scores, liver transplantation should be considered.[7]

In the treatment of AIH, steroid-based induction therapy followed by azathioprine-based maintenance therapy is commonly used.[1,8] Treatment response is typically evaluated after 1 month (to assess response vs. non-response) and again at 6 months (to assess complete biochemical response vs. incomplete response).[4,11,12] For patients with an incomplete response, second-line therapies such as mycophenolate mofetil (MMF) or tacrolimus are preferred, while cyclosporine, 6-mercaptopurine (6-MP), and 6-thioguanine (6-TG) are also recommended alternatives.[4,11,12] In cases of relapse following remission, re-initiation of first-line therapy is generally advised, along with consideration for long-term treatment.[5,11] Recently, several novel therapeutic candidates for AIH have been studied, including tofacitinib, infliximab, tocilizumab, IL-2 mutein, and ustekinumab, which target the JAK/STAT, TNF-α, IL-6, IL-2, and IL-12/IL-23 pathways, respectively.[13,14] In addition, cell-based therapies are under investigation, such as regulatory T cell (Treg) infusion, anti-BAFF receptor antibody targeting B cells, and therapies targeting natural killer cells.[13,14]

In conclusion, autoimmune hepatitis has various spectrum, including chronic hepatitis, AS-AIH, and AIH-ALF, which make challenges for clinician in the diagnosis and management according to the clinical features. Moreover, DI-ALH should be differentiated from AIH, with observation of relapse as the specific hallmark of AIH. Besides the high rate of relapse, the possibility of incomplete response is still challenging in the management of AIH. Several 2nd-line therapies are introduced, and novel candidate therapies are under investigated to improve the patient's clinical outcomes.

In conclusion, AIH presents with a broad clinical spectrum, including chronic hepatitis, AS-AIH, and AIH-ALF, posing diagnostic and therapeutic challenges for clinicians. In addition, DI-ALH should be carefully differentiated from AIH, with relapse following treatment withdrawal serving as a key distinguishing feature of true AIH. Despite the generally favorable prognosis, the high relapse rate and potential for incomplete response remain major challenges in AIH management. Several second-line therapies have been introduced, and novel therapeutic candidates are currently under investigation to improve clinical outcomes in affected patients.

References

1. KASL clinical practice guidelines for management of autoimmune hepatitis 2022. Clin Mol Hepatol 2023;29:542-592.
2. Katsumi T, Ueno Y. Epidemiology and surveillance of autoimmune hepatitis in Asia. Liver Int 2022;42:2015-2022.
3. Flikshteyn B, Amer K, Tafesh Z, Pyrsopoulos NT. Diagnosis of Autoimmune Hepatitis. Clin Liver Dis 2024;28:37-50.
4. Wang G, Tanaka A, Zhao H, Jia J, Ma X, Harada K, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidance: the diagnosis and management of patients with autoimmune hepatitis. Hepatol Int 2021;15:223-257.
5. Mack CL, Adams D, Assis DN, Kerkar N, Manns MP, Mayo MJ, et al. Diagnosis and Management of Autoimmune Hepatitis in Adults and Children: 2019 Practice Guidance and Guidelines From the American Association for the Study of Liver Diseases. Hepatology 2020;72:671-722.
6. Andrade RJ, Aithal GP, de Boer YS, Liberal R, Gerbes A, Regev A, et al. Nomenclature, diagnosis and management of drug-induced autoimmune-like hepatitis (DI-ALH): An expert opinion meeting report. J Hepatol 2023;79:853-866.
7. Tanaka A, Harada K. Acute presentation of autoimmune hepatitis -from acute hepatitis to ALF and ACLF. Hepatol Int 2024;18:1385-1395.
8. Heneghan MA, Lohse AW. Update in clinical science: Autoimmune hepatitis. J Hepatol 2025;82:926-937.
9. Komori A, Kugiyama Y. Hard-to-treat autoimmune hepatitis and primary biliary cholangitis: The dawn of a new era of pharmacological treatment. Clin Mol Hepatol 2025;31:90-104.
10. De Martin E, Coilly A, Chazouillères O, Roux O, Peron JM, Houssel-Debry P, et al. Early liver transplantation for corticosteroid non-responders with acute severe autoimmune hepatitis: The SURFASA score. J Hepatol 2021;74:1325-1334.
11. Pape S, Snijders R, Gevers TJG, Chazouilleres O, Dalekos GN, Hirschfield GM, et al. Systematic review of response criteria and endpoints in autoimmune hepatitis by the International Autoimmune Hepatitis Group. J Hepatol 2022;76:841-849.
12. Komori A. Recent updates on the management of autoimmune hepatitis. Clin Mol Hepatol 2021;27:58-69.
13. Snijders R, Assis DN, Oo YH, Sebode M, Taubert R, Willemse J, et al. Research gaps and opportunities in autoimmune hepatitis-Results of the international autoimmune hepatitis group research workshop 2022. Liver Int 2023;43:1375-1384.
14. Lohse AW, Sebode M, Jørgensen MH, Ytting H, Karlsen TH, Kelly D, et al. Second-line and third-line therapy for autoimmune hepatitis: A position statement from the European Reference Network on Hepatological Diseases and the International Autoimmune Hepatitis Group. J Hepatol 2020;73:1496-1506.

Atsushi Tanaka

Teikyo University, Japan

Self Introduction

Prof. Atsushi Tanaka received his M.D. from the University of Tokyo, Japan, in 1988. After spending three years as a resident physician at St. Luke's International Hospital in Tokyo, he received his Ph.D. degree from the University of Tokyo in 1996, and then stayed at the University of California, Davis, from 1996 to 1999 as a visiting scholar with M. Eric Gershwin, M.D., where he elucidated T cell mechanisms involved in the pathogenesis and progression of primary biliary cholangitis (PBC).

Returning to Japan in 2000, he rose through the academic ranks to become Professor of Medicine at Teikyo University School of Medicine in 2011. His area of expertise is autoimmune liver diseases, especially autoimmune hepatitis (AIH), PBC, primary sclerosing cholangitis (PSC), and IgG4-related sclerosing cholangitis. He has authored more than 250 peer-reviewed manuscripts on these topics. He has provided outstanding leadership to hepatology in Japan, including ongoing service as Chairman of the Drafting Committee for Hepatitis Management Guidelines of the Japan Society of Hepatology (JSH). Currently, he is also the PI of the Intractable Hepatobiliary Disease Study Group supported by the Ministry of Health, Labor and Welfare of Japan, and is one of the leaders in autoimmune liver disease research in Japan. He is an active member of the APASL Clinical Practice Guidelines Committee for AIH and PBC, and has been a member of the steering committee of the Global PBC Group since 2021.

Research Interests

Autoimmune Liver Disease, Drug-Induced Liver Injury, and Rare Liver Diseases

Representative Publications

1. Atsushi Tanaka, Kenji Notohara, Maki Tobari, et al. A clinicopathological study of IgG4-related autoimmune hepatitis and IgG4-hepatopathy. J Gastroenterol, in press.
2. Laurent Lam, Pierre-Antoine Soret, Atsushi Tanaka, et al, on behalf of the Global & ERN Rare-Liver PBC Study Groups. Dynamics of liver stiffness measurement and clinical course of primary biliary cholangitis. Clin Gastroenterol Hepatol, 2024 Dec;22(12):2432-2441.e2.
3. Atsushi Tanaka, Kenichi Harada. Acute Presentation of Autoimmune Hepatitis –from acute hepatitis to ALF and ACLF-. Hepatol Int, 2024 Oct;18(5):1385-1395.
4. Atsushi Tanaka, Xiong Ma, Atsushi Takahashi, John M. Vierling. Primary biliary cholangitis. Lancet, 2024 Sep 14;404(10457):1053-1066.
5. Atsushi Tanaka, Keiji Tsuji, Yasuyuki Komiyama, et al. RECAM-J 2023 – validation and development of the Japanese version of RECAM for the diagnosis of DILI. Hepatol Res, 2024 Jun;54(6):503-512.

Current Status and Research Trends of Autoimmune Liver Diseases in Japan

Atsushi Tanaka *Teikyo University, Japan*

In Japan, as in Western countries, research trends in autoimmune liver diseases (AILDs) have recently focused predominantly on clinical researches. A national research group funded by the Japanese government, titled "Research on Intractable Hepato-Biliary Diseases," has been established, and I have served as the principal investigator for the past five years. This consortium primarily targets autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC), and has constructed nationwide disease registries through collaboration with numerous medical institutions in Japan. Currently, the registries contain clinical data on 2,579 cases of PBC, 3,528 cases of AIH, and over 500 cases of PSC, which are actively being utilized for various clinical studies.

Regarding PBC, we have utilized bezafibrate as a second-line therapy for ursodeoxycholic acid (UDCA)-nonresponsive cases since around 2000. A collaborative study with European institutions demonstrated improved long-term outcomes in patients treated with bezafibrate compared to untreated patients.[1] Additionally, we reported that the albumin-bilirubin (ALBI) grade is useful in prognostic prediction in Japanese PBC patients.[2] While previous European studies have highlighted impaired health-related quality of life (HRQOL) in PBC due to diverse subjective symptoms, our own survey using the PBC-40 instrument revealed similar findings in Japanese patients.[3] Eight years after the initial study, we are currently conducting a follow-up HRQOL survey and plan to compare the results longitudinally. As a culmination of these clinical studies, our comprehensive review of PBC was published in The Lancet in 2024.[4]

For AIH, we reported national trends based on the registry data,[5] highlighting a recent increase in acute-onset cases,[6] and proposed a conceptual framework to better understand this disease presentation.[7] Regarding PSC, we clarified the current status in Japan based on registry data,[8] and found that UDCA is associated with improved long-term prognosis.[9] Furthermore, our nationwide epidemiological studies of all three diseases revealed increasing prevalence, along with a relative rise in the proportion of male patients with PBC and AIH.[10] A case-control study suggested that improved sanitation compared to previous decades may be associated with the rising incidence of male PBC patients.[11]

Thus, significant progress has been made in clinical research over the past decade. However, basic and translational research that could potentially lead to a cure remains insufficient, partly due to these areas

being outside the scope of the aforementioned research group funded by the Japanese government. Nevertheless, there is growing interest in the role of gut microbiota. Notably, Nakamoto and colleagues at Keio University reported that Klebsiella species are closely implicated in the pathogenesis of PSC,[12] and have begun exploring the therapeutic potential of bacteriophage therapy.[13] In PBC, Kawata's group at Hamamatsu Medical University reported in murine PBC models that a high-fat diet alters bile acid composition and gut microbiota, thereby exacerbating cholangitis.[14]

In Japan, clinical research that can directly inform therapeutic strategies and health policy tends to receive more funding than basic research, which often yields slower outcomes. Nevertheless, many unresolved questions remain in the field of AILDs. Moving forward, we aim to expand basic research efforts, for instance, to identify novel prognostic biomarkers and develop breakthrough therapies capable of significantly altering disease outcomes. I do hope to continue our collaboration with hepatologists in Korea even more than before.

References

1. Tanaka, A., et al., J Hepatol, 2021. 75(3): p. 565-571.
2. Yamashita, Y., et al., JHEP Rep, 2023. 5(4): p. 100662.
3. Yagi, M., et al., Sci Rep, 2018. 8(1): p. 12542.
4. Tanaka, A., et al., Lancet, 2024. 404(10457): p. 1053-1066.
5. Takahashi, A., et al., J Gastroenterol, 2017. 52(5): p. 631-640.
6. Takahashi, A., et al., Sci Rep, 2020. 10(1): p. 14250.
7. Tanaka, A. and K. Harada, Hepatol Int, 2024. 18(5): p. 1385-1395.
8. Tanaka, A., et al., J Hepatobiliary Pancreat Sci, 2017. 24(4): p. 217-225.
9. Arizumi, T., et al., J Gastroenterol, 2022. 57(11): p. 902-912.
10. Tanaka, A., et al., Hepatol Res, 2019. 49(8): p. 881-889.
11. Matsumoto, K., et al., Hepatol Res, 2023. 53(10): p. 989-997.
12. Nakamoto, N., et al., Nat Microbiol, 2019. 4(3): p. 492-503.
13. Ichikawa, M., et al., Nat Commun, 2023. 14(1): p. 3261.
14. Umemura, M., et al., J Autoimmun, 2024. 148: p. 103287.

Yu Rim Lee

Kyungpook National University

Self Introduction

Postgraduate Training and Position

2011.03-2015.02	Residency of Internal Medicine in Kyungpook National University Hospital
2015.03-2017.02	Fellowship of Gastroenterology & Hepatology in Kyungpook National University Hospital
2017.03-2019.02	Full-time Instructor, Department of Internal medicine, Chilgok Kyungpook National University Hospital, Daegu, Korea
2020.03-2024.03	Assistant professor, Department of Internal medicine, Chilgok Kyungpook National University Hospital, Daegu, Korea
2024.04-Present	Associate professor, Department of Internal medicine, Chilgok Kyungpook National University Hospital, Daegu, Korea

Education

2010.02	M.D., Yeungnam University, School of Medicine, Daegu, Korea
2018.02	Ph.D. Kyungpook National University, School of Medicine

Professional Societies

The Korean Association for the Study of the Liver
The Korean Liver Cancer Association
The Korean Society of Gastroenterology

Research Interests

Hepatocellular Carcinoma, Liver Cirrhosis, Viral Hepatitis, MASLD

Representative Publications

1. The Clinical Significance of Myosteatosis in Survival Outcomes in Patients with Hepatocellular Carcinoma Treated with Sorafenib. Cancers (Basel) 2024;16(2):454.
2. Comparative associations of MASLD and MAFLD with the presence and severity of coronary artery calcification. Sci Rep 2024;14(1):22917.
3. Diagnostic performance of procalcitonin for bacterial infection in severe alcoholic hepatitis compared with C-reactive protein. BMC Gastroenterol 2024;24(1):428.
4. Outcome of Atezolizumab Plus Bevacizumab Combination Therapy in High-Risk Patients with Advanced Hepatocellular Carcinoma. Cancers (Basel) 2024;16(4):838.

Updates in Diagnosis and Management of Rare Vascular Liver Diseases

Yu Rim Lee *Kyungpook National University*

Rare vascular liver diseases are a group of rare disorders resulting from abnormalities in the vascular system within or around the liver. Their diagnosis and management are rapidly evolving due to emerging disease concepts, advances in imaging techniques, and the development of novel therapies.

Budd-Chiari syndrome is a rare condition characterized by obstruction of the hepatic veins or the inferior vena cava, leading to elevated portal pressure. Etiologies include obstruction of hepatic venous outflow by thrombus due to coagulation disorders, as well as secondary causes such as hepatic venous invasion by tumors, abscesses, or parasites, and external compression by a membranous obstruction of the inferior vena cava. Clinical manifestations range from asymptomatic cases to hepatic dysfunction, including hepatomegaly, abdominal pain, and ascites. Doppler ultrasonography is the first-line diagnostic modality, with contrast-enhanced CT, MRI, and venography used to confirm venous obstruction or stenosis. Management depends on the underlying cause, anatomical features, and disease severity, and typically involves a stepwise approach: initiation of anticoagulation, balloon angioplasty with or without stent placement, transjugular intrahepatic portosystemic shunt in refractory cases, and liver transplantation when necessary.

Sinusoidal Obstruction Syndrome (SOS) is a potentially fatal form of liver injury characterized by hepatic endothelial cell damage caused by toxic and inflammatory responses. Sinusoidal endothelial cells become necrotic and desquamated, resulting in partial or complete obstruction of the central venules. SOS thus causes a post-sinusoidal form of portal hypertension. SOS occurs primarily as a complication of high-dose myeloablative chemotherapy administered before hematopoietic stem cell transplantation (HSCT). Acute SOS occurs within 1 to 3 weeks of exposure and presents with right upper quadrant abdominal pain, weight gain with edema, hepatomegaly, and ascites. Aminotransferases (AST and ALT) are often markedly elevated, sometimes accompanied by jaundice. Standardized diagnostic criteria for SOS, namely the Seattle and Baltimore criteria, have been established; nonetheless, presentations may be atypical. The definitive diagnosis is histological; however, performing a liver biopsy is difficult in these patients due to cytopenias and other comorbidities, particularly in the HSCT population. Clinically significant portal hypertension (HVPG ≥ 10 mmHg) without an alternative etiology is highly specific for confirming SOS. Data from randomized controlled trials regarding ursodeoxycholic acid for the prophy-

laxis of SOS have yielded inconsistent results; nevertheless, a meta-analysis of study findings proposed an overall benefit. Consequently, ursodeoxycholic acid is recommended as prophylactic therapy for SOS in patients receiving allogeneic HSCT. Defibrotide is the only FDA-approved therapy for SOS and is generally given for moderate to severe cases.

Rare vascular liver diseases exhibit diverse etiologies and pathophysiological mechanisms. Accurate diagnosis and personalized therapeutic approaches are essential for optimal management. To enhance diagnostic accuracy and improve patient outcomes, further long-term follow-up data and the therapeutic developments are needed.

References

1. Northup PG, Garcia - Pagan JC, Garcia - Tsao G, et al. Vascular liver disorders, portal vein thrombosis, and procedural bleeding in patients with liver disease: 2020 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;73(1):366–413. doi:10.1002/hep.31646
2. De Gottardi A, Rautou PE, Schouten J, et al. Porto-sinusoidal vascular disease: proposal and description of a novel entity. Lancet Gastroenterol Hepatol. 2019;4(5):399–411.
3. DeLeve LD, Valla DC, Garcia-Tsao G, et al. Vascular disorders of the liver. Hepatology. 2009;49(5):1729–64.
4. Plessier A, Valla DC, et al. Budd-Chiari syndrome. Semin Liver Dis. 2008;28(3):259–69.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri.)

KASL Symposium 1

Innovative Strategies in Cirrhosis Care

Chairs:

Barjesh Chander Sharma (Govind Ballabh Pant Hospital, India)
Jae Young Jang (Soonchunhyang Univ.)

Manoj Kumar Sharma

Institute of Liver and Biliary Sciences, India

Self Introduction

Education

1994	MBBS, Rajasthan University, India
2001	MD Internal Medicine, Rajasthan University, India
2005	DM (Fellowship) Gastroenterology, Delhi University, India
2008	Assistant Professor (Hepatology) at ILBS, New Delhi, India
2018	Professor and Head (Hepatology and Liver Transplantation) at ILBS, New Delhi, India

Professional Experience

Since 2021	Secretary General cum Treasurer, APASL
Since 2012	Associate Dean APASL School of Hepatology
Since 2018	Chairman Guidelines committee APASL
Since 2015	Assistant Director, World Gastroenterology Organization (WGO) New Delhi International Training Center at Institute of Liver and Biliary Sciences, New Delhi
Since 2018	Board of Directors, Asia Pacific Digestive Week (APDW) Federation Associate Editor, Hepatology International. 155 Original Publications, H-Index 50.

Research Interests

Portal Hypertension, Acute Variceal Bleed, ACLF, Coagulation and Liver

Representative Publications

1. Kumar M, Madke T , Mukund A, Patidar, Shasthry SM , Bihari C , Agarwal P, Jindal A , Bajpai M, Maiwall R , Choudhary A, Rajan V ,Arora V , Thevathia H, Meena BL , Singh SP, Maheshwari A , Bhardwaj A, Kumar G , Sarin SK. Comparison of relaxed verses standard cut-offs of rotational thromboelastometry for guiding blood product use before invasive procedures in advanced cirrhosis: a randomized controlled trial. Hepatology International 2025[accepted]
2. Rudra O, Kumar M, Arora V, Rajan V, Tomar A, Maras J, Sarin SK. Coagulation parameters with Albumin In decompensated cirrhosis (CoPA-D): An open-label randomised control trial. 2025 [under publication]
3. Kumar M, Venishetty S, Jindal A, Bihari C, Maiwall R, Vijayaraghavan R, Saggere Muralikrishna S, Arora V, Kumar G, Sarin SK. Tranexamic acid in upper gastrointestinal bleed in patients with cirrhosis: A randomized controlled trial. Hepatology. 2024 ;1;80(2):376-388.
4. Kumar M, Ahmad J, Maiwall R, Choudhury A, Bajpai M, Mitra LG, Saluja V, Mohan Agarwal P, Bihari C, Shasthry SM, Jindal A, Bhardwaj A, Kumar G, Sarin SK. Thromboelastography-Guided Blood Component Use in Patients With Cirrhosis With Nonvariceal Bleeding: A Randomized Controlled Trial. Hepatology. 2020 Jan;71(1):235-246.

Primary Hemostasis in Cirrhosis: A Modern Perspective on Coagulopathy

Manoj Kumar Sharma *Institute of Liver and Biliary Sciences, India*

Hemostasis has 4 main events: primary hemostasis, secondary hemostasis, fibrin clot formation and stabilization , and inhibition of coagulation [inhibition of thrombin generation and fibrin clot breakdown (fibrinolysis)]. Primary and secondary hemostatic processes and fibrinolysis are intrinsically linked. Activated neutrophils and RBCs also have effect on platelets.

Laboratory methods to assess hemostasis include conventional tests (PT/aPTT, platelet count, bleeding time); tests for fibrinogen and fibrinolysis (thrombin time, fibrinogen, d-dimer, FDPs); thrombin generation assays; VETs (including TEG, ROTEM, Sono-Clot); individual factor levels ; and platelet functionality assays. There are no laboratory tests can assess vessel walls or endothelial cells. Various platelet function tests (including PFA, LTA, whole blood aggregometry, and flow cytometry) analyze separately the different facets of platelet function; and there is no pivotal screening test for platelet functionality.

Patients with cirrhosis develop complex alterations in coagulation system including primary hemostasis that include both hypocoagulable and hypercoagulable features. The average patient with cirrhosis appears to be in a state of rebalanced hemostasis; however,

this rebalanced state may be less stable than that of healthy subjects and susceptible to a perturbation by many factors that may increase the risk of both bleeding and thrombosis.

Severe thrombocytopenia is not indicative of the bleeding risk in patients undergoing invasive procedures and does not dictate per se the need for pre-procedural prophylaxis. A more comprehensive and individualized risk assessment should combine hemostatic impairment, the severity of decompensation and systemic inflammation, and the presence of additional factors that may impair platelet function, such as acute kidney injury and bacterial infections.

In acute variceal bleed (AVB), coagulation correction including platelet transfusions is not warranted and may be harmful. Tranexamic acid use in CTP- B and C cirrhosis with AVB leads to less failure to control bleed and failure to prevent rebleed.

VET based blood products transfusions lead to less blood products use as compared to conventional test (INR, platelets, and fibrinogen).

Albumin infusions can worsen coagulation parameters.

Adipose tissue can be a source of vWF.

VITRO score and PLT ratio are promising biomarkers to predict the risk of hepatic decompensation and survival in both compensated and decompensated patients. Still, the role of coagulation abnormalities including those in primary hemostasis in predicting prognosis of cirrhosis patients require further studies.

Further investigations into the in vivo interplay between platelets, circulating blood elements, and endothelial cells will be needed to understand coagulopathy in cirrhosis and their clinical importance.

Eun Ju Cho

Seoul National University

Self Introduction

Prof. Cho graduated from Seoul National University College of Medicine (Seoul, Korea) in 2005. She got a Master's and a Doctor's degree of Medicine from the same college in 2011 and 2013, respectively. After she accomplished residency (from 2006 to 2010) and fellowship (from 2010 to 2012) at Seoul National University Hospital (Seoul, Korea), she joined the faculty at the Seoul National University Hospital since 2014.

Research Interests

Prof. Cho's major research interests involve (i) discovery and evaluation of biomarkers for HCC and (ii) MASLD.

Representative Publications

1. Choi YM, Kim DH, Cho EJ, Kim Z, Jang J, Kim H, Yu SJ, Kim BJ. The sV184A Variant in HBsAg Specific to HBV Subgenotype C2 Leads to Enhanced Viral Replication and Apoptotic Cell Death Induced by PERK-eIF2α-CHOP-Mediated ER Stress. J Med Virol. 2025 Feb;97(2):e70253.
2. Cho EJ, Chung GE, Yoo JJ, Cho Y, Lee KN, Shin DW, Kim YJ, Yoon JH, Han K, Yu SJ. Association of nonalcoholic fatty liver disease with new-onset atrial fibrillation stratified by age groups. Cardiovasc Diabetol. 2024 Sep 12;23(1):340.
3. Kim SJ, Jung CW, Anh NH, Yoon YC, Long NP, Hong SS, Cho EJ, Kwon SW. Metabolic phenotyping combined with transcriptomics metadata fortifies the diagnosis of early-stage Hepatocellular carcinoma. J Adv Res. 2024 Sep 6:S2090-1232(24)00391-6.
4. Cho EJ, Kim B, Yu SJ, Hong SK, Choi Y, Yi NJ, Lee KW, Suh KS, Yoon JH, Park T. Urinary microbiome-based metagenomic signature for the noninvasive diagnosis of hepatocellular carcinoma. Br J Cancer. 2024 Apr;130(6):970-975.
5. Kim SC, Kim DW, Cho EJ, Lee JY, Kim J, Kwon C, Kim-Ha J, Hong SK, Choi Y, Yi NJ, Lee KW, Suh KS, Kim W, Kim W, Kim H, Kim YJ, Yoon JH, Yu SJ, Kim YJ. A circulating cell-free DNA methylation signature for the detection of hepatocellular carcinoma. Mol Cancer. 2023 Oct 6;22(1):164.

Metabolomic Biomarkers for Risk Stratification and Prognosis Prediction in Cirrhotic Patients

Eun Ju Cho *Seoul National University*

Metabolomics offers a novel approach to improving risk stratification and outcome prediction in patients with cirrhosis, addressing key limitations of conventional scoring systems such as MELD and Child-Pugh. These traditional indices lack sensitivity to dynamic metabolic changes, underscoring the need for biomarkers that reflect ongoing disease activity and predict events such as hepatic decompensation, hepatocellular carcinoma (HCC), and mortality.

Advances in analytical technologies have enabled the identification of reproducible metabolic signatures associated with cirrhosis progression. Notable alterations include reduced levels of branched-chain amino acids, increased aromatic amino acids, disruptions in lipid metabolism—particularly elevated ceramides and lysophosphatidylcholines—and higher concentrations of bile acids and microbiota-derived metabolites such as phenylacetylglutamine. Integrating these biomarkers into existing scoring systems, such as APRI and FIB-4, enhances prognostic accuracy and supports more tailored clinical decision-making.

Recent studies showed that metabolites such as ceramide and methionine are associated with the severity of portal hypertension, providing a potential non-invasive alternative to hepatic venous pressure gradient measurement. Furthermore, metabolomics-based models such as CLIF-C MET demonstrate superior predictive performance compared to conventional tools in assessing outcomes in acute-on-chronic liver failure. In the context of HCC surveillance, metabolomic profiling has shown improved diagnostic accuracy over alpha-fetoprotein and may also be valuable in monitoring post-transplant complications, including rejection and recurrence. Despite these promising developments, challenges persist, including the need for assay standardization, cost-effectiveness analyses, and prospective validation in diverse patient populations.

In conclusion, the integration of metabolomics into clinical practice represents a significant step toward precision medicine in hepatology. These approaches offer the potential to individualize risk assessment and guide timely interventions, ultimately aiming to improve clinical outcomes in patients with cirrhosis.

References

1. Yang L, Wang F, Liu S, Xian Z, Yang S, Xu Y, Shu L, Yan X, He J, Li X, Peng C, Bi C, Yuan Y, Chen S, Han L, Yang R, Li Y. Unique metabolomics characteristics for distinguishing cirrhosis related to different liver diseases: A systematic review and meta-analysis. Diabetes Metab Syndr. 2024 Jun;18(6):103068.
2. Luo YQ, Zhang CY, Nong XZ, Gao Y, Wang L, Ji G, Wu T. Metabolomics in cirrhosis: Recent advances and opportunities. Clin Chim Acta. 2024 Apr 15;557:117886.
3. Liu G, Wang X, Fan X, Luo X. Metabolomics profiles in acute-on-chronic liver failure: Unveiling pathogenesis and predicting progression. Front Pharmacol. 2022 Aug 19;13:953297.
4. Li P, Liang X, Luo J, Li J. Omics in acute-on-chronic liver failure. Liver Int. 2025 Mar;45(3):e15634.
5. Lan T, Tacke F. Diagnostics and omics technologies for the detection and prediction of metabolic dysfunction-associated steatotic liver disease-related malignancies. Metabolism. 2024 Dec;161:156015.

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Byeong Geun Song

Sungkyunkwan University

Self Introduction

Prof. Byeong Geun Song is an Associate Professor of the Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine.

He graduated from Sungkyunkwan University School of Medicine with his medical degree in 2013 and completed his residency in Internal Medicine and fellowship in Gastroenterology at Samsung Medical Center. He received his Master's degree in Medicine from the same institution in 2018.

Since 2018, he has served in various roles at Samsung Medical Center, including Clinical Instructor, Clinical Fellow, and Clinical Assistant Professor.

He currently serves as a member of the Scientific Committee and External Affairs Committee of the Korean Association for the Study of the Liver (KASL).

Research Interests

Steatotic Liver Disease, Hepatocellular Carcinoma (HCC) Risk Stratification and Biomarker Discovery, Portal Hypertension and Non-Invasive Diagnosis of CSPH, Population-Based Cohort Studies Using Health Screening and Claims Data

Representative Publications

1. Song BG, Goh MJ, Kang W, et al. Serum ferritin levels and liver-related events in individuals with steatotic liver disease: A longitudinal cohort study. Aliment Pharmacol Ther. 2024. https://doi.org/10.1111/apt.18402
2. Song BG, Kim A, Goh MJ, et al. Risk of hepatocellular carcinoma by steatotic liver disease and its newly proposed subclassification. Liver Cancer. 2024. https://doi.org/10.1159/000538301
3. Song BG, Choi SC, Goh MJ, et al. Metabolic dysfunction-associated fatty liver disease and the risk of hepatocellular carcinoma. JHEP Rep. 2023. https://doi.org/10.1016/j.jhepr.2023.100810
4. Song BG, Goh MJ, Kang W, et al. Validation of non-invasive diagnosis of CSPH in patients with compensated advanced chronic liver disease according to Baveno VII. Liver Int. 2023;43:1966–74. https://doi.org/10.1111/liv.15632
5. Song BG, Sinn DH, Kang W, et al. Changes in the prevalence of hepatitis B and metabolic abnormalities among young men in Korea. Korean J Intern Med. 2022;37(5):1082–7. https://doi.org/10.3904/kjim.2021.452

Recompensation in Cirrhosis: Mechanisms, Predictors, and Therapeutic Strategies

Byeong Geun Song *Sungkyunkwan University*

Cirrhosis, long regarded as an irreversible progressive disease following decompensation, has recently been redefined with the concept of "recompensation." Introduced formally in the Baveno VII consensus, recompensation refers to the reversal of decompensated cirrhosis through control of the underlying etiology, sustained clinical stability, and improvement in liver function. This emerging concept challenges the unidirectional trajectory of cirrhosis and proposes a dynamic model of disease evolution.

Recompensation requires three core elements: (1) removal or control of the causative etiology (e.g., HBV, HCV, alcohol), (2) resolution of clinical decompensating events (ascites, hepatic encephalopathy, and variceal bleeding) for at least 12 months without therapy, and (3) biochemical stabilization of liver function (bilirubin, INR, albumin). Pathophysiological mechanisms include fibrosis regression, vascular remodeling, inflammation resolution, and reduced portal hypertension.

Clinical evidence supports the feasibility of recompensation in various etiologies: in HBV-related cirrhosis, long-term nucleos(t)ide analog therapy results in recompensation in approximately 56% of patients. In HCV, recompensation can occur 2–3 years after achieving sustained virologic response. Alcohol-related liver disease shows recompensation in about 18% of abstinent individuals. Primary biliary cholangitis (PBC) patients who respond to UDCA demonstrate favorable outcomes. However, recompensation remains rare in metabolic dysfunction-associated steatotic liver disease (MASLD), where bariatric surgery may assist selected patients.

Key predictors of recompensation include low MELD and Child-Pugh scores, preserved albumin, absence of severe complications, and early initiation of etiologic treatment. Novel prediction tools such as the Brec-PAS score (platelet count, albumin, sodium) show promising performance in HBV.

Etiologic therapy remains the cornerstone of recompensation. Non-etiologic therapies—such as statins, non-selective beta-blockers (NSBBs), and lifestyle interventions—support recompensation by improving portal pressure and metabolic profile, although their independent role remains unproven.

While current Baveno VII criteria exclude transjugular intrahepatic portosystemic shunt (TIPS) from defining recompensation, evidence suggests that early TIPS in selected patients can induce recompensation-like states, with significant reductions in HCC incidence and all-cause mortality.

Recompensation has important clinical implications, including potential delisting from liver transplantation. Long-term surveillance remains essential due to residual HCC risk. Future research should aim to refine criteria, validate predictors, and establish recompensation as a meaningful clinical endpoint.

References

1. De Franchis R, et al. Baveno VII – Renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959–74.
2. Piano S, et al. Recompensation in cirrhosis: pathophysiology and clinical implications. JHEP Rep. 2024;6(12):101233.
3. Wang Q, et al. Reversal of decompensated HBV cirrhosis with antiviral therapy: A multicenter study. J Hepatol. 2022;77(6):1564–72.
4. Kim TH, et al. Predictors of recompensation in HBV cirrhosis. Aliment Pharmacol Ther. 2022;55(1):83–96.
5. Hui VW-K, et al. Validation of a prediction score for recompensation. JHEP Rep. 2023;5(9):100814.
6. Deng Y, et al. Long-term outcomes of recompensation in HBV-related cirrhosis. JHEP Rep. 2024;6(7):101091.
7. Hofer BS, et al. Recompensation in alcohol-related cirrhosis. Liver Int. 2023;43(10):2220–31.
8. Pose E, et al. Delisting from liver transplant after recompensation. J Hepatol. 2021;75(2):275–83.
9. Hofer BS, et al. PBC and recompensation. Aliment Pharmacol Ther. 2024;59(8):962–72.
10. Feng G, et al. Mechanisms of recompensation in MASLD. Nat Rev Gastroenterol Hepatol. 2024;21(1):46–56.
11. Singal AK, et al. Recompensation and transplant delisting. Am J Gastroenterol. 2024.
12. Sánchez J, et al. Outcomes after recompensation induced by TIPS. Liver Int. 2024;44(11):3072–82.
13. Piecha F, et al. Hepatic cell death markers post-TIPS. Liver Int. 2025;45(4):e16156.
14. Tonon M, et al. Management after recompensation. Liver Transpl. 2024;30(11):1181–7.
15. Sharma S, et al. Recompensation as a novel clinical endpoint. J Clin Exp Hepatol. 2023;13(2):329–34.

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Dominique Damais-Thabut

Sorbonne University, France

Self Introduction

Professional Experience

Physician in France
Medical School in Paris
Hepatogastroenterologist since 2000
Post-doctorant Mayo Clinic, 2009-2010
Head of the Liver-Devoted ICU from 2005-2018
Professor in Hepatology, Intensive Care Unit, AP-HP Sorbonne-Université, Pitié-Salpêtrière Hospital, Paris, France
Head of Department of Hepato-Gastroenterology Since 2018.10

Professional Experience

Deputy Dean of the Faculty of Health, Sorbonne-Université, Paris, France
Baveno VIII Steering Committee
Head of Baveno VI, VII Bleeding Group
President Elect ISHEN
Associate Editor Journal of Hepatology
Coordination of EASL Guidelines on Abdominal Extrahepatic Surgery and Portal Hypertension, 2025

Research Interests

Portal Hypertension, Hepatic Encephalopathy

Representative Publications

1. Desplats V, Haudebourg L, Verger N, Assaraf J, Mouri S, Bouzbib C, Thabut D. Acute encephalopathy without hyperammonemia has a different presentation than overt HE and displays a similarly severe prognosis. Hepatology 2025.
2. Sultanik P, Kheloufi L, Leproux A, Bouzbib C, Mouri S, Santiago A, Thabut D. Other causes of neurocognitive impairment than covert hepatic encephalopathy (CHE) are very frequent, either alone or associated with CHE, in cirrhotic patients with cognitive complaints. Aliment Pharmacol Ther 2024;60(6): 749-764.
3. Allaire M, Thabut D. Portal hypertension and variceal bleeding in patients with liver cancer: Evidence gaps for prevention and management. Hepatology 2024;79(1): 213-223.
4. Thabut D, Kudo M. Treatment of portal hypertension in patients with HCC in the era of Baveno VII. J Hepatol 2023;78(3): 658-662.
5. Rudler M, Hernández-Gea V, Procopet BD, Giráldez A, Amitrano L, Villanueva C, Thabut D. Hepatic encephalopathy is not a contraindication to pre-emptive TIPS in high-risk patients with cirrhosis with variceal bleeding. Gut 2023;72(4): 749-758.
6. Validation of Baveno VI Criteria for Screening and Surveillance of Esophageal Varices in Patients With Compensated Cirrhosis and a Sustained Response to Antiviral Therapy. Thabut D, Bureau C, Layese R, Bourcier V, Hammouche M, Cagnot C, Marcellin P, Guyader D, Pol S, Larrey D, De Lédinghen V, Ouzan D, Zoulim F, Roulot D, Tran A, Bronowicki JP, Zarski JP, Goria O, Calès P, Péron JM, Alric L, Bourlière M, Mathurin P, Blanc JF, Abergel A, Serfaty L, Mallat A, Grangé JD, Attali P, Bacq Y, Wartelle-Bladou C, Dao T, Pilette C, Silvain C, Christidis C, Capron D, Bernard-Chabert B, Hillaire S, Di Martino V, Sutton A, Audureau E, Roudot-Thoraval F, Nahon P; ANRS CO12 CirVir group. Gastroenterology. 2019 Mar;156(4):997-1009.e5.

Treatment of Portal Hypertension in Patients with Hepatocellular Carcinoma in the Era of Baveno VII

Dominique Damais-Thabut *Sorbonne University, France*

Clinically significant portal hypertension (CSPH) is independently associated with hepatocellular carcinoma (HCC) occurrence. Prevalence of CSPH is very high in HCC patients, ranging from 35% in early stages to more than 50% in advanced stages of HCC. Portal hypertension (PHT) is independently associated with mortality idn patients with variceal bleeding. PHT influences HCC treatments at any stage. Baveno VII conference raised the issue of targeting CSPH av-nd not varices, in order to prevent liver decompensation and not only variceal bleeding in cirrhotic patients. Some simplified algorithms, mainly including liver stiffness and platelets count, were proposed to decrease the number of upper endoscopies to diagnose CSPH. In this lecture we will see how those algorithms aplly to HCC patients. Moreover we will describe primary prophylaxis of liver decompensation and variceal bleeding, as well as secondary prophylaxis. Primary prophylaxis is underprescribed and should be performed in all eligible patients, as variceal bleeding is at poor prognosis and precludes HCC therapies. Moreover, under systemic therapy a previous history of variceal bleeding is constantly retrieved as a predictor of bleeding under systemic therapy by atezolizumab-bevacizumab. If carvedilol is recommended at first line in non HCC patients, banding may also be a good option in HCC patients in primary prophylaxis. Secondary prophylaxis should be handled properly, as it increases survival in HCC patients. TIPS can be indicated to facilitate HCC therapies like resection, radioembolisation, and can be a bridge to liver transplant. Last, studies devoted to HCC patients must be performed to improve the knowledge as there are specific issues in this subset of patients

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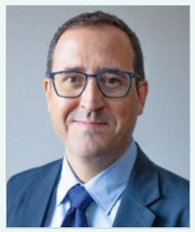
TLW Special Interest Group

Integrating Multi-Omics for Precision Oncology

Chairs:

Chien-Hung Chen (National Taiwan Univ., Taiwan)
Jaeyoun Cheong (Ajou Univ.)



Augusto Villanueva

NYU Langone, USA

Self Introduction

Prof. Augusto Villanueva, MD, PhD, is the Medical Director of the Liver Cancer Program at NYU Langone in New York. He earned his medical degree from the University of Santiago de Compostela in Spain. Before assuming his current roles, he was Associate Professor in the Liver Cancer Program at Mount Sinai and prior to that he was Senior Lecturer and Consultant Hepatologist at the Institute of Liver Studies at King's College Hospital in London.

A NIH-funded physician-scientist, Prof. Villanueva combines his clinical expertise as a hepatologist with pioneering research focused on intratumor heterogeneity in cancer evolution and the development of novel minimally invasive biomarkers through liquid biopsy. He has authored more than 160 publications, accumulating over 30,000 citations and achieving an H-index of 72. His work has been featured in premier journals, including The New England Journal of Medicine, Nature Genetics, Nature Biotechnology, Nature Communications, Gastroenterology, Hepatology, Journal of Hepatology, Gut, Journal of Clinical Investigation, and Oncogene. Prof. Villanueva ranks among the top 1% of highly cited researchers in 2024 (Clarivate) and has contributed to the field through more than 15 book chapters as well as editing a book on resistance to targeted therapies in hepatocellular carcinoma. He has served as Executive Secretary of the International Liver Cancer Association.

Research Interests

Early Detection of Liver Cancer, Liquid Biopsy, Biomarker Development

Representative Publications

1. Singal AG, Sanduzzi-Zamparelli M, Nahon P, Ronot M, Hoshida Y, Rich N, Reig M, Vilgrain V, Marrero J, Llovet JM, Parikh ND, Villanueva A. International Liver cancer Association (ILCA) White Paper on Hepatocellular carcinoma Risk Stratification and Surveillance. J Hepatol 2023.
2. Von Felden J, Garcia-Lezana T, Dogra N, Gonzalez-Kozlova E, Ahsen ME, Craig A, Gifford S, Wunsch B, Smith JT, Kim S, Diaz JEL, Chen X, Labgaa I, Haber P, Olsen R, Han D, Restrepo P, D'Avola D, Hernandez-Meza G, Allette K, Sebra R, Saberi B, Tabrizian P, Asgharpour A, Dieterich D, Llovet JM, Cordon-Cardo C, Tewari A, Schwartz M, Stolovitzky G, Losic B, Villanueva A. Unannotated small RNA clusters associated with circulating extracellular vesicles detect early stage liver cancer. Gut 2021.
3. Moctezuma-Velazquez C, Lewis S, Lee K, Amodeo S, Llovet JM, Schwartz M, Abraldes JG, Villanueva A. Non-invasive imaging criteria for the diagnosis of hepatocellular carcinoma in non-cirrhotic hepatitis B virus patients. JHEP Reports 2021
4. Singal AG, Hoshida Y, Pinato DJ, Marrero J, Nault JC, Paradis V, Tayob N, Sherman M, Lim YS, Feng Z, Lok AS, Rinaudo JA, Srivastava S, Llovet JM, Villanueva A. International Liver Cancer Association (ILCA) white paper on biomarker development for hepatocellular carcinoma. Gastroenterology 2021
5. Hernandez-Meza G*, von Felden J*, Gonzalez-Kozlova E, Garcia-Lezana T, Peix J, Portela A, Craig AG, Sayols S, Schwartz M, Losic B, Mazzaferro V, Esteller M, Llovet JM, Villanueva A. DNA methylation profiling of human hepatocarcinogenesis. Hepatology 2021

Integration of Clinical, Computational, and Genomic Resources for Early Hepatocellular Carcinoma Detection

Augusto Villanueva *NYU Langone, USA*

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and a major contributor to cancer-related deaths globally. Due to its asymptomatic progression and challenges in early diagnosis, many patients are diagnosed at advanced stages when curative treatments are limited.[1] To address this, the integration of clinical, computational, and genomic resources offers a comprehensive framework for improving early detection and personalized intervention strategies.

Clinical assessments play a crucial role in risk stratification and early diagnosis of HCC, and they are still the mainstay for early HCC detection as per clinical practice guidelines.[2] Routine surveillance includes abdominal ultrasound and alpha-feto-protein (AFP) every 6 months. These combined have a sensitivity of 63% for the detection of HCC at a curable stage. While AFP alone has limitations in sensitivity and specificity, its combination with additional markers enhances diagnostic accuracy. Other markers, such as AFP-L3 and DCP have been extensively tested for early HCC detection but despite promising results, they are not still incorporated in clinical guidelines. The GALAD score, which is a combination of these 3 blood markers along with age and sex is the most advanced in developmental stage.[3,4] Genomic research has unveiled critical insights into the molecular mechanisms driving HCC.[5] Whole-genome sequencing and transcriptomic analyses reveal specific mutations, copy number variations, and epigenetic modifications associated with early disease onset. Aberrant activation of oncogenic pathways, such as WNT/β-catenin, PI3K/AKT, and TP53 mutations, contributes to tumorigenesis and offers targets for early intervention. In terms of early HCC detection, many studies have tried to incorporate this information in tools that could outperform the accuracy of abdominal US and AFP. Most of them were develop under the liquid biopsy technology, which entails the analysis of tumor components released to the bloodstream including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs) and extracellular vesicles (EVs).[6] Mutation and methylation analysis of ctDNA are the most advanced in terms of development, but again, still without enough evidence to be recommended in clinical practice. In early phase 2 biomarker studies, analysis of ctDNA and small RNAs in EVs have reached sensitivities of 80% for small HCC.[7,8] More recently, analysis of fragment size of ctDNA has also provided promising results in terms of early HCC detection.[9]

Artificial intelligence (AI) and machine learning (ML) have transformed disease prediction models by

analyzing vast clinical datasets with unparalleled precision. AI-driven image analysis enables radiologists to detect minute hepatic abnormalities that might be overlooked in conventional assessments. ML algorithms trained on electronic health records, laboratory results, and genetic profiles have demonstrated improved predictive accuracy for HCC occurrence. Computational models also integrate multi-omic data, allowing researchers to identify novel biomarkers and molecular signatures indicative of early tumorigenesis. Thus, there is an increased interest to leverage these technologies in the HCC surveillance space. By integrating patient history, biomarkers, AI-driven analytics, and molecular insights, researchers and clinicians can develop more effective screening protocols and personalized treatment strategies. Continued interdisciplinary collaboration and technological innovation are crucial in reducing HCC mortality rates and improving long-term patient outcomes.

References

1. Villanueva A. Hepatocellular Carcinoma. N Engl J Med 2019;380(15):1450–62.
2. Singal AG, Llovet JM, Yarchoan M, et al. AASLD practice guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology [Internet] 2023;Available from: http://dx.doi.org/10.1097/HEP.0000000000000466
3. Marsh TL, Parikh ND, Roberts LR, et al. A phase 3 biomarker validation of GALAD for the detection of hepatocellular carcinoma in cirrhosis. Gastroenterology [Internet] 2024;Available from: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S001650852405460X.pdf?locale=en_US&searchIndex=
4. El-Serag HB, Jin Q, Nabihah T, et al. HES V2.0 outperforms GALAD for detection of HCC: A phase 3 biomarker study in the United States. Hepatology [Internet] 2024;Available from: http://dx.doi.org/10.1097/HEP.0000000000000953
5. Llovet JM, Pinyol R, Kelley RK, et al. Molecular pathogenesis and systemic therapies for hepatocellular carcinoma. Nature Cancer 2022;3(4):386–401.
6. von Felden J, Garcia-Lezana T, Schulze K, Losic B, Villanueva A. Liquid biopsy in the clinical management of hepatocellular carcinoma. Gut [Internet] 2020 [cited 2020 Sep 4];Available from: https://gut.bmj.com/content/early/2020/09/03/gutjnl-2019-320282
7. Xu R-H, Wei W, Krawczyk M, et al. Circulating tumour DNA methylation markers for diagnosis and prognosis of hepatocellular carcinoma. Nat Mater 2017;16(11):1155–61.
8. von Felden J, Garcia-Lezana T, Dogra N, et al. Unannotated small RNA clusters associated with circulating extracellular vesicles detect early stage liver cancer. Gut [Internet] 2021;Available from: http://dx.doi.org/10.1136/gutjnl-2021-325036
9. Foda ZH, Annapragada AV, Boyapati K, et al. Detecting liver cancer using cell-free DNA fragmentomes. Cancer Discov [Internet] 2022;Available from: http://dx.doi.org/10.1158/2159-8290.CD-22-0659

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025
May 29 - 31, 2025 | HICO, Gyeongju, Korea

Renumathy Dhanasekaran

Stanford University, USA

Self Introduction

Prof. Renu Dhanasekaran is a physician scientist specializing in liver cancer research and patient care. She completed her Gastroenterology fellowship at Mayo Clinic, Rochester, and has a PhD in Cancer Biology from Stanford University. In her clinical practice, she is dedicated to the management of liver cancer, running a specialized clinic at Stanford for patients with liver tumors.

Her research focuses on the immunobiology of liver cancer aiming to deepen understanding of its molecular pathogenesis. Her lab adopts a bench-to-bedside approach to identify novel biomarkers and therapeutic targets for liver cancer. She is widely published and funded by organizations like the NIH, ACG, AASLD, Cancer League, Doris Duke, and others. She is a recipient of the Laure Aurelian Research Endowment award and a mentor in the AGA Future Leader program. Her long-term goal is to improve clinical outcomes for patients with liver cancer through personalized care and translational research.

Research Interests

Liver Cancer, Immunobiology, Genomics, MASH

Representative Publications

1. TCGA Network. Comprehensive and Integrative Genomic Characterization of Hepatocellular Carcinoma. Cell. 2017 PMCID: PMC5680778. Dhanasekaran R*- Manuscript Coordinator.
2. Dhanasekaran R*, Baylot V*, Kim M, Kuruvilla S, Bellovin DI, Adeniji N, Rajan KD A, Lai I, Gabay M, Tong L, Krishnan M, Park J, Hu T, Barbhuiya MA, Gentles AJ, Kannan K, Tran PT, Felsher DW. MYC and Twist1 cooperate to drive metastasis by eliciting crosstalk between cancer and innate immunity. Elife. 2020 Jan 14;9. PMCID: PMC6959993.
3. Dhanasekaran R*, Hansen AS, Park J, Lemaitre L, Lai I, Adeniji N, Kuruvilla S, Suresh A, Zhang J, Swamy V, Felsher DW*. MYC Overexpression Drives Immune Evasion in Hepatocellular Carcinoma that is Reversible Through Restoration of Pro-Inflammatory Macrophages. Cancer Res. 2023; PMCID: PMC9931653 *Co-Corresponding Authors.
4. Krishnan M, Rajan A, Arjunan V, Park J, Marques F, Bermudez A, Girvan O, Hoang N, Yin J, Nguyen M, Kothary N, Pitteri S, Felsher D, Dhanasekaran R. Genomic Analysis of Vascular Invasion in HCC Reveals Molecular Drivers and Predictive Biomarkers. Hepatology. 2020. PMCID: PMC8115767.
5. Lemaitre L*, Adeniji N*, Suresh A*, Reguram R, Zhang J, Park J, Reddy A, Trevino AE, Mayer AT, Deutzmann A, Hansen AS, Tong L, Arjunan V, Kambham N, Visser BC, Dua MM, Bonham CA, Kothary N, D'Angio HB, Preska R, Rosen Y, Zou J, Charu V, Felsher DW, Dhanasekaran R. Spatial analysis reveals targetable macrophage-mediated mechanisms of immune evasion in hepatocellular carcinoma minimal residual disease. Nat Cancer. 2024 Sep 20; PMID: 39304772.

Molecular Insights into Hepatocellular Carcinoma Recurrence from Minimal Residual Disease after Therapy

Renumathy Dhanasekaran *Stanford University, USA*

Valerie Chew

Duke-NUS Medical School, Singapore

Self Introduction

Prof. Valerie Chew graduated with PhD in immunology from Agency of Science, Technology and Research (A*STAR), Singapore. She now serves as a Principal Investigator in Translational Immunology Institute (TII), SingHealth and holds a position of Associate Professor in Duke-NUS Medical School, Singapore. Her research delves into deciphering the intricate immune landscape and crosstalk within the tumor microenvironment of hepatocellular carcinoma (HCC), with a keen focus on uncovering biomarkers and therapeutic avenues.

Research Interests

- Understanding the Mechanisms of Tumour Immunity in Hepatocellular Carcinoma (HCC)
- Identification of Potential Biomarkers to Predict Prognosis and Treatment Outcome in HCC Patients
- Design of Novel Immunotherapies for Patients with HCC

Representative Publications

1. S Chuah, J Lee, Y Song, et al D Tai, V Chew*. Uncoupling immune trajectories of response and adverse events from anti-PD-1 immunotherapy in hepatocellular carcinoma. J Hepatology. 2022
2. P Nguyen, S Ma et al P Chow, W Zhai and V Chew*. Intratumoural immune heterogeneity as a hallmark of tumour evolution and progression in hepatocellular carcinoma. Nature Com. 12, 227 (2021).
3. CJ Lim, YH Lee, et al. V Chew*. Multidimensional analyses reveal distinct immune microenvironment in hepatitis B virus-related hepatocellular carcinoma. Gut. (2019) May;68(5):916-927
4. V Chew*, YH Lee, et al. Immune activation underlies a sustained clinical response to Yttrium-90 radioembolisation in hepatocellular carcinoma. Gut (2019), 68(2): 335-346.
5. Chew V^{+}, Chen JM, Lee DM, et al. Chemokine-driven lymphocyte infiltration: an early intratumoural event determining long-term survival in resectable hepatocellular carcinoma. Gut (2012); 61(3):427-38. Chew V^{+}, Tow C, Teo M, et al. Inflammatory tumor microenvironment is associated with superior survival in hepatocellular carcinoma patients. Journal of hepatology (2010), 52(3): 370-379.

Immune Microenvironment and Therapeutic Discovery in Hepatocellular Carcinoma Using Single-Cell Omics Analysis

Valerie Chew *Duke-NUS Medical School, Singapore*

Summary

Hepatocellular carcinoma (HCC) is the third leading cause of cancer mortality globally[1] and its incidence and mortality are predicted to rise by more than 50% globally by 2040[2]. The currently available immunotherapies using immune-checkpoint blockade (ICB) for advanced HCC benefit only 20%-30% of the patients in either monotherapy or combination settings[3-5]. This relatively low response rate warrants a deeper understanding of the complex nature of the tumour microenvironment (TME) in HCC. Using cutting-edge single-cell immune and transcriptomic analyses, our team aims to decipher the underlying **mechanisms of immune suppression or escape** within HCC, the mechanisms of resistance to therapy, and devise novel immunotherapies to counteract immunosuppression, overcome resistance and enhance HCC treatment efficacy.

In recent years, our team employed cutting-edge technologies such as Time-of-Flight Mass Cytometry **(CyTOF), single-cell RNA sequencing (scRNA-seq)** and **spatial transcriptomics (ST)** analysis to conduct multi- and high-dimensional single-cell analysis, enabling us to comprehensively understand the TME of HCC. For instance, we uncovered an immunosuppressive gradient of the TME in HCC with the accumulation of regulatory T cells (Tregs), PD-1^{+} tissue-resident memory CD8+ T cells (TRMs) and pro-tumoural tumor-associated macrophages (TAMs)[6]. This immunosuppression could be driven by several factors including chronic hepatitis B viral **(HBV)** infection[7] or hypoxia[8]. For instance, by analyzing the immune landscapes of HBV-related and non-viral-related HCCs, we identified distinct immunosuppressive subsets, PD-1+Tregs and PD-1+CD8+ TRMs, as enriched in HBV-related HCC[7]. This work provides a potential explanation for the superior therapeutic response to anti-PD-1 ICB, particularly in HBV-related HCC[9]. We have also expanded our investigation into immune intratumoral heterogeneity (immune-ITH) in HCC, demonstrating a relationship between tumour-immune co-evolution and disease progression[10], which occurs as a progressive process that peaks at intermediate-stage HCC tumours[11].

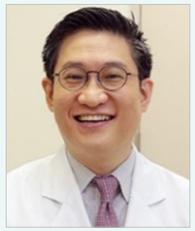
More importantly, our team also works on identification of **peripheral immune biomarkers to predict treatment response** in patients with HCC. The use of biomarkers from the solid tumour biopsies often poses clinical challenge as being an invasive procedure. Using our multi-omics approach, we identified immune biomarkers in peripheral blood using pre-treatment PBMCs from HCC patients treated with yt-

trium-90 (Y90) radioembolization therapy or selective internal radiation therapy (SIRT)[12]. We found that the $CD8^+$ T cells from pre-treatment blood samples of responders versus non-responders expressed higher levels of PD-1, Tim-3, CXCR6 and CCR5, suggesting its homing potential to TME upon SIRT. It is believed that SIRT exerts its clinical benefit via an activation of delayed and sustained immune response, called the "abscopal effect"[13]. We also analyzed immune cells from the peripheral blood and tumour tissues of HCC patients treated with **anti-PD-1 ICB** using scRNA-seq before and after treatment in a Singapore cohort with a validation cohort from South Korea[14] (in collaboration with Dr Changhoon Yoo, Asan Medical Center). We identified the key immune subsets of $CXCR3^+CD8^+$ T effector memory (TEM) cells and $HLA\text{-}DR^+$ antigen presenting cells (APCs), as the common immune subsets involved in both treatment response and the lack of immune-related adverse effects (irAEs). Next, we performed comprehensive cell-cell interaction analysis (CellphoneDB[15]) and uncovered the **distinct tumor necrosis factor (TNF) interactions** enriched in T cell from patients who responded to anti-PD-1 ICB but did not experience greater than Grade 2 irAEs. These findings suggest that targeting specific TNF pathways could enhance treatment response while controlling irAEs. Indeed, Preclinical testing revealed that combining **anti-TNFR2 with anti-PD-1 blockade** significantly enhanced anti-tumor responses, resulting in complete tumor regression without a significant increase in toxicity.

Collectively, our previous studies provide valuable insights into the immunological composition, heterogeneity, and mechanisms of immune evasion in HCC. Building upon these findings, our team aim to further unravel the mechanisms of immune evasion in HCC, with the ultimate goal of developing **targeted immunotherapeutic strategies** that effectively **enhance clinical response and improve patient outcomes.**

References

1. Bray, F. et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68, 394-424 (2018). https://doi.org:10.3322/caac.21492
2. Rumgay, H. et al. Global burden of primary liver cancer in 2020 and predictions to 2040. J Hepatol (2022). https://doi.org:10.1016/j.jhep.2022.08.021
3. El-Khoueiry, A. B. et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. Lancet 389, 2492-2502 (2017). https://doi.org:10.1016/S0140-6736(17)31046-2
4. Zhu, A. X. et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. Lancet Oncol 19, 940-952 (2018). https://doi.org:10.1016/S1470-2045(18)30351-6
5. Finn, R. S. et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 382, 1894-1905 (2020). https://doi.org:10.1056/NEJMoa1915745
6. Chew, V. et al. Delineation of an immunosuppressive gradient in hepatocellular carcinoma using high-dimensional proteomic and transcriptomic analyses. Proceedings of the National Academy of Sciences of the United States of America 114, E5900-E5909 (2017). https://doi.org:10.1073/pnas.1706559114
7. Lim, C. J. et al. Multidimensional analyses reveal distinct immune microenvironment in hepatitis B virus-related hepatocellular carcinoma. Gut (2018). https://doi.org:10.1136/gutjnl-2018-316510
8. Suthen, S. et al. Hypoxia-driven immunosuppression by Treg and type-2 conventional dendritic cells in HCC. Hepatology (2022). https://doi.org:10.1002/hep.32419
9. Pfister, D. et al. NASH limits anti-tumour surveillance in immunotherapy-treated HCC. Nature 592, 450-456 (2021). https://doi.org:10.1038/s41586-021-03362-0
10. Nguyen, P. H. D. et al. Intratumoural immune heterogeneity as a hallmark of tumour evolution and progression in hepatocellular carcinoma. Nat Commun 12, 227 (2021). https://doi.org:10.1038/s41467-020-20171-7
11. Nguyen, P. H. D. et al. Trajectory of immune evasion and cancer progression in hepatocellular carcinoma. Nat Commun 13, 1441 (2022). https://doi.org:10.1038/s41467-022-29122-w
12. Chew, V. et al. Immune activation underlies a sustained clinical response to Yttrium-90 radioembolisation in hepatocellular carcinoma. Gut (2018). https://doi.org:10.1136/gutjnl-2017-315485
13. Ng, J. & Dai, T. Radiation therapy and the abscopal effect: a concept comes of age. Ann Transl Med 4, 118 (2016). https://doi.org:10.21037/atm.2016.01.32
14. Chuah, S. et al. Uncoupling immune trajectories of response and adverse events from anti-PD-1 immunotherapy in hepatocellular carcinoma. J Hepatol (2022). https://doi.org:10.1016/j.jhep.2022.03.039
15. Efremova, M., Vento-Tormo, M., Teichmann, S. A. & Vento-Tormo, R. CellPhoneDB: inferring cell-cell communication from combined expression of multi-subunit ligand-receptor complexes. Nat Protoc 15, 1484-1506 (2020). https://doi.org:10.1038/s41596-020-0292-x



Ju Hyun Shim

University of Ulsan

Self Introduction

Employment

Professor,
Department of Gastroenterology, Asan Medical Center, Seoul, Korea

Post Graduate Training

2020.03-	Professor, Dept of Gastroenterology & Liver Center, Asan Medical Center
2015.03-2020.02	Associate Professor, Dept of Gastroenterology & Liver Center, Asan Medical Center
2010.03-2015.02	Assistant Professor, Dept of Gastroenterology & Liver Center, Asan Medical Center
2008.03-2010.02	Fellowship, Dept of Gastroenterology, Asan Medical Center
2007.03-2008.02	Public Health Doctor, National Cancer Center, Goyang, Korea
2001.03-2005.02	Residency, Seoul National University Hospital, Seoul, Korea
2000.03-2001.02	Internship, Seoul National University Hospital, Seoul, Korea

Education

2009.03-2011.02	Doctor's degree, University of Ulsan College of Medicine, Seoul, Korea
2003.03-2005.02	Master's degree, College of Medicine, Seoul National University, Seoul, Korea

TLW Special Interest Group | DAY 2: May 30 (Fri.) | ROOM 7 [1F]

Genomic Characteristics of RB1-Deficient Hepatocellular Carcinoma and Its Therapeutic Candidates

Ju Hyun Shim *University of Ulsan*

Hepatocellular carcinoma (HCC), the most prevalent form of primary liver cancer, is the fourth most-frequent cause of cancer-related death, and ranks sixth in terms of incident cases. In fact, the World Health Organization estimates that more than 1 million patients will die from liver cancer in 2030. The unfortunate reality is that only a quarter of HCC tumors are susceptible to FDA-approved drugs or compounds now in clinical development, and none have specific alterations considered to predict responsiveness to such tailored therapy.

Deregulation of the cell cycle via functional disruption of the *retinoblastoma* (RB1) pathway is a canonical hallmark of cancer. In previous genomic studies of HCC, 3-8% of the series had somatic *RB1* mutations defined as non-silent mutations and copy number alterations, and their frequency was increased in advanced-stage HCCs. Importantly, clinical and biochemical experiments have shown that genetic impairment of *RB1* is associated with aggressive behavior and poor outcomes in a number of cancer types, including HCC. Also loss of *RB1* has been shown to confer resistance to common targeted therapies combating solid malignancies. However, the clinical implications of the different types of *RB1* alteration in HCC remain poorly understood.

In my talk, I will introduce the effects of one subtype of *RB1* loss-of-function alteration of HCCs in genomic and molecular terms in addition to its clinical implications, and also suggest by high-throughput drug screening processes a class of compound effective in treating this *RB1*-defective subclass.

References

1. Villanueva A. Hepatocellular Carcinoma. N Engl J Med 2019;380:1450-1462.
2. W. H. Organization. Projections of mortality and causes of death, 2016 to 2060. Available from:
3. Harding JJ, Nandakumar S, Armenia J, Khalil DN, Albano M, Ly M, et al. Prospective Genotyping of Hepatocellular Carcinoma: Clinical Implications of Next-Generation Sequencing for Matching Patients to Targeted and Immune Therapies. Clin Cancer Res 2019;25:2116-2126.
4. Knudsen ES, Pruitt SC, Hershberger PA, Witkiewicz AK, Goodrich DW. Cell Cycle and Beyond: Exploiting New RB1 Controlled Mechanisms for Cancer Therapy. Trends Cancer 2019;5:308-324.
5. Nault JC, Martin Y, Caruso S, Hirsch TZ, Bayard Q, Calderaro J, et al. Clinical Impact of Genomic Diversity From Early to Advanced Hepatocellular Carcinoma. Hepatology 2020;71:164-182.
6. Muller M, Bird TG, Nault JC. The landscape of gene mutations in cirrhosis and hepatocellular carcinoma. J Hepatol

2020;72:990-1002.
7. Ahn SM, Jang SJ, Shim JH, Kim D, Hong SM, Sung CO, et al. Genomic portrait of resectable hepatocellular carcinomas: implications of RB1 and FGF19 aberrations for patient stratification. Hepatology 2014;60:1972-1982.
8. Choi S, Kim HR, Sung CO, Kim J, Kim S, Ahn SM, et al. Genomic Alterations in the RB Pathway Indicate Prognostic Outcomes of Early-Stage Lung Adenocarcinoma. Clin Cancer Res 2015;21:2613-2623.
9. Chen WS, Alshalalfa M, Zhao SG, Liu Y, Mahal BA, Quigley DA, et al. Novel RB1-Loss Transcriptomic Signature Is Associated with Poor Clinical Outcomes across Cancer Types. Clin Cancer Res 2019;25:4290-4299.
10. Feugeas O, Guriec N, Babin-Boilletot A, Marcellin L, Simon P, Babin S, et al. Loss of heterozygosity of the RB gene is a poor prognostic factor in patients with osteosarcoma. J Clin Oncol 1996;14:467-472.
11. Condorelli R, Spring L, O'Shaughnessy J, Lacroix L, Bailleux C, Scott V, et al. Polyclonal RB1 mutations and acquired resistance to CDK 4/6 inhibitors in patients with metastatic breast cancer. Ann Oncol 2018;29:640-645.
12. Bollard J, Miguela V, Ruiz de Galarreta M, Venkatesh A, Bian CB, Roberto MP, et al. Palbociclib (PD-0332991), a selective CDK4/6 inhibitor, restricts tumour growth in preclinical models of hepatocellular carcinoma. Gut 2017;66:1286-1296.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat.)

KASL Special Interest Group 4.
The KASL Viral Hepatitis Study Group

Advancing Insights into Hepatitis B Virus Pathogenesis and Therapy

Chairs:

Hyung Joon Yim (Korea Univ.)
Takehisa Watanabe (Kumamoto Univ., Japan)

Yewan Park

Kyung Hee University

Self Introduction

Education

2020.03-2024.02 Department of Digital Health (for Ph.D. in Digital Health), Sungkyunkwan University Graduate School, Seoul, Korea
2009.03-2014.02 Medicine Doctor, Korea University School of Medicine, Seoul, Korea
2013.03-2018.02 Bachelor of Statistics, College of Department of Statistics and Data Science, Korea National Open University
2005.03-2009.02 Bachelor of Education, Department of Biology Education, College of Education, Seoul National University, Seoul, Korea

Research and Professional Experience

2025.03-Present Assistant Professor, Kyung Hee University Hospital, Seoul Korea
2021.06-2025.02 Clinical Assistant Professor, Division of Gastroenterology and Hepatology, Kyung Hee University Hospital, Seoul Korea
2019.03-2021.05 Clinical Fellow, Division of Gastroenterology and Hepatology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea
2015.03-2019.02 Residency, Department of Medicine, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea
2013.03-2014.02 Rotating Internship, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea

Board Certification

2019.03 Korean Board of Internal Medicine (number: 18022)
2018.08 Korean Board of Gastrointestinal endoscopy (number: 2020-7776)

Membership

Korean Association of Internal Medicine
Korean Society of Gastroenterology
Korean Society of Gastrointestinal Endoscopy
Korean Association for the Study of the Liver Disease
Korean Liver Cancer Association

KASL Special Interest Group 4. | DAY 3: May 31 (Sat.) | ROOM 1 [3F]

Maternal Chronic Hepatitis B Virus Infection and Its Potential Impact on Fetal Development and Congenital Anomalies

Yewan Park *Kyung Hee University*

Chronic hepatitis B virus (HBV) infection affects over 250 million people globally, with a substantial number of cases occurring in women of reproductive age. In pregnant women, clinical and public health strategies have traditionally focused on preventing vertical transmission to the newborn. While these efforts, including antiviral prophylaxis and immunization, have been highly effective, emerging research highlights that the impact of maternal HBV infection may extend well beyond the risk of perinatal transmission. This presentation aims to explore the broader maternal and fetal health consequences associated with chronic HBV infection during pregnancy.

Recent studies have shown that chronic HBV infection can disrupt immune modulation in pregnancy. A Th1-dominant cytokine profile and elevated levels of proinflammatory mediators such as TNF-α, IFN-γ, and IL-12 have been observed in HBV-positive pregnant women, suggesting altered immune tolerance during gestation. These changes may contribute to adverse pregnancy outcomes, such as gestational diabetes mellitus (GDM). Meta-analyses have demonstrated that HBV-positive women have a significantly higher risk of GDM, with adjusted odds ratios around 1.47 compared to HBV-negative counterparts, even after controlling for confounders.

Additionally, HBV infection has been associated with an increased risk of preterm birth. Systematic reviews have found higher odds of both preterm labor and birth among infected women, indicating a possible link between maternal HBV-related inflammation and early parturition. Furthermore, studies have identified HBV DNA, HBsAg, and HBcAg in placental tissue, oocytes, and even embryos, raising concerns about germline and intrauterine infection. These findings suggest that HBV may interfere with fetal development beyond transmission alone.

Importantly, large-scale national cohort studies and meta-analyses have suggested that maternal HBV infection may also elevate the risk of congenital anomalies, including congenital heart disease (CHD). The magnitude of risk appears to vary with maternal viral load and HBeAg status. Although the exact mechanisms remain unclear, these observations underscore the need to assess not only infection status but also viral activity and host immune responses during pregnancy.

Given the current limitations in the literature, including inconsistent adjustments for confounding variables and a lack of HBV genotype and DNA data, future research should prioritize well-powered, prospective studies that incorporate detailed viral and immunologic profiling. A more comprehensive understanding of HBV's impact on fetal development is essential for optimizing care for HBV-infected pregnant women and their children.

Takehisa Watanabe

Kumamoto University, Japan

Self Introduction

Prof. Takehisa Watanabe, from the Department of Gastroenterology at Kumamoto University. He dedicated to the clinical practice and research of liver diseases. Recently, he has been working on the development of new drugs for HBV, aiming to contribute to the reduction of HBV patients worldwide.

Furthermore, he aspire to make a societal contribution by unraveling the pathogenesis of liver diseases that has not yet been clarified, from an epigenetics perspective.

Research Interests

HBV, Chronic Hepatitis, Steatotic Liver Disease, Metabolic Disorder, Epigenetics

Representative Publications

1. Watanabe T, Hayashi S, Y Tanaka et al. A novel, small anti-HBV compound reduces HBsAg and HBV DNA by destabilizing HBV RNA. J Gastroenterol. 2024 Feb 5. doi: 10.1007/s00535-023-02070-y.
2. Watanabe T, Hayashi S, Tanaka Y. Drug Discovery Study Aimed at a Functional Cure for HBV. Viruses 2022, 14:1393.
3. Suzuki T, Matsuura K, Watanabe T, Tanaka Y, et al. Clinical usefulness of a novel high-sensitivity hepatitis B core-related antigen assay to determine the initiation of treatment for HBV reactivation. J Gastroenterol. 2022; 57:486-494.
4. Narahara S, Watanabe T, Tanaka Y, et al. Clusterin and Related Scoring Index as Potential Early Predictors of Response to Sorafenib in Hepatocellular Carcinoma. Hepatol Comm. 2022; 6:1198-1212.
5. Satou Y, Miyazato P, Watanabe T, et al. The retrovirus HTLV-1 inserts an ectopic CTCF-binding site into the human genome. Proc Natl Acad Sci USA 2016, 11, 3054-59.

KASL Special Interest Group 4. | DAY 3: May 31 (Sat.) | ROOM 1 [3F]

A Novel Anti-HBV Compound Reduces HBsAg and HBV-DNA by Destabilizing HBV-RNA

Takehisa Watanabe *Kumamoto University, Japan*

Since HBV cannot be completely eliminated once it infects hepatocytes, the primary therapeutic goal for chronic hepatitis B is to achieve sustained viral suppression. Although nucleos(t)ide analogues (NAs), which are orally available and generally well tolerated, effectively inhibit HBV DNA synthesis, they have limited impact on viral protein production mediated by HBV RNA. As a result, the development of novel therapeutic agents capable of reducing hepatitis B surface antigen (HBsAg) levels is urgently needed to achieve a functional cure.

Small interfering RNAs (siRNAs) and antisense oligonucleotides (ASOs), both of which are well-characterized RNA-targeting modalities, are currently under development for this purpose. Although these agents have demonstrated promising HBsAg-lowering effects, their injectable administration poses challenges related to convenience and broad clinical applicability.

We have been developing a compound designed to be orally administrable, capable of reducing HBsAg levels, and exhibiting an acceptable safety profile. Given the global burden of chronic hepatitis B, particularly in low- and middle-income countries where healthcare resources may be limited, an effective oral therapy offers significant advantages in terms of accessibility, patient compliance, and broader clinical applicability.

We screened 30,000 compounds using HepG2.2.15 cells and HBV-infected human hepatocytes (PXB cells), and selected candidates that reduced HBsAg and HBV-DNA levels in culture supernatants. Through further optimization, we identified SAG-524, a small-compound that effectively reduces HBV-DNA and HBsAg levels at low concentrations with low cytotoxicity. It is suitable for oral administration and exhibits anti-HBV activity across different HBV genotypes.

MoA studies showed that SAG-524 reduces HBV-RNA levels, including pgRNA and PreS/S mRNA, by making them less stable and more susceptible to degradation. This effect appears to be specific to HBV. Further analysis suggests that SAG-524 binds to PAPD5, an RNA poly(A) polymerase involved in HBV-RNA stability, and inhibits its function.

In vivo studies using chimeric mice with humanized livers (PXB mice) demonstrated that oral administration of SAG-524 significantly reduced both HBsAg and HBV DNA levels. When combined with en-

tecavir (ETV), SAG-524 further enhanced the reduction of serum HBV DNA compared to ETV alone and achieved additional decreases in HBsAg and cccDNA. In preclinical safety studies conducted in mice and monkeys, no significant toxicity was observed even at doses up to 1000 mg/kg/day.

SAG-524, a novel RNA destabilizer developed with the goal of achieving a functional cure for hepatitis B, is currently undergoing preparation for clinical evaluation. Given its dual ability to reduce both viral proteins and replicative intermediates, SAG-524 may represent an important new therapeutic option for the management of chronic hepatitis B.

References

1. World Health Organization. Hepatitis B Fact Sheet. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b
2. Watanabe T, Hayashi S, Zhaoyu Y, Inada H, Nagaoka K, Tateyama M, Tanaka Y. A novel, small anti-HBV compound reduces HBsAg and HBV-DNA by destabilizing HBV-RNA. J Gastroenterol. 2024 Apr;59(4):315-328.
3. Watanabe T, Hayashi S, Tanaka Y. Drug Discovery Study Aimed at a Functional Cure for HBV. Viruses. 2022 Jun 26;14(7):1393.

Yeonjung Ha

CHA University

Self Introduction

Education and Professional Experience

2003-2009 Inje University College of Medicine, M.D. (Summa Cum Laude)
2009 Internship, Asan Medical Center
2010-2013 Residency, Internal Medicine, Asan Medical Center
2012-2014 University of Ulsan College of Medicine, M.S.
2013 Short-Term Training, Prince of Wales Hospital, Hong Kong S.A.R., China
2014-2015 Clinical Fellowship, Gastroenterology, Asan Medical Center
2014-2017 University of Ulsan College of Medicine, Ph.D.
2016-2023 Assistant Professor, Gastroenterology, CHA Bundang Medical Center
2017-2019 Visiting Scientist, Mayo Clinic, United States
2024 Associate Professor, Gastroenterology, CHA Bundang Medical Center

Research Interests

- Hepatocellular Carcinoma
- Predictive Modeling
- Metabolic Dysfunction-Associated Steatotic Liver Disease

Representative Publications

1. Ha Y, Lee S, Lim J, et al. A Machine Learning Model to Predict De Novo Hepatocellular Carcinoma Beyond Year 5 of Antiviral Therapy in Patients with Chronic Hepatitis B. Liver Int 2025;45(4):e16139. DOI: 10.1111/liv.16139.
2. Cheon J, Kim H, Kim HS, (…), Ha Y et al. Atezolizumab plus bevacizumab in patients with child-Pugh B advanced hepatocellular carcinoma. Ther Adv Med Oncol 2023;15:17588359221148541. DOI: 10.1177/17588359221148541.
3. Ha Y, Lim J, Chon YE, et al. Five-year on-treatment variables-based PPACS model predicts subsequent hepatocellular carcinoma in entecavir/tenofovir-treated patients. Int J Cancer 2023;153(12):2045-2054. DOI: 10.1002/ijc.34704.
4. Yang H, Kang B, Ha Y, et al. High serum IL-6 correlates with reduced clinical benefit of atezolizumab and bevacizumab in unresectable hepatocellular carcinoma. JHEP Reports : innovation in hepatology 2023;5(4):100672. DOI: 10.1016/j.jhepr.2023.100672.
5. Ha Y, Kim JH, Cheon J, Jeon GS, Kim C, Chon HJ. Risk of Variceal Bleeding in Patients with Advanced Hepatocellular Carcinoma Receiving Atezolizumab/Bevacizumab. Clin Gastroenterol Hepatol 2023;21(9):2421-2423.e2. DOI: 10.1016/j.cgh.2022.07.035.

AI-Based Hepatocellular Carcinoma Risk Prediction in Chronic Hepatitis B Virus Patients

Yeonjung Ha *CHA University*

Hepatocellular carcinoma (HCC) represents a major global health burden, ranking as the sixth most common malignancy and the third leading cause of cancer-related mortality worldwide. Hepatitis B virus (HBV) infection remains a predominant risk factor for HCC, particularly in regions with high HBV endemicity. Despite advances in antiviral therapy that suppress viral replication and reduce disease progression, a considerable proportion of chronic hepatitis B (CHB) patients remain at risk for developing HCC. Accordingly, accurate and individualized risk stratification models are crucial for guiding surveillance intensity, clinical decision-making, and early therapeutic intervention.

Traditional HCC prediction tools such as the REACH-B, GAG-HCC, or PAGE-B scores have offered clinical utility by incorporating readily available clinical parameters. However, these models often rely on linear assumptions and fixed weightings that fail to capture the complex, nonlinear interactions among virological, host, and metabolic parameters that drive carcinogenesis. Furthermore, their performance tends to decline when externally validated. This limitation has prompted increasing interest in the use of artificial intelligence (AI) to develop more robust, data-driven models capable of learning intricate patterns from high-dimensional clinical datasets.

AI-based risk prediction models are well-suited to address the heterogeneity inherent in patients with CHB. Machine learning algorithms can integrate diverse types of inputs without requiring a priori assumptions regarding variable relationships. Supervised learning models, such as random forests, gradient boosting machines, and neural networks, have demonstrated improved performance over conventional scoring systems in retrospective studies. Moreover, time-to-event models such as survival forests or deep Cox networks offer dynamic risk estimates, aligning better with the evolving nature of chronic liver disease. Also, the integration of AI with real-world data from electronic health records and biorepositories has further enabled continuous model updating, enhancing both clinical relevance and temporal validity.

Despite these promising advances, the deployment of AI-based HCC prediction tools into clinical practice faces several challenges. First, the interpretability of complex models remains limited, although tools such as SHAP (SHapley Additive exPlanations) values and LIME (Local Interpretable Model-agnostic Explanations) are increasingly used to enhance transparency. Second, differences in data quality,

coding practices, and population structure between training and external validation datasets can introduce bias or overfitting, underscoring the importance of prospective validation and cross-population calibration. Third, regulatory approval and integration into clinical workflows will require rigorous testing to ensure reproducibility, safety, and equitable performance across subgroups.

From a translational perspective, AI-based HCC risk models could significantly impact current surveillance strategies. By refining patient selection for biannual imaging, they can optimize resource allocation and reduce unnecessary imaging in low-risk individuals while ensuring high-risk patients receive timely detection. The growing availability of multi-omics data, such as transcriptomics, proteomics, and microbiome profiles, holds potential for further personalization of risk estimation through integrative AI approaches.

In conclusion, AI-based models represent a promising frontier in HCC risk prediction for patients with CHB, offering superior flexibility, scalability, and predictive power over conventional tools. By leveraging large-scale datasets and advanced algorithms, these models can more accurately stratify risk, support individualized care, and ultimately improve HCC-related outcomes. However, future efforts must focus on model interpretability, clinical integration, and real-world validation. As the field progresses, interdisciplinary collaboration among hepatologists, data scientists, and policy-makers will be critical in realizing the full potential of AI in management of patients with CHB, including HCC prediction.

THE LIVER WEEK 2025

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DAY 3: May 31 (Sat.)

KASL-AASLD Joint Symposium 2

Looking into the Future of Hepatology

Chairs:

Silvia Sookoian (Maimonides Univ., Argentina)
Sook-Hyang Jeong (Seoul National Univ.)

Seung Up Kim

Yonsei University

Self Introduction

Prof. Seung Up Kim is a member of Korean Association of the Study of the Liver and Korean Liver Cancer Study Group. He has more than 300 SCI(E) original, peer reviewed publications as primary or corresponding author.

He acted as an Editor-in-Chief of Clinical and Molecular Hepatology from 2019 to 2013 and impact factor increased from 4 to 14. He also acts as an Associate Editor of Journal of Gastroenterology and Hepatology and Gut and liver, an Editorial Board of Clinical Gastroenterology and Hepatology, and an Academic Editor of PLoS One, Clinical and Translational Hepatology, and International Journal of Molecular Science. He is an invited referee for more than 20 SCI(E) journals including Lancet Gastroenterology and Hepatology, Gastroenterology, Hepatology, Journal of Hepatology, Gut, etc.

Research Interests

His Major Research Interests Include Metabolic Associated Steatotic Liver Disease, Sarcopenia, Viral Hepatitis, Liver Fibrosis, Liver Cirrhosis, and Liver Cancer.

Representative Publications

1. Vibration-Controlled Transient Elastography Scores to Predict Liver-Related Events in Steatotic Liver Disease. Lin H, Lee HW, Yip TC, Tsochatzis E, Petta S, Bugianesi E, Yoneda M, Zheng MH, Hagström H, Boursier J, Calleja JL, Goh GB, Chan WK, Gallego-Durán R, Sanyal AJ, de Lédinghen V, Newsome PN, Fan JG, Castéra L, Lai M, Harrison SA, Fournier-Poizat C, Wong GL, Pennisi G, Armandi A, Nakajima A, Liu WY, Shang Y, de Saint-Loup M, Llop E, Teh KK, Lara-Romero C, Asgharpour A, Mahgoub S, Chan MS, Canivet CM, Romero-Gomez M, Kim SU, Wong VW; VCTE-Prognosis Study Group.JAMA. 2024 Apr 16;331(15):1287-1297. doi: 10.1001/jama.2024.1447.
2. Prognostic performance of the two-step clinical care pathway in metabolic dysfunction-associated steatotic liver disease. Yip TC, Lee HW, Lin H, Tsochatzis E, Petta S, Bugianesi E, Yoneda M, Zheng MH, Hagström H, Boursier J, Calleja JL, Goh GB, Chan WK, Gallego-Durán R, Sanyal AJ, de Lédinghen V, Newsome PN, Fan JG, Castéra L, Lai M, Fournier-Poizat C, Wong GL, Pennisi G, Armandi A, Nakajima A, Liu WY, Shang Y, de Saint-Loup M, Llop E, Teh KKJ, Lara-Romero C, Asgharpour A, Mahgoub S, Chan MS, Canivet CM, Romero-Gomez M, Kim SU, Wong VW.J Hepatol. 2025 Jan 23:S0168-8278(25)00021-2. doi: 10.1016/j.jhep.2025.01.014.
3. AI-Safe-C score: Assessing liver-related event risks in patients without cirrhosis after successful direct-acting antiviral treatment. Lin H, Cheuk-Fung Yip T, Lee HW, Meng X, Che-To Lai J, Ahn SH, Pang W, Lai-Hung Wong G, Zeng L, Wai-Sun Wong V, de Lédinghen V, Kim SU.J Hepatol. 2025 Mar;82(3):456-463. doi: 10.1016/j.jhep.2024.09.020.
4. PAGE-B incorporating moderate HBV DNA levels predicts risk of HCC among patients entering into HBeAg-positive chronic hepatitis B. Chun HS, Papatheodoridis GV, Lee M, Lee HA, Kim YH, Kim SH, Oh YS, Park SJ, Kim J, Lee HA, Kim HY, Kim TH, Yoon EL, Jun DW, Ahn SH, Sypsa V, Yurdaydin C, Lampertico P, Calleja JL, Janssen H, Dalekos GN, Goulis J, Berg T, Buti M, Kim SU, Kim YJ.J Hepatol. 2024 Jan;80(1):20-30. doi: 10.1016/j.jhep.2023.09.011
5. Metabolic dysfunction-associated steatotic liver disease and risk of cardiovascular disease. Lee HH, Lee HA, Kim EJ, Kim HY, Kim HC, Ahn SH, Lee H, Kim SU.Gut. 2024 Feb 23;73(3):533-540. doi: 10.1136/gutjnl-2023-331003.

Anti-Fibrotic and Anti-Cirrhotic Approaches in Chronic Liver Disease

Seung Up Kim *Yonsei University*

Chronic liver disease (CLD), encompassing a spectrum of etiologies such as viral hepatitis, alcohol-related liver disease (ALD), nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH), autoimmune liver diseases, and metabolic/genetic disorders, continues to impose a substantial global health burden. Central to the pathogenesis of CLD is progressive hepatic fibrosis—a dynamic and potentially reversible process characterized by excessive extracellular matrix (ECM) accumulation—ultimately culminating in cirrhosis, portal hypertension, and hepatocellular carcinoma (HCC). With advances in pathophysiological understanding and non-invasive diagnostics, the paradigm of liver fibrosis and cirrhosis has shifted from a static endpoint to a modifiable disease state. This lecture explores evolving anti-fibrotic and anti-cirrhotic strategies, examining therapeutic targets, clinical evidence, and translational implications.

Pathophysiology of Hepatic Fibrogenesis and Cirrhosis:

Liver fibrosis results from sustained hepatic injury leading to the activation of hepatic stellate cells (HSCs), portal fibroblasts, and myofibroblasts, which collectively synthesize and deposit ECM components. These processes are driven by inflammatory cytokines, oxidative stress, gut-liver axis dysregulation, metabolic insults, and immune dysregulation. Key fibrogenic pathways include TGF-β/Smad, PDGF, Wnt/β-catenin, and integrin signaling. Furthermore, hepatic fibrogenesis involves epithelial–mesenchymal transition (EMT), endothelial dysfunction, and loss of hepatocyte regenerative capacity.

Cirrhosis, historically considered irreversible, is now recognized as a disease stage with therapeutic potential for regression—particularly during the compensated phase. Cirrhosis involves both architectural distortion and vascular remodeling, with the interplay between angiogenesis, capillarization of sinusoids, and portal hypertension perpetuating decompensation. Understanding this complex microenvironment is critical to designing effective anti-cirrhotic therapies.

Rationale for Anti-Fibrotic and Anti-Cirrhotic Approaches:

Given the clinical and economic burden of cirrhosis, preventing or reversing fibrosis is a public health imperative. Traditional management has focused on treating the underlying etiology. However, even

with viral suppression or metabolic control, fibrosis regression is variable, underscoring the need for direct anti-fibrotic agents. Therapeutic targets include modulating HSC activity, reducing ECM production, promoting ECM degradation, attenuating inflammation, and restoring liver regeneration.

Anti-cirrhotic strategies expand this paradigm to address portal hypertension, liver stiffness, hepatic venous outflow, and the risk of decompensation and HCC. The recognition of "compensated advanced chronic liver disease" (cACLD) as a target population has enabled trials of anti-cirrhotic therapies with clinically meaningful endpoints.

Current Therapeutic Landscape:

1. Etiology-Specific Therapy:

- o Viral Hepatitis: Long-term suppression of HBV with nucleos(t)ide analogs and SVR in HCV with DAAs are associated with significant fibrosis regression, though not universal.
- o NAFLD/NASH: Lifestyle modification remains the cornerstone, but weight loss is difficult to achieve and maintain. Several pharmacologic agents (e.g., GLP-1 receptor agonists, FXR agonists, pan-PPAR agonists) show promise in targeting metabolic pathways and improving fibrosis in NASH.
- o Alcoholic Liver Disease: Abstinence can lead to fibrosis regression, but anti-fibrotic therapies for ALD remain underexplored.

2. Direct Anti-Fibrotic Agents:

- o HSC Modulators: Compounds targeting TGF-β (e.g., fresolimumab), PDGF receptors (e.g., imatinib), and LOXL2 (e.g., simtuzumab) have shown variable results. Most have failed in phase II/III trials, underscoring the need for better target validation and combination approaches.
- o Inflammatory Pathway Modulators: Cenicriviroc (CCR2/CCR5 antagonist) and selonsertib (ASK1 inhibitor) initially showed promise but were not confirmed in larger trials.
- o Anti-fibrotic Candidates in NAFLD: Obeticholic acid (FXR agonist) demonstrated fibrosis improvement in phase III trials but raised safety concerns. Resmetirom (thyroid hormone receptor-β agonist) and lanifibranor (pan-PPAR agonist) have shown fibrosis improvement in ongoing studies.

3. Anti-Cirrhotic Interventions:

- o Portal Hypertension Modulation: Non-selective beta-blockers (NSBBs) have emerged as disease-modifying agents, reducing decompensation risk in cACLD.
- o Endothelial Function and Angiogenesis: Statins, by improving endothelial nitric oxide synthase (eNOS) activity, offer potential anti-fibrotic and anti-cirrhotic effects.
- o Regenerative Therapies: FGF analogs and hepatocyte growth factor (HGF) pathways are being explored to enhance liver regeneration. Mesenchymal stem cell therapy has shown early-phase promise but remains investigational.

Biomarkers and Non-Invasive Assessment:

To assess treatment response, non-invasive tests (NITs) including transient elastography, serum biomarkers (e.g., ELF, FIB-4, PRO-C3), and imaging modalities (e.g., MRE, contrast-enhanced ultrasound) are essential. Dynamic changes in liver stiffness and biomarker levels offer surrogate endpoints in trials. Recent efforts aim to develop composite scores integrating fibrosis stage, portal hypertension, and inflammation.

Challenges and Future Directions:

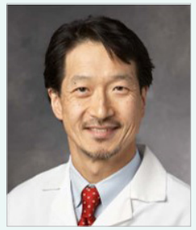
Despite advances, significant challenges remain. Fibrosis is a multifactorial process, and single-target therapies may be insufficient. Inter-patient variability in fibrosis regression is influenced by genetic, epigenetic, and environmental factors. Trial design complexity, lack of validated endpoints, and regulatory hurdles impede drug development. Additionally, distinguishing fibrosis regression from architectural remodeling without biopsy remains a challenge.

Future Strategies Include:

- Combination therapies that target multiple pathogenic pathways.
- Patient stratification using omics-based approaches to personalize therapy.
- Repurposing existing drugs (e.g., statins, ARBs, metformin) for liver fibrosis.
- Advanced imaging and digital pathology to better quantify fibrosis and cirrhosis.
- Artificial intelligence in predicting outcomes and treatment response.

Conclusion:

Anti-fibrotic and anti-cirrhotic therapy in chronic liver disease is an evolving field, transitioning from a singular focus on etiology to a broader, mechanism-based approach. Although no FDA-approved direct anti-fibrotic agents currently exist, the momentum of research and clinical trials is encouraging. A multipronged approach—targeting inflammation, fibrogenesis, vascular remodeling, and regeneration—offers the best prospect for preventing decompensation and improving outcomes. As our understanding of fibrotic biology and cirrhotic progression deepens, precision medicine will likely play a pivotal role in tailoring treatment to maximize benefit and minimize risk.



Future Directions in Liver Transplant Allocation Policies: Beyond MELD

W. Ray Kim *Mayo Clinic, USA*

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Ki Tae Suk

Hallym University

Self Introduction

Educational

1993.2-1999	Medical Degree, Yonsei University, Wonju College of Medicine, Korea
2003.2-2015	Master of Medicine, Graduate School, Yonsei University, Seoul, Korea
2010.8-2012	Doctor of Medicine, Graduate School, Yonsei University, Seoul, Korea
2014.9-2016	Post-Doctor Research Scholar, Medicine, Columbia University, New York, USA
2016.9-Present	Professor, Hallym University, Chuncheon, Korea

Research Interests

Liver Disease	Cirrhosis and Hepatocellular Carcinoma
Microbiota	Metabolites of Microbiome
	Post-Bioitcs
	Multi-Omics Associated Mechanism
Pharmabiotics	Therapeutics and Diagnostic Marker

Representative Publications

1. Suk KT. A metabolomics approach to the validation of predictive metabolites and phenotypic expression in non-alcoholic fatty liver disease. Life Sci. 2023 Mar 30:121626.
2. Suk KT. Characteristics of microbiome-derived metabolomics according to the progression of alcoholic liver disease. Hepatol Int. 2023 Mar 31.
3. Suk KT, Yoon JH, Kim MY et al. Transplantation with autologous bone marrow-derived mesenchymal stem cells for alcoholic cirrhosis: Phase 2 trial. Hepatology. 2016 Dec;64(6):2185-2197.
4. Suk KT, Mederacke I, Gwak GY, Cho SW, Adeyemi A, Friedman R, Schwabe RF. Opposite roles of cannabinoid receptors 1 and 2 in hepatocarcinogenesis. Gut. 2016 Oct;65(10):1721-32.
5. Suk KT. Lactobacillus lactis and Pediococcus pentosaceus-driven reprogramming of gut microbiome and metabolome ameliorates the progression of non-alcoholic fatty liver disease. Clin Transl Med. 2021 Dec;11(12):e634.

Gut Microbiome-Targeted Therapies to Enhance Treatment Outcomes of Liver Diseases

Ki Tae Suk *Hallym University*

Liver-gut communication is vital in fatty liver diseases, and gut microbes are the key regulators in maintaining liver homeostasis. Chronic alcohol abuse and persistent overnutrition create dysbiosis in gut ecology, which can contribute to fatty liver disease. In this review, we discuss the gut microbial compositional changes that occur in alcoholic and nonalcoholic fatty liver diseases and how this gut microbial dysbiosis and its metabolic products are involved in fatty liver disease pathophysiology.

The gut microbiome and microbial metabolomic influences on liver diseases and their diagnosis, prognosis, and treatment are still controversial. Research studies have provocatively claimed that the gut microbiome, metabolomics understanding, and microbial metabolite screening are key approaches to understanding liver cancer and liver diseases. An advance of logical innovations in metabolomics profiling, the metabolome inclusion, challenges, and the reproducibility of the investigations at every stage are devoted to this domain to link the common molecules across multiple liver diseases, such as fatty liver, hepatitis, and cirrhosis. These molecules are not immediately recognizable because of the huge underlying and synthetic variety present inside the liver cellular metabolome. This review focuses on microenvironmental metabolic stimuli in the gut-liver axis. Microbial small-molecule profiling (i.e., semi-quantitative monitoring, metabolic discrimination, target profiling, and untargeted profiling) in biological fluids has been incompletely addressed. Here, we have reviewed the differential expression of the metabolome of short-chain fatty acids (SCFAs), tryptophan, one-carbon metabolism and bile acid, and the gut microbiota effects are summarized and discussed. We further present proof-of-evidence for gut microbiota-based metabolomics that manipulates the host's gut or liver microbes, mechanosensitive metabolite reactions and potential metabolic pathways. We conclude with a forward-looking perspective on future attention to the "dark matter" of the gut microbiota and microbial metabolomics.

Renumathy Dhanasekaran

Stanford University, USA

Self Introduction

Prof. Renu Dhanasekaran is a physician scientist specializing in liver cancer research and patient care. She completed her Gastroenterology fellowship at Mayo Clinic, Rochester, and has a PhD in Cancer Biology from Stanford University. In her clinical practice, she is dedicated to the management of liver cancer, running a specialized clinic at Stanford for patients with liver tumors.

Her research focuses on the immunobiology of liver cancer aiming to deepen understanding of its molecular pathogenesis. Her lab adopts a bench-to-bedside approach to identify novel biomarkers and therapeutic targets for liver cancer. She is widely published and funded by organizations like the NIH, ACG, AASLD, Cancer League, Doris Duke, and others. She is a recipient of the Laure Aurelian Research Endowment award and a mentor in the AGA Future Leader program. Her long-term goal is to improve clinical outcomes for patients with liver cancer through personalized care and translational research.

Research Interests

Liver Cancer, Immunobiology, Genomics, MASH

Representative Publications

1. TCGA Network. Comprehensive and Integrative Genomic Characterization of Hepatocellular Carcinoma. Cell. 2017 PMCID: PMC5680778. Dhanasekaran R*- Manuscript Coordinator.
2. Dhanasekaran R*, Baylot V*, Kim M, Kuruvilla S, Bellovin DI, Adeniji N, Rajan KD A, Lai I, Gabay M, Tong L, Krishnan M, Park J, Hu T, Barbhuiya MA, Gentles AJ, Kannan K, Tran PT, Felsher DW. MYC and Twist1 cooperate to drive metastasis by eliciting crosstalk between cancer and innate immunity. Elife. 2020 Jan 14;9. PMCID: PMC6959993.
3. Dhanasekaran R*, Hansen AS, Park J, Lemaitre L, Lai I, Adeniji N, Kuruvilla S, Suresh A, Zhang J, Swamy V, Felsher DW*. MYC Overexpression Drives Immune Evasion in Hepatocellular Carcinoma that is Reversible Through Restoration of Pro-Inflammatory Macrophages. Cancer Res. 2023; PMCID: PMC9931653 *Co-Corresponding Authors.
4. Krishnan M, Rajan A, Arjunan V, Park J, Marques F, Bermudez A, Girvan O, Hoang N, Yin J, Nguyen M, Kothary N, Pitteri S, Felsher D, Dhanasekaran R. Genomic Analysis of Vascular Invasion in HCC Reveals Molecular Drivers and Predictive Biomarkers. Hepatology. 2020. PMCID: PMC8115767.
5. Lemaitre L*, Adeniji N*, Suresh A*, Reguram R, Zhang J, Park J, Reddy A, Trevino AE, Mayer AT, Deutzmann A, Hansen AS, Tong L, Arjunan V, Kambham N, Visser BC, Dua MM, Bonham CA, Kothary N, D'Angio HB, Preska R, Rosen Y, Zou J, Charu V, Felsher DW, Dhanasekaran R. Spatial analysis reveals targetable macrophage-mediated mechanisms of immune evasion in hepatocellular carcinoma minimal residual disease. Nat Cancer. 2024 Sep 20; PMID: 39304772.

Molecular and Immunological Biomarkers for Hepatocellular Carcinoma to Guide Personalized Treatment Decisions

Renumathy Dhanasekaran *Stanford University, USA*

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!

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DAY 3: May 31 (Sat.)

President's Choice Lecture

Chair:

Yoon Jun Kim (Seoul National Univ.)

Management of Portal Hypertension in Advanced Cirrhosis

Shiv Kumar Sarin *Institute of Liver and Biliary Sciences, India*

THE LIVER WEEK 2025

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KASL Symposium 3

Emerging Concepts, Challenges, and Therapeutic Frontiers of Metabolic Dysfunction-Associated Steatotic Liver Disease

Chairs:

Tatsuya Kanto (Japan Institute for Health Security, Japan)
Won Kim (Seoul National Univ.)

Murim Choi

Seoul National University

Self Introduction

Murim Choi's main scientific question is to elucidate the genetic mechanisms of human diseases. To address this, his expertise lies in the functional interpretation of human genetic variants using genomic and bioinformatic methodologies. He graduated from Seoul National University (SNU), Seoul, Korea, majoring in molecular biology (BS and MS). During the Ph.D. course at Duke University, he studied cardiovascular system development in mice.

In his postdoctoral training at Yale University, he studied human genetics, setting up a whole exome sequencing pipeline and applying it to various human diseases to identify causal genes.

In SNU, his group has recently established a bioinformatic pipeline that allows screening of eQTL signals only functioning in the metabolic dysfunction-associated steatotic liver disease (MASLD) status and validated its utility. His lab has recently established protocols for advanced functional genomics approaches, including single-cell sequencing, saturation mutagenesis, modifier screening, and cell tracing techniques, to understand the genetic mechanisms underlying disease progression. He has a strong interest in clinical and translational research, especially in elucidating genotype-phenotype relationships that may lead to human diseases. He was selected as a member of the Young Korean Academy of Science and Technology and is currently a Samsung Research Fellow. He is a Senior Editor for eLife and serves editor roles for Experimental Molecular Medicine and Molecules and Cells.

Research Interests

Genetics of Diseases and Functional Genomics

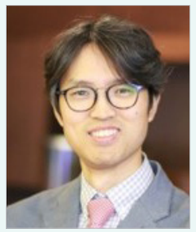
Representative Publications

1. Hong et al., Identification of genes conferring individual-level variation responsible for metabolic dysfunction-associated steatohepatitis using single-cell eQTL analysis. Nat. Genet. (2025) in press
2. Jeon et al., Inhibiting EZH2 complements steroid effects in Duchenne muscular dystrophy. Sci Adv. (2025) 11:eadr4443
3. Sim et al., Increased inflammatory signature in myeloid cells of non-small cell lung cancer patients with high clonal hematopoiesis burden. Elife (2024) 13:RP96951.
4. Lee et al., Somatic uniparental disomy mitigates the most damaging EFL1 allele combination in Shwachman-Diamond syndrome. Blood (2021) 138:2117-2128.
5. Yoo et al., Disease-specific eQTL screening reveals an anti-fibrotic effect of AGXT2 in non-alcoholic fatty liver disease. J Hepatol. (2021) 75:514-523.

Identification of Genes Conferring Individual-Level Variation Responsible for MASLD Using Single-Cell eQTL Analysis

Murim Choi *Seoul National University*

Genetic understanding of chronic diseases is challenging due to the large contribution of non-genetic factors and the involvement of many genes and variants. Nevertheless, in the last 15 years, we have witnessed substantial improvements in discovering novel genes and variants that are associated with chronic diseases, mostly due to large-scale genome-wide association studies (GWAS). Indeed, numerous GWAS variants impose susceptibility or resistance with varying strengths (i.e., odds ratios). However, there are still many gaps that require further understanding of variant functions for individual-level variation of chronic diseases that influences the severity and clinical profiles of individual patients. Metabolic dysfunction-associated steatotic liver disease (MASLD) impacts a quarter of adults in developed countries and pose a substantial risk of fibrotic liver and liver cancer. To elucidate individual-level gene expression regulation and its role in modulating disease symptoms and susceptibilities, we undertook a single-cell expression quantitative loci (sc-eQTL) analysis and devised a novel analytic framework. The resulting data enabled us to identify and evaluate functional variants. We propose that various types of eQTLs confer an essential addition to the GWAS variants in an individual- and context-dependent manner.



Sang Bong Ahn

Eulji University

Self Introduction

Prof. Ahn graduated from Hanyang University College of Medicine with his medical degree in 2023 and completed his internship and residency at Hanyang University Hospital.

He is a Professor of the Department of Gastroenterology, Nowon Eulji Medical Center and is currently holding a position of Chief of Gastroenterology and Head of Internal Medicine simultaneously.

Research Interests

MAFLD, Hepatitis B

Representative Publications

1. Diagnostic performance of non-invasive tests in patients with MetALD in a health check-up cohort. J Hepatol 2024 Nov
2. Impact of components of metabolic syndrome on long-term outcomes of CHB with nucleos(t)ide analogue treatment. Clin Mol Hepatol 2025 Mar
3. Clinical Course and Prognosis of Long-Term Survivors of Hepatocellular Carcinoma. Aliment Pharmacol Ther 2025 Apr
4. Harnessing Metabolic Indices as a Predictive Tool for Cardiovascular Disease in a Korean Population without Known Major Cardiovascular Event. Diabetes Metab J 2024 May
5. Barriers to care linkage and educational impact on unnecessary MASLD referrals. Front Med 2024 Jul

GLP-1 Receptor Agonists in MASLD: Current Clinical Status and Future Directions

Sang Bong Ahn *Eulji University*

Metabolic dysfunction-associated steatotic liver disease (MASLD) is currently the most prevalent form of chronic liver disease globally. Projections from recent modeling studies suggest that the incidence rates of both MASLD and its more advanced form, metabolic dysfunction-associated steatohepatitis (MASH), are expected to rise by approximately 21% and 63%, respectively, by 2030. It is estimated that around 20–30% of individuals with MASLD may progress to MASH.

The prevalence of MASLD and MASH is significantly higher among individuals with type 2 diabetes (T2D), affecting 60–70% and 37%, respectively, compared to 25–30% and 5–14% in the general population. This is largely due to shared risk factors such as insulin resistance, dyslipidemia, abdominal obesity, and hypertension—all hallmarks of metabolic syndrome. The presence of multiple metabolic abnormalities increases the likelihood of MASLD progression. Moreover, MASLD is closely associated with cardiovascular disease (CVD), which remains the leading cause of death in this population, accounting for roughly 25% of mortality. This strong link is primarily attributed to overlapping cardiometabolic risk profiles.

Given the significant pathophysiological overlap between MASLD, obesity, and T2D, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have attracted attention as a potential therapeutic strategy. While these agents are currently approved for the treatment of T2D and/or obesity, they have yet to receive indication for MASLD or MASH. Nonetheless, GLP-1 RAs address core metabolic disturbances and lipid toxicity implicated in MASLD development.

Clinical trials have consistently shown that GLP-1 RAs can improve cardiovascular risk factors by lowering blood pressure, improving lipid profiles, and promoting weight loss. Cardiovascular outcome trials—including LEADER (liraglutide), REWIND (dulaglutide), HARMONY (albiglutide), and SUSTAIN-6 (semaglutide)—have demonstrated a reduction in major adverse cardiovascular events, particularly in patients with preexisting atherosclerotic CVD.

Newer agents such as tirzepatide (a dual GLP-1 and glucose-dependent insulinotropic polypeptide [GIP] receptor agonist) and cotadutide (a GLP-1/glucagon receptor coagonist) have shown potential for reducing hepatic steatosis, suppressing de novo lipogenesis, and achieving MASH resolution. Additional investigational drugs like survodutide (being evaluated in people with T2D, overweight, or obesity) and efinopegdutide (in clinical trials for NAFLD and precirrhotic NASH) are also under development. Furthermore, retatrutide, a triple agonist of GLP-1, GIP, and glucagon receptors, is being explored as a novel therapeutic option.

In summary, GLP-1 RAs represent a promising treatment avenue for MASLD and MASH by addressing shared metabolic and inflammatory derangements found in obesity and T2D.

Kris V. Kowdley

Washington State University, USA

Self Introduction

Prof. Kris V. Kowdley, is Director of Liver Institute Northwest and professor, Elson S. Floyd College of Medicine at Washington State University. He received his B.S. in Biology and Anthropology from Columbia University, and his medical degree from Mount Sinai School of Medicine. He completed his internship and residency at Oregon Health Science University and a Fellowship in Gastroenterology and Hepatology at Tufts University School of Medicine.

He is internationally recognized as a clinician, educator, and researcher in liver disease. He has led several major international clinical trials of new treatments for hepatitis C, primary biliary cholangitis, primary sclerosing cholangitis and nonalcoholic steatohepatitis.

He is the author of more than 1,000 articles, book chapters, reviews, abstracts and commentaries, and his scholarly work has been cited more than 75,000 times (h-index 125), according to Google Scholar. He is on the Web of Science list of "Highly Cited Researchers" (top 1% by citations for field) for 2019-2024.

Research Interests

MASH, Hepatic Iron Overload Disorders, Cholestatic Liver Disease, Chronic Viral Hepatitis

Representative Publications

1. Sanyal AJ, Chalasani N, Kowdley KV, McCullough A, Diehl AM, Bass NM, Neuschwander-Tetri BA, Lavine JE, Tonascia J, Unalp A, Van Natta M, Clark J, Brunt EM, Kleiner DE, Hoofnagle JH, Robuck PR; NASH CRN. Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. N Engl J Med. 2010 May 6;362(18):1675-85. doi: 10.1056/NEJMoa0907929. Epub 2010 Apr 28. PMID: 20427778; PMCID: PMC2928471.
2. Kowdley KV, Bowlus CL, Levy C, Akarca US, Alvares-da-Silva MR, Andreone P, Arrese M, Corpechot C, Francque SM, Heneghan MA, Invernizzi P, Jones D, Kruger FC, Lawitz E, Mayo MJ, Shiffman ML, Swain MG, Valera JM, Vargas V, Vierling JM, Villamil A, Addy C, Dietrich J, Germain JM, Mazain S, Rafailovic D, Taddé B, Miller B, Shu J, Zein CO, Schattenberg JM; ELATIVE Study Investigators' Group; ELATIVE Study Investigators' Group. Efficacy and Safety of Elafibranor in Primary Biliary Cholangitis. N Engl J Med. 2024 Feb 29;390(9):795-805. doi: 10.1056/NEJMoa2306185. Epub 2023 Nov 13. PMID: 37962077.
3. Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, Shiffman ML, Schiff E, Ghalib R, Ryan M, Rustgi V, Chojkier M, Herring R, Di Bisceglie AM, Pockros PJ, Subramanian GM, An D, Svarovskaia E, Hyland RH, Pang PS, Symonds WT, McHutchison JG, Muir AJ, Pound D, Fried MW; ION-3 Investigators. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med. 2014 May 15;370(20):1879-88. doi: 10.1056/NEJMoa1402355. Epub 2014 Apr 10. PMID: 24720702.
4. Kowdley KV, Lawitz E, Poordad F, Cohen DE, Nelson DR, Zeuzem S, Everson GT, Kwo P, Foster GR, Sulkowski MS, Xie W, Pilot-Matias T, Liossis G, Larsen L, Khatri A, Podsadecki T, Bernstein B. Phase 2b trial of interferon-free therapy for hepatitis C virus genotype 1. N Engl J Med. 2014 Jan 16;370(3):222-32. doi:10.1056/NEJMoa1306227. PMID: 24428468.
5. Kowdley KV, Modi NB, Peltekian K, Vierling JM, Ferris C, Valone FH, Gupta S. Rusfertide for the treatment of iron overload in HFE-related haemochromatosis: an open-label, multicentre, proof-of-concept phase 2 trial. Lancet Gastroenterol Hepatol. 2023 Dec;8(12):1118-1128. doi: 10.1016/S2468-1253(23)00250-9. Epub 2023 Oct 17. PMID: 37863080.

Resmetirom's Promise and the Challenges Ahead

Kris V. Kowdley *Washington State University, USA*

The US FDA has approved resmetirom for treatment of adults with at-risk MASH and moderate to advanced liver fibrosis consistent (stages F2 and F3), in conjunction with diet and exercise. The label specifically excludes the use of resmetirom in patients with early fibrosis which is consistent with Stage F0-F1, pregnant or lactating women, pediatric patients, or those with cirrhosis. Patients with early stage (F0-F1) fibrosis are at a very low risk of adverse liver outcomes and the AASLD recommends that this subset of patients be managed with intensive lifestyle modifications and optimization of cardiovascular risk factors. In patients meeting criteria for treatment, the FDA label recommends 80 mg once daily for patients weighing less than 100 kgs and 100 mg once daily for those weighing over 100 kgs.

Patients with "at-risk" MASH are those with Stage 2 fibrosis or higher with histological evidence of MASH and are at a significantly higher risk of liver morbidity and mortality. Prior to initiating resmetirom in any patient it is crucial to rule out other common causes of liver disease such as alcohol-associated liver disease, autoimmune liver diseases, infectious or genetic liver diseases. The gold standard to determine the stage of fibrosis remains a liver biopsy. However, the FDA does not mandate a liver biopsy for fibrosis staging and depending on the type of practice, provider expertise and patient preference, non-invasive testing (NIT) can be considered as an alternative to biopsy.

In the absence of a liver biopsy, the use of a combination of NITs can increase the precision for staging hepatic fibrosis. Several NITs are currently being used in clinical practice and per current AASLD guidelines the preferred tests include vibration controlled transient elastography (VCTE), enhanced liver fibrosis (ELF) test and magnetic resonance elastography (MRE). Additionally, several new composite scores including Fibroscan-aspartate aminotransferase (FAST), Magnetic Resonance Imaging-Aspartate Aminotransferase and Magnetic Resonance Elastography-FIB-4 (MRE-FIB4) scores have been adopted by society guidelines. However, while NITs are advantageous, they are not without limitations and lack the precision to reliably differentiate between borderline stages of fibrosis. For this reason, patients with early fibrosis should not be started on resmetirom based on NIT assessment alone; a liver biopsy is recommended instead for accurate staging in such cases.

Most clinical prediction scores such as FIB-4 score and NAFLD fibrosis score are commonly used as screening tools to rule out or rule in advanced fibrosis but lack the specificity needed to definitive-

ly identify 'at risk' MASH patients. Among the serum-based NITs the ELF test is considered the most reliable, with values ranging between 7.5 and 9.8 indicative of 'at-risk' MASH patients. VCTE, an imaging-based NIT, may not be as readily available in primary care and general gastroenterology settings, but is another accurate test with liver stiffness measurements ranging between 8.0 and 13.6 suggestive of moderate to advanced fibrosis. More advanced imaging techniques, such as MRE, while highly accurate, are typically limited to large academic centers. For MRE, thresholds indicative of F2/F3 fibrosis may range between 2.5 and 4.5 kPa.

In cases where the results from different NITs are discordant, a liver biopsy should be considered for definitive diagnosis.

Silvia Sookoian

Maimonides University, Argentina

Self Introduction

Prof. Silvia Sookoian, MD, PhD., is a Senior Research Scientist at the CONICET (National Scientific and Technical Research Council). She graduated cum laude from the University of Buenos Aires School of Medicine. Her professional role as a physician scientist involves the translation of scientific knowledge in Hepatology into patient care. The primary focus of her current clinical and translational research is on the genetic, epigenetic and molecular mechanisms implicated in the pathogenesis and progression of MASLD. Dr. Sookoian has published extensively in the field of Liver Diseases, including MASLD (former NAFLD) and hepatitis C. She has been in clinical practice since 1987 (Clinical Training Board certificated in Internal Medicine; Fellowship in Hepatology). She received training in Hepatology (Karolinska Institute, Huddinge University Hospital. Sweden 1997 Hepatology Centres of Excellence Program; Pathology (Armed Forces Institute of Pathology. Washington DC. 2000); Genetics of complex diseases (Cold Spring Harbor Laboratories. NY, USA, and Wellcome Trust Advanced Courses 2006).

She currently holds a position of Head of the Clinical and Molecular Hepatology. CENITRES (Translational Health Research Centre). Maimonides University, Buenos Aires. Argentina. Full Professor of Medicine. Dean of the Faculty of Health Science at the Maimonides University. Buenos Aires. Argentina. Fellow of the American Association for the Study of the Liver Disease (AASLD). Elected 2016. Editorial Boards: GUT (2015-current). HEPATOLOGY Country USA (2016-2021). Journal of Lipid Research (2019-current). International Editorial Board Journal of Alimentary Pharmacology and Therapeutics. (2020-current). Liver International (2020- current). Hepatobiliary Surgery and Nutrition (HBSN) (2020-current). Journal of Hepatology (2025-current). Associate Editor: Hepatobiliary Surgery and Nutrition (HBSN) (2021-current). Clinical and Molecular Hepatology (2020-current). Journal of Lipid Research (2024-current). Liver International (2025-current). Other relevant international professional service: Member of the Program Evaluation Committee American Association for the Study of Liver Disease (AASLD) 2010-2013. Member of the Steering Committee Steatosis and Steatohepatitis Special Interest Group of AASLD and Co-Chair of its global outreach subcommittee (2018-2020). Member of the Latin American Regional Advisory Council of AASLD). Abstract review committee American Association for the Study of Liver Diseases (AASLD) Steatosis and Steatohepatitis. Scientific Committee Italian Liver Foundation. 2023-current. Co-Organizer of the Keystone Symposia, MASH and Fibrosis: From Molecular Phenotypes to Precision Therapeutics, Fairmont Banff Springs, Banff, AB, Canada, 2024.

Research Interests

Contributions to science: With over 220 publications and an h-index of 57 (Scopus, 2025), our group research has made significant contributions to the understanding of metabolic associated steatotic liver disease (MASLD). Our early work directly addressed the pathogenesis of MASLD, focusing on the critical role of genetic and epigenetic factors in disease progression. Using cutting-edge OMICs techniques, including transcriptomics, genomics, epigenomics, and metagenomics, our group has elucidated key biological mechanisms underlying MASLD.

Representative Publications

1. Epigenetic regulation of insulin resistance in nonalcoholic fatty liver disease: impact of liver methylation of the peroxisome proliferator-activated receptor γ coactivator 1 α promoter. Hepatology. 2010, 52(6):1992-2000.
2. Epigenetic modification of liver mitochondrial DNA is associated with histological severity of nonalcoholic fatty liver disease. Gut. 2013;62(9):1356-63.
3. Circulating microRNA signature in non-alcoholic fatty liver disease: from serum non-coding RNAs to liver histology and disease pathogenesis. GUT 2015 May;64(5):800-12.
4. Nonalcoholic fatty liver disease. Nature Reviews Disease Primers 2015;1:15080. doi: 10.1038/nrdp.2015.80.
5. Genetic pathways in nonalcoholic fatty liver disease: Insights from systems biology. Hepatology. 2020 Jul;72(1):330-346.

New Drug Discovery in MASLD Based on Multi-Omics

Silvia Sookoian *Maimonides University, Argentina*

Discovering new drugs for MASLD (Metabolic Dysfunction-Associated Steatotic Liver Disease) requires understanding its complex mechanisms through multi-omics approaches. This also involves considering comorbidities like obesity, insulin resistance, and metabolic disorders. Multi-omics combines different types of data—genomics, transcriptomics, proteomics, metabolomics, and epigenomics—which assists researchers in identifying biomarkers, molecular pathways, and potential drug targets. By examining these datasets, scientists can identify new drug candidates that may influence disease progression or address liver damage. This all-encompassing approach supports a more individualized treatment strategy and reveals mechanisms in liver dysfunction, inflammation, fibrosis, and fatty liver progression.

Key goals of multi-omics-based drug discovery include:

- Identifying specific genetic, metabolic, and inflammatory pathways that contribute to MASLD.
- Uncovering novel therapeutic targets for intervention.
- Evaluating the efficacy of existing and new drug candidates across various biological levels.
- Developing precision medicine approaches tailored to individual patients' omic profiles.

Some key concepts will be addressed, including:

1. Genomics

Genomics studies the entire genome (DNA) and is essential in multi-omics. For MASLD, it identifies genetic variants linked to liver fat accumulation, metabolic dysfunction, and progression to severe forms like MASH or cirrhosis. How it's leveraged: Target Identification; Personalized Medicine: Genomic information can also guide the development of personalized treatments; Gene Editing: Techniques like CRISPR allow for the direct manipulation of genes, providing a powerful tool for testing the impact of genetic changes on disease and potential drug responses.

2. Epigenomics

Epigenomics is the study of modifications in gene expression regulation that do not involve changes to the underlying DNA sequence. This includes mechanisms such as DNA methylation, histone modifications, and non-coding RNA regulation. These epigenetic modifications are often influenced by

environmental factors such as diet, lifestyle, and pharmaceuticals and play a crucial role in diseases like MASLD. How it's leveraged: Target Identification: Epigenetic modifications can reveal new drug targets. For instance, drugs that reverse aberrant DNA methylation or histone modifications could be developed to progressive MASLD, where epigenetic changes play a role in disease progression; Therapeutic Development: Epigenetic drugs (like DNA methyltransferase inhibitors or histone deacetylase inhibitors) aim to "reset" the epigenetic state of the genome to normal; Drug Response and Resistance: Epigenetic changes can influence how cells respond to treatment, including the development of drug resistance. Understanding these changes can help researchers design drugs that overcome resistance mechanisms and improve therapeutic efficacy.

3. Transcriptomics

This field studies all RNA transcripts (mRNA, lncRNA, etc.) produced by the genome. By analyzing gene expression in liver cells, researchers can reveal the molecular mechanisms of MASLD and identify gene networks involved in liver steatosis, inflammation, fibrosis, and metabolic disturbances. How it's leveraged: Biomarker Discovery: By comparing gene expression profiles of diseased and healthy tissues, researchers can identify potential biomarkers for early diagnosis, disease progression, or drug response; Disease Pathway Insights: Transcriptomics can identify changes in gene expression that contribute to disease mechanisms.

4. Proteomics

Proteomics studies all proteins expressed in cells or tissues at a specific time, providing insight into the liver's functional state in MASLD. Protein biomarkers can also be targets for drug development. How it's leveraged: Target Validation: Proteomics can help validate drug targets identified through genomics and transcriptomics; Biomarker Identification: Proteins are often used as biomarkers for diagnosing diseases or predicting drug response; Drug Discovery and Optimization: Proteomics can identify protein-drug interactions, helping researchers understand how a drug binds to its target and how it affects cellular pathways. This can be crucial for optimizing drug efficacy and reducing off-target effects.

5. Metabolomics

Metabolomics involves the study of metabolites (small molecules such as lipids, sugars, amino acids) within a biological system. Metabolomic profiling of liver tissue and blood can indicate changes in the metabolic state in MASLD, offering information on potential biomarkers for early diagnosis, progression, and therapeutic response. How it's leveraged: Identifying Disease Signatures: Metabolomics can help identify unique metabolic profiles associated with specific diseases; Drug Mechanism of Action: By monitoring changes in metabolite levels in response to a drug, researchers can gain insights into the drug's effects on metabolism. Personalized Treatment: Metabolomics can aid in determining which metabolic profiles are associated with favorable drug responses, allowing for more tailored and effective treatments.

6. Metagenomics

By sequencing the genetic material from a patient's microbiota—such as those found in the gut, circulation or liver tissue—metagenomics can provide insights into how microbial communities influence disease susceptibility, treatment responses, and overall health.

7. Integration of Multi-Omics Data

The real power of multi-omics comes from integrating data from genomics, transcriptomics, proteomics, metabolomics, and epigenomics. By combining information across these layers, researchers can build a more holistic understanding of MASLD and identify new therapeutic strategies. How it's leveraged: Systems Biology: By combining genomic, transcriptomic, proteomic, and metabolomic data, researchers can build more accurate models of disease pathways. These models help identify critical nodes (e.g., proteins, genes, metabolites) that can be targeted by drugs; Predictive Modeling: Integrating omics data helps build predictive models for drug efficacy and toxicity. Researchers can predict how a drug will impact the entire system by studying the interactions between different molecular components in health and disease, which may help reduce the risk of failures in clinical trials. Precision Medicine: Multi-omics data allows for the development of precision medicine, where therapies are tailored to individuals based on their unique molecular profiles. This improves treatment outcomes by ensuring that patients receive drugs that are most likely to work for their specific biological makeup.

Conclusion

Multi-omics approaches in MASLD drug discovery offer a promising way to understand the molecular mechanisms of this disease. By using genomics, transcriptomics, proteomics, metabolomics, and epigenomics, researchers can find new biomarkers and therapeutic targets, advancing precision medicine for MASLD treatment. As omics technologies evolve, they hold potential for developing more effective, personalized therapies to manage or reverse MASLD, giving hope to patients.

References

1. Genetics in non-alcoholic fatty liver disease: The role of risk alleles through the lens of immune response. Clin Mol Hepatol. 2023 Feb;29(Suppl):S184-S195. doi: 10.3350/cmh.2022.0318
2. Personalized medicine in nonalcoholic fatty liver disease. Clin Mol Hepatol. 2022 Oct;28(4):935-938. doi: 10.3350/cmh.2022.0175.
3. Precision medicine in nonalcoholic fatty liver disease: New therapeutic insights from genetics and systems biology. Clin Mol Hepatol. 2020 Oct;26(4):461-475. doi: 10.3350/cmh.2020.0136.
4. Genetic Pathways in Nonalcoholic Fatty Liver Disease: Insights From Systems Biology. Hepatology. 2020 Jul;72(1):330-346. doi: 10.1002/hep.31229.
5. Cross talk between the liver microbiome and epigenome in patients with metabolic dysfunction-associated steatotic liver disease. EBioMedicine. 2024 Mar;101:104996. doi: 10.1016/j.ebiom.2024.104996.

6. Epigenetic modification of liver mitochondrial DNA is associated with histological severity of nonalcoholic fatty liver disease. Gut. 2013 Sep;62(9):1356-63. doi: 10.1136/gutjnl-2012-302962.
7. Epigenetic regulation of insulin resistance in nonalcoholic fatty liver disease: impact of liver methylation of the peroxisome proliferator-activated receptor gamma coactivator 1alpha promoter. Hepatology. 2010 Dec;52(6):1992-2000. doi: 10.1002/hep.23927
8. The lipidome in nonalcoholic fatty liver disease: actionable targets. J Lipid Res. 2021;62:100073. doi: 10.1016/j.jlr.2021.100073.
9. The Proteomics of MASLD Progression: Insights From Functional Analysis to Drive the Development of New Therapeutic Solutions. Aliment Pharmacol Ther. 2025 Feb;61(4):614-627. doi: 10.1111/apt.18468.
10. Intrahepatic bacterial metataxonomic signature in non-alcoholic fatty liver disease. Gut. 2020 Aug;69(8):1483-1491. doi: 10.1136/gutjnl-2019-318811.

THE LIVER WEEK 2025

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LIVER WEEK 2025

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DAY 3: May 31 (Sat.)

KLCA Symposium 3

Revisiting and Expanding Hepatocellular Carcinoma Treatment Paradigms: From Standard to Innovative Therapies

Chairs:

Jong Young Choi (Chung-Ang Univ.)
Augusto Villanueva (Icahn School of Medicine at Mount Sinai, USA)

Yi-Hsiang Huang

National Yang Ming Chiao Tung University, Taiwan

Self Introduction

Prof. Yi-Hsiang Huang is the President (2023-2027) of Taiwan Liver Cancer Association (TLCA), and the Director of Medical Research at the Taipei Veterans General Hospital (since 2025 Jan). He is also the Chair Professor for the Institute of Clinical Medicine at the National Yang Ming Chiao Tung University. Completing his medical and PhD training at National Yang Ming University, he furthered his training as a research fellow at the Vaccine Branch of National Cancer Institute, National Institute of Health, USA from 2006 to 2007. Prof. Huang became a full professor at the Institute of Clinical Medicine, NYCU in 2011, and the Chair Professor at NYCU since Aug. 2022.

He has served as the council member of Asia-Pacific Primary Liver Cancer Expert Association (APPLE) since Jul. 2023; the executive committee member of Taiwan Association for the Study of the Liver (TASL) since Sep. 2023; the secretary general of the Chinese Medical Association (CMA) of Taiwan (2020-2026), the council member of the Taiwan Academy of Tumor Ablation (TATA), the Chairman of the 2025 Asia Pacific Association for the Study of the Liver (APASL) STC Oncology.

Research Interests

Prof. Huang's study interest is in the virology and immunology of viral hepatitis and HCC, including HBV reactivation related to immunosuppressive and immune checkpoint inhibitors therapy, and HCC treatment across locoregional to systemic therapy.

Representative Publications

1. Mon HC, Lee PC, Hung YP, Hung YW, Wu CJ, Lee CJ, Chi CT, Lee IC, Hou MC, Huang YH*. Functional cure of hepatitis B in patients with cancer undergoing immune checkpoint inhibitor therapy. J Hepatol 2025 Jan; 82(1): 51-61 (*corresponding author)
2. Hung YW, Lee IC, Chi CT, Lee RC, Liu CA, Chiu NC, Hwang HE, Chao Y, Hou MC, Huang YH*. Radiologic Patterns Determine the Outcomes of Initial and Subsequent Transarterial Chemoembolization in Intermediate-Stage Hepatocellular Carcinoma. Liver Cancer. 2024 Feb;13 (1): 29-40. (*corresponding author)
3. Lee PC, Wu CJ, Hung YW, Lee CJ, Chi CT, Lee IC, Yu-Lun K, Chou SH, Luo JC, Hou MC, Huang YH*. Gut microbiota and metabolites associate with outcomes of immune checkpoint inhibitors-treated unresectable hepatocellular carcinoma. J Immunother Cancer 2022 Jun;10(6):e004779. (*corresponding author)
4. Chen MH*, Lee IC, Chen MH, Hou MC, Tsai CY, Huang YH*. Abatacept is second to rituximab at risk of HBsAg reverse seroconversion in patients with rheumatic disease. Annals of Rheumatic Diseases 2021 Nov;80(11):1393–1399. (*corresponding author)
5. Lee IC, Huang JY, Chen TC, Yen CH, Chiu NC, Hwang HE, Huang JG, Liu CA, Chau GY, Lee RC, Hung YP, Chao Y, Ho SY*, Huang YH*. Evolutionary Learning Derived Clinical-Radiomic Models for Predicting Early Recurrence of Hepatocellular Carcinoma After Resection. Liver Cancer. 2021 Nov;10(6):572-582 (*corresponding author)

Systemic Therapy and Transarterial Chemoembolization in BCLC Intermediate Stage: A Survival Boost?

Yi-Hsiang Huang *National Yang Ming Chiao Tung University, Taiwan*

Hepatocellular carcinoma (HCC) is characterized by heterogeneity in tumor burden and liver histology, especially in the intermediate stage. Transarterial chemoembolization (TACE) has long been the standard of care for intermediate stage HCC. Recent advances in systemic therapies have expanded its feasibility to intermediate stage HCC. Systemic therapy has long been the treatment option for TACE refractory status for intermediate stage HCC. Switching to sorafenib or lenvatinib can prolong the survival for TACE refractory cases. In general, tumor burden is a key factor associated with treatment response and survival to TACE. TACE unsuitability has been proposed for patients with up-to-7 out status. In our studies, 7-11 criteria and radiologic pattern can further predict the tumor response to TACE. For patients with high tumor burden or poor radiologic patterns, systemic therapy should be considered.

Targeted kinase inhibitors (TKI) including sorafenib and lenvatinib in combination with TACE can provide better time-to-unTACEable progression in intermediate stage HCC with high tumor burden from TACTIS and TACTIS-L trials. Following the success of the IMbrave 150 and Himalaya studies, immune checkpoint inhibitors (ICI) have become the upfront treatment for advanced HCC. It is hypothesized that locoregional treatment (LRT) can enhance the response of ICI by providing tumor antigen shedding. Therefore, immune boost LRT or TACE is an emerging issue for intermediate stage HCC. New data from the EMERALD-1 and LEAP-012 studies show that immunotherapy combined with TACE can indeed improve tumor response rate and progression-free survival compared with TACE alone. However, the overall survival data from both trials are not yet mature. Currently, up to a quarter of patients with intermediate stage HCC can be curative conversion by systemic therapy combining with or followed by LRT. All these issue will be discussed further in the presentation.

Hyo-Cheol Kim

Seoul National University

Self Introduction

Prof. Hyo-Cheol Kim is a clinical professor at the Seoul National University Hospital, in Seoul, Republic of Korea. He completed his residency in diagnostic radiology at the Seoul National University Hospital (1999–2003) and is board- certified in radiology. In 2008, he finished his fellowship training in interventional radiology at the Seoul National University Hospital and has been a professor of interventional radiology there since then.

His clinical interests include chemoembolization and radioembolization for hepatocellular carcinoma. From Dec 2017, He joined JVIR editorial member as associate editor. He also gave a lecture on cTACE at the Guerbet Asia Pacific Preceptorship program and lectured on radioembolization at the SIR-Spheres® Center of Education: advanced course.

Educational

1992.03-1998.02	Seoul National University College of Medicine
1999.03-2003.02	Residency in Radiology, Seoul National University Hospital
2003.05-2006.04	Military Medical Officer, Captain, 19th Fighter Wing
2006.03-2008.02	Fellow in Radiology, Seoul National University Hospital
2008.03-2013.09	Clinical Assistant Professor, Seoul National University Hospital
2013.10-2018.08	Clinical Associate Professor, Seoul National University Hospital
2018.09-Present	Clinical Professor in Interventional Radiology section, Seoul National University Hospital

Journal Editorial Member

2017.12-Present	JVIR Associate Editor
2018.02-Present	KJR Section Editor

Representative Publications

1. Kim HC, Miyayama S, Choi JW, Kim GM, Chung JW. Hepatocellular carcinoma supplied by the inferior phrenic artery or cystic artery: anatomic and technical considerations. Radiographics. 2023 Jan;43(1):e220076.
2. Kim HC, Kim GM. Radiation pneumonitis following Yttrium-90 radioembolization: A Korean multicenter study. Front Oncol. 2023 Jan 16;13:977160.
3. Chung SW, Cho H, Shin H, Park J, Kim JY, Hong JH, Hur MH, Park MK, Lee YB, Yu SJ, Lee M, Kim YJ, Paeng JC, Yoon JH, Chung JW, Lee JH, Kim HC. Transarterial chemoembolization as an alternative to radioembolization is associated with earlier tumor recurrence than in radioembolization-eligible patients. Front Oncol. 2023 Feb 28;13:1081479.
3. Choi R, Lee M, Choi JW, Kim HC. Safety of Radioembolization via the Cystic Artery in patients with Hepatocellular Carcinoma and Parasitized Arterial Supply. J Vasc Interv Radiol. 2023 Oct;34(10):1802-1808.
4. Choi JW, Suh M, Paeng JC, Kim JH, Kim HC. Radiation Major Hepatectomy Using Ablative Dose Yttrium-90 Radioembolization in Patients with Hepatocellular Carcinoma 5 cm or Larger. J Vasc Interv Radiol. 2024 Feb;35(2):203-212.
5. Kim HC, Suh M, Paeng JC, Lee JH, Lee M, Chung JW, Choi JW. Streamlining Radioembolization without Lung Shunt Estimation versus Regular Radioembolization in Patients with Hepatocellular Carcinoma within the Milan Criteria. J Vasc Interv Radiol. 2025 Jan;36(1):78-87.e1

TACE/TARE in Advanced Hepatocellular Carcinoma: Can They Coexist with Systemic Therapy?

Hyo-Cheol Kim *Seoul National University*

Current Role of TACE and TARE

TACE has long been the standard of care for intermediate-stage HCC (Barcelona Clinic Liver Cancer [BCLC] stage B), characterized by multifocal disease without vascular invasion or extrahepatic spread. It involves the intra-arterial delivery of chemotherapy followed by embolic agents to block blood flow, leading to ischemic necrosis of the tumor. TARE, in contrast, delivers radioactive microspheres (usually Yttrium-90) via the hepatic artery, offering a more targeted radiation-based approach.

While both modalities have demonstrated efficacy in controlling intrahepatic tumors and delaying progression, their roles in advanced HCC (BCLC stage C), particularly in patients with portal vein thrombosis (PVT) or extrahepatic spread, are more controversial. In such cases, systemic therapy is the mainstay treatment. However, TARE, which causes less ischemic injury than TACE, has been explored in patients with PVT due to its safety profile and potential to downstage disease.

Emergence and Impact of Systemic Therapies

The introduction of systemic agents such as sorafenib and lenvatinib revolutionized treatment for advanced HCC by offering survival benefits in patients with preserved liver function. More recently, the combination of immune checkpoint inhibitors (e.g., atezolizumab plus bevacizumab, durvalumab plus tremelimumab) has shown superior efficacy over tyrosine kinase inhibitors (TKIs) alone. These combinations have shifted the treatment paradigm toward immunotherapy-first approaches.

Given this evolution, there has been increasing interest in integrating locoregional and systemic therapies. Rather than viewing TACE/TARE and systemic therapy as mutually exclusive, the focus has shifted to synergistic strategies that may improve outcomes beyond what either modality can achieve alone.

Rationale for Combination Approaches

The theoretical basis for combining TACE or TARE with systemic therapy lies in the complementary mechanisms of action. Locoregional therapies target intrahepatic disease, offering cytoreduction and possibly converting tumors into resectable or transplantable states. However, they may also trigger hypoxia-induced pro-angiogenic factors such as VEGF, promoting tumor recurrence and systemic spread.

Systemic agents, especially those targeting angiogenesis or modulating the immune system, may counteract these effects.

For example, combining TACE with anti-VEGF therapy like sorafenib was hypothesized to suppress the surge in VEGF post-embolization. Similarly, TARE may induce immunogenic cell death, creating a microenvironment conducive to checkpoint inhibition. These synergistic interactions provide a strong rationale for combination strategies in advanced HCC.

Clinical Evidence and Ongoing Trials

Several clinical trials have investigated the feasibility and efficacy of combining locoregional and systemic therapies:

TACE + Sorafenib: The SPACE and TACE 2 trials failed to show significant improvements in overall survival or progression-free survival when combining TACE with sorafenib. However, these trials highlighted the challenges of patient selection and timing of administration.

TARE + Sorafenib: The SARAH and SIRveNIB trials compared TARE with sorafenib monotherapy and showed comparable survival outcomes, but TARE offered better tolerability and quality of life in some patients.

TACE/TARE + Immunotherapy: This is currently the most exciting area of research. Trials like EMERALD-1, LEAP-012, and CheckMate 74W are evaluating combinations of TACE with immune checkpoint inhibitors (e.g., atezolizumab, nivolumab) and anti-angiogenic agents (e.g., bevacizumab, lenvatinib). Preliminary data from early-phase studies suggest that such combinations are safe and may offer improved response rates.

The outcomes of these trials are expected to provide critical insights into whether TACE and TARE can coexist with systemic therapies in a clinically meaningful way.

Challenges and Considerations

Despite promising prospects, several challenges remain:

Patient Selection: Identifying which patients are most likely to benefit from combination therapy remains a key issue. Factors such as liver function (Child-Pugh score), tumor burden, and presence of extrahepatic disease must be carefully considered.

Treatment Sequencing and Timing: Determining the optimal timing (e.g., concurrent vs. sequential) and sequencing of locoregional and systemic therapies is complex. Some studies suggest initiating systemic therapy first to control disease, followed by TACE/TARE for intrahepatic dominance.

Toxicity Management: Combining treatments increases the risk of adverse events, including hepatic decompensation. Careful monitoring and multidisciplinary management are essential.

Cost and Accessibility: Combination therapies are often costly and may not be available in all healthcare settings. Health economics will influence their widespread adoption.

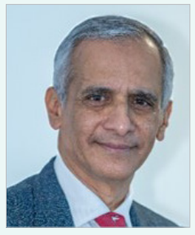
Future Perspectives

The future of HCC management is moving toward a personalized, multidisciplinary approach. Biomarkers predicting response to therapy, such as immune signatures or radiologic features, may guide selection of patients for combination treatments. Moreover, advances in imaging and artificial intelligence could improve response assessment and enable more precise targeting of locoregional therapies.

As immunotherapy continues to evolve, the concept of "immunogenic priming" through TACE or TARE could become a cornerstone strategy. In addition, novel agents targeting different immune pathways or tumor microenvironment components could further enhance synergy with locoregional treatments.

Conclusion

TACE and TARE have long played a central role in managing unresectable HCC, particularly in the intermediate stage. With the advent of effective systemic therapies, especially immunotherapy, the paradigm is shifting from an either-or approach to a combined modality strategy. While challenges such as toxicity, patient selection, and optimal sequencing remain, the convergence of locoregional and systemic treatments holds great promise. As ongoing trials mature and novel combinations are explored, it is increasingly likely that TACE and TARE will continue to coexist—and synergize—with systemic therapies in the evolving landscape of advanced HCC treatment.



Jacob George

The University of Sydney, Australia

Self Introduction

Jacob George is the Robert W. Storr Professor of Hepatic Medicine at the Storr Liver Centre, Westmead Institute for Medical Research, University of Sydney and Head of the Department of Gastroenterology and Hepatology at Westmead Hospital.

He undertakes basic and clinical research on MAFLD, hepatitis C, liver cancer and hepatic fibrosis.

He is a senior Editor for Seminars in Liver Disease and Journal of Hepatology Reports. He has published extensively.

Research Interests

MAFLD, HCC, Hepatitis C

Representative Publications

1. Li Z, et al. Presence of onco-fetal neighborhoods in hepatocellular carcinoma is associated with relapse and response to immunotherapy. Nature Cancer 2024; 5(1):167-186
2. Pan Z, et al. M. Inhibition of MERTK reduces organ fibrosis in mouse models of fibrotic disease. Science Translational Medicine 2024;16(741):eadj0133.
3. Eslam M, et al. IFN- λ 3, not IFN- λ 4, likely mediates IFNL3/IFNL4 haplotype-dependent hepatic inflammation and fibrosis. Nature Genetics 2017;49:795-800.
4. Eslam M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. Journal of Hepatology 2020;73(1):202-209.
5. Daniels SJ, et al. ADAPT: An algorithm incorporating PRO-C3 accurately identifies patients with NAFLD and advanced fibrosis. Hepatology 2019;69:1075-1086

The Emerging Role of Immuno-Oncology Therapy in Neo- and Adjuvant Treatment for Hepatocellular Carcinoma

Jacob George *The University of Sydney, Australia*

Liver cancer is the fifth most common and third most lethal cancer worldwide with global incidence and mortality rates predicted to rise 55% by 2040. In the Asia Pacific, HCC accounted for 584,000 new cases in 2020, representing two thirds of total incidence of liver cancer worldwide and 72% of total HCC deaths. The treatment of HCC has seen increasingly aggressive curative and loco-regional approaches that have improved the survival of patients. As a majority of patients still present at late stages, the advent of immunotherapy-based systemic regimens (IMbrave 150, STRIDE) has radically altered the outcomes for patients with advanced cancers. However, an unmet clinical need remains the need to reduce recurrence rates after curative treatments, particularly surgical resection. In this group, recurrence rates of up to 63% at 5 years and higher in patients with high-risk features (large tumour size, multiple tumours, poor tumour differentiation, or vascular invasion) has been reported. For the majority, recurrence events typically appear within the first 2 years. Given these data, recent studies have tried adjuvant, and neo-adjuvant approaches to therapy in combination with surgical resection. Unfortunately, while the IMbrave050 trial had initially encouraging results for recurrence free survival, the RFS benefit was not sustained over time, while overall survival continued to be immature at the updated interim analysis. Neoadjuvant immunotherapy-based regimens have provided encouraging phase 2 data. While there are a lot of reasons for why neoadjuvant therapy might offer advantages over adjuvant approaches, treatment regimens in this scenario have to first and foremost, be informed by the dynamics of tumour and stromal biology and kinetics.

Jeong Heo

Pusan National University

Self Introduction

Prof. Jeong Heo, M.D., Ph.D., is a full professor of Internal Medicine, Pusan National University and Digestive Disease Center, Pusan National University Hospital. He is a medical doctor and scientist, having received his medicinae doctor and doctoral (Internal Medicine) degrees from College of Medicine, Pusan National University, in Busan Republic of Korea.

During his career, Prof. Heo held a number of academic positions, university and hospital appointments as well as principal investigator in many clinical trials for Phase I-IV of hepatitis B, C and hepatocellular carcinoma. He has also received research grants from the Korean Ministry of Education, Science and Technology. Prof. Heo has published more than 300 peer-reviewed manuscripts.

Research Interests

Cure of Chronic Hepatitis B, Immunotherapy of Hepatocellular Carcinoma

Representative Publications

1. Buti M, Heo J, Tanaka Y, et al. Sequential Peg-IFN after bepirovirsen may reduce post-treatment relapse in chronic hepatitis B. J Hepatol. 2025 Feb;82(2):222-234.
2. Lim HY, Heo J, Peguero JA, et al. Efficacy and safety of bintrafusp alfa in 2 phase I expansion cohorts with advanced HCC. Hepatology. 2025 Jan 1;81(1):32-43.
3. Hwang SY, Woo HY, Heo J, et al. Outcome of Atezolizumab Plus Bevacizumab Combination Therapy in High-Risk Patients with Advanced Hepatocellular Carcinoma. Cancers (Basel). 2024 Feb 19;16(4):838.
4. Heo J, Liang JD, Kim CW, et al. Safety and dose escalation of the targeted oncolytic adenovirus OBP-301 for refractory advanced liver cancer: Phase I clinical trial. Mol Ther. 2023 Jul 5;31(7):2077-2088.
5. Yuen MF, Heo J, Jang JW, et al. Safety, tolerability and antiviral activity of the antisense oligonucleotide bepirovirsen in patients with chronic hepatitis B: a phase 2 randomized controlled trial. Nat Med. 2021 Oct;27(10):1725-1734.

KLCA Symposium 3 | DAY 3: May 31 (Sat.) | ROOM 2 [3F]

Cancer Vaccines in Hepatocellular Carcinoma: Current Status and Future Directions

Jeong Heo *Pusan National University*

Hepatocellular carcinoma (HCC) is a prevalent and deadly form of liver cancer, often associated with chronic hepatitis B and C infections. Despite advancements in traditional treatments like surgery, chemotherapy including targeted therapy, and radiotherapy, HCC remains challenging to treat, especially in advanced stages. Immune-based therapies are gaining attention in the treatment of HCC. In particular, immunotherapies such as immune checkpoint inhibitors (ICIs) have brought about a major change in the treatment of HCC. Combination therapy of atezolizumab (anti-PD-L1) and bevacizumab (anti-VEGF) is used as first-line treatment for advanced HCC and has shown a median survival time of approximately 19 months and an objective response rate of 30%. In addition, many basic and clinical studies on immunology and immune-based treatment of HCC are actively underway. Novel immunotherapies include innovative approaches such as cell therapy. The role of vaccines in HCC treatment is also being studied, and they work by inducing an immune response to attack cancer cells. Although these vaccine treatments are still in their early stages, they are likely to play an important role in the treatment of HCC in the future.

Major Tumor-Associated Antigens (TAAs) from Hepatocellular Carcinoma (HCC)

In HCC, TAAs are proteins that are overexpressed or abnormally expressed in cancer cells. These antigens are recognized by the immune system and can be used as targets for cancer diagnosis and treatment. Major TAAs include the following (Table 1.). These TAAs are pivotal in advancing HCC diagnostics and therapeutics, offering innovative opportunities for immune-based treatments.

1. Glypican-3 (GPC3): Overexpressed in ~80% of HCC cases; involved in key signaling pathways (e.g., Wnt, YAP). Serves as both a diagnostic marker and a therapeutic target (e.g., CAR-T cell therapies and vaccines)[1,2].

2. Alpha-Fetoprotein (AFP): A serum biomarker targeting AFP-expressing HCC cells through vaccines and combination therapies[3]. Challenges include immune exhaustion, but promising preclinical and clinical results have been observed[4].

3. Melanoma Antigen Gene-1 (MAGE-1): Explored in vaccine therapy; boosts immune responses when combined with immune checkpoint inhibitors[5,6]. Potential for metastatic HCC treatment[6].

4. Heat Shock Protein 70 (HSP70): Aims to activate cytotoxic T cells (CTLs) against HSP70-expressing tumors. Combination therapies enhance effectiveness[7,8].

5. Glutamine Synthetase (GS): Targeted by vaccines to induce CTLs. Research suggests improved outcomes with immune checkpoint inhibitors[9-11].

6. TMEM176A/B: Modulates immune regulation and enhances the antitumor response[12]. Promising results when combined with immune checkpoint inhibitors like nivolumab[12,13].

Table 1. Strategic Vaccine Targets in Hepatocellular Carcinoma

Target	Mechanism	Combination Therapy	Clinical Trials	Potential
Glypican-3 (GPC3)	Involved in signaling pathways like Wnt, IGF, YAP, Hedgehog. Inhibits tumor growth	Therapies like monoclonal antibodies, CAR-T cells, GPC-3 vaccines aim for clinical improvement	Focused on its role as a diagnostic marker and treatment through targeted immunotherapy	High specificity in HCC diagnosis; promising therapeutic target
Alpha-Fetoprotein (AFP)	Stimulates immune response using AFP-specific CD8+ T cells	Combining AFP vaccines with anti-PD-L1 immune checkpoint inhibitors enhances therapy	Tested in preclinical models and clinical trials for inducing immune responses to kill tumors	Effective in combination therapies; faces challenges like immune exhaustion
Melanoma Antigen Gene-1 (MAGE-1)	Induces MAGE-1-specific CD8+ T cells to target cancer cells	Combined with anti-PD-1 inhibitors for increased survival and tumor clearance	MAGE-1-directed TCR-T cell therapy evaluated in advanced/metastatic tumor clinical trials	Enhanced effectiveness with immunotherapies; promising for metastatic cases
Heat Shock Protein 70 (HSP70)	Generates CTLs targeting HSP70-expressing tumor cells	Enhanced immune response when combined with therapies like immune checkpoint inhibitors	Ongoing trials focus on vaccine-induced immune activation and impact on tumor control	Strong immune activation; complementary with other therapies
Glutamine Synthetase (GS)	Produces CTLs to kill GS-expressing cancer cells	Immune checkpoint inhibitors improve vaccine efficacy and antitumor response	Evaluated for immune response and tumor suppression in clinical trials	Promising immune-targeted therapy when combined with immunotherapies
TMEM176A/B	Modulates immune responses against TMEM176A/B-positive HCC cells	Combined with nivolumab for enhanced antitumor response and checkpoint inhibitor effectiveness	Trials assess safety, immune modulation, and therapeutic impact on tumor progression	Novel regulatory targets with therapeutic potential in combination immunotherapy strategies

* CAR-T, chimeric antigen receptor T-cell therapy; HCC, hepatocellular carcinoma; CTL, Cytotoxic T Lymphocytes

Current Status of Cancer Vaccines in HCC

1. Types of Cancer Vaccines

Therapeutic Vaccines: Aim to treat existing cancer by enhancing the immune response against tumor cells. Examples include dendritic cell vaccines and peptide-based vaccines.[14,15].

Prophylactic Vaccines: Aim to prevent cancer development, particularly for virus-associated cancers like hepatitis B virus and human papillomavirus[14].

2. Vaccine Platforms (Table 2)

Peptide-Based Vaccines: Use specific peptides to target TAAs, such as GPC3 and AFP, and elicit immune responses[16.17].

Dendritic Cell-Based Vaccines: Utilize antigen-presenting dendritic cells to activate T cells and initiate targeted immune responses[18].

Viral Vector-Based Vaccines: Employ engineered viruses (e.g., adenovirus) to deliver antigens and stimulate robust immune responses[14].

DNA and mRNA Vaccines: Use genetic material to instruct cells to produce antigens, inducing potent immune responses. mRNA vaccines show significant promise[19].

Table 2. Platforms for HCC Vaccine Development

Vaccine Platform	Mechanism	Key Features	Clinical Insights
Peptide-based Vaccines	Utilize specific peptides to target TAAs like GPC3 and AFP	Trigger immune responses by targeting overexpressed TAAs in HCC	Clinical trials show promising results in eliciting immune responses and improving survival rates
Dendritic Cell-based Vaccines	Isolate patient's dendritic cells, load them with tumor antigens, and reintroduce them	Activates T cells via potent antigen-presenting dendritic cells	Demonstrated safety and efficacy in HCC clinical trials
Viral Vector-based Vaccines	Use engineered viruses (e.g., adenovirus, vesicular stomatitis virus) to deliver antigens	Induce strong and durable immune responses through viral vectors	Explored for robust immune stimulation against HCC antigens
DNA and mRNA Vaccines	Introducing genetic material (DNA or mRNA) to instruct cells to produce tumor antigens	DNA encodes tumor antigens; mRNA produces antigens within cells, inducing potent immune responses	Preclinical and clinical studies show promise, with mRNA gaining attention for its effectiveness

* TAAs, tumor-associated antigens; GPC3, glypican-3; AFP, alpha-fetoprotein

Therapeutic Cancer Vaccines

1. Principle

Therapeutic cancer vaccines are designed to:

Identify Tumor Antigens: Target antigens specific to cancer cells, distinguishing them from healthy cells.

Stimulate Immune Response: Activate immune cells to recognize and attack cancer cells, fostering a strong immune response[20].

2. Mechanism

Antigen Presentation: TAAs or TSAs are introduced via platforms like peptide-, cell-, virus-, or nucleic acid-based vaccines. Antigen-presenting cells (e.g., dendritic cells) process and present antigens using MHC molecules[20].

Activation of Immune Cells: The presented antigens are recognized by T cells, leading to their activation. Cytotoxic T cells (CD8+ T cells) are particularly important as they can directly kill cancer cells expressing the target antigens[20].

Immune Memory: The immune system develops a memory of the cancer antigens, which helps in recognizing and attacking cancer cells if they reappear. This long-term immune memory is crucial for preventing cancer recurrence[21].

3. Application in HCC

Focus on antigens like AFP and GPC3. Experimental and clinical trials are exploring vaccine platforms (e.g., peptide-based, dendritic cell-based) for efficacy and safety[21]. These vaccines show potential in enhancing immune responses against HCC and improving treatment outcomes[22].

Limitations of Therapeutic Cancer Vaccines in HCC

1. Tumor Immune Microenvironment: HCC creates an immunosuppressive environment (e.g., regulatory T cells, cytokines) that hampers vaccine efficacy[23]. Chronic inflammation and infections like hepatitis B/C further complicate immune responses[24].

2. Antigen Selection: Choosing highly specific and effective TAAs is difficult. Some TAAs, like GPC3, risk off-target effects due to expression in normal tissues[25].

3. Immune Evasion: HCC cells evade immune detection by downregulating antigen presentation (e.g., MHC molecules) or utilizing immune checkpoints (e.g., PD-1, CTLA-4), reducing vaccine effectiveness[23].

4. Clinical Outcomes: Despite preclinical promise, many vaccines fail in large-scale trials due to tumor heterogeneity and variability in patient immune responses[26]. Trials like HepaVac-101[27] and GNOS-PV02[28] show potential but require further validation.

5. Manufacturing and Delivery: High costs and complexity in production and delivery pose challenges[17,22,26]. Personalized vaccines require tailored processes, adding to the complexity.

Future Directions in Therapeutic Cancer Vaccines for HCC

1. Combination Therapies: Using cancer vaccines alongside treatments like chemotherapy, radiotherapy, and immune checkpoint inhibitors (e.g., PD-1/PD-L1 blockers) enhances immune responses, tackles immune evasion, and maximizes therapeutic benefits for better patient outcomes[15,29,30].

2. Personalized Medicine: Tailored vaccines based on individual tumor profiles leverage TSAs and neoantigens unique to each patient[31]. Advances in sequencing and bioinformatics enable the creation of highly specific vaccines, showing promise in improving clinical outcomes (e.g., prolonged progression-free survival)[32,33].

3. Innovative Platforms: New vaccine technologies such as mRNA, DNA, and viral vector-based platforms, along with novel adjuvants (e.g., TLR and cGAS-STING pathway stimulators), are being developed to boost immune responses and combat immunosuppression, broadening vaccine applications[34-37].

4. Clinical Trials: Extensive trials validate vaccine safety and efficacy[38]. Phase I, II, and III trials assess immune response, efficacy, and rare side effects. Promising examples, like the HepaVac-101 trial[27], highlight the potential of personalized vaccines for HCC treatment.

Conclusion

In conclusion, while there are significant challenges in developing effective cancer vaccines for HCC, the potential benefits are substantial. By leveraging combination therapies, personalized medicine, and innovative platforms, we can enhance the immune response against HCC and improve patient outcomes. Continued research and extensive clinical trials are crucial to bringing these promising therapies to patients and ultimately improving survival rates for those battling HCC.

Acknowledgments

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Declaration of interests
The authors declare no competing interests.

References

1. Devan AR, Nair B, Pradeep GK, et al. The role of glypican-3 in hepatocellular carcinoma: Insights into diagnosis and therapeutic potential. Eur J Med Res. 2024 Oct 5;29(1):490. doi: 10.1186/s40001-024-02073-2. PMID: 39369212; PMCID: PMC11453014.
2. Zheng X, Liu X, Lei Y, et al. Glypican-3: A Novel and Promising Target for the Treatment of Hepatocellular Carcinoma. Front Oncol. 2022 Feb 16;12:824208. doi: 10.3389/fonc.2022.824208. PMID: 35251989; PMCID: PMC8889910.

3. Lu X, Deng S, Xu J, et al. Combination of AFP vaccine and immune checkpoint inhibitors slows hepatocellular carcinoma progression in preclinical models. J Clin Invest. 2023 Jun 1;133(11):e163291. doi: 10.1172/JCI163291. PMID: 37040183; PMCID: PMC10231990.
4. A Phase I/II Trial Testing Immunization With Dendritic Cells Pulsed With Four AFP Peptides in Patients With Hepatocellular Carcinoma. https://clinicaltrials.gov/study/NCT00022334. 2020.
5. Wermke M, Holderried TAW, Luke JJ, et al. First-in-human dose escalation trial to evaluate the clinical safety and efficacy of an anti-MAGEA1 autologous TCR-transgenic T cell therapy in relapsed and refractory solid tumors. J Immunother Cancer. 2024 Jul 22;12(7):e008668. doi: 10.1136/jitc-2023-008668. PMID: 39038917; PMCID: PMC11268062.
6. McAuliffe J, Chan HF, Noblecourt L, et al. Heterologous prime-boost vaccination targeting MAGE-type antigens promotes tumor T-cell infiltration and improves checkpoint blockade therapy. J Immunother Cancer. 2021 Sep;9(9):e003218. doi: 10.1136/jitc-2021-003218. PMID: 34479921; PMCID: PMC8420668.
7. Wang XY, Kazim L, Repasky EA, et al. Characterization of heat shock protein 110 and glucose-regulated protein 170 as cancer vaccines and the effect of fever-range hyperthermia on vaccine activity. J Immunol. 2001 Jan 1;166(1):490-7. doi: 10.4049/jimmunol.166.1.490. PMID: 11123328.
8. Wang XY, Arnouk H, Chen X, et al. Extracellular targeting of endoplasmic reticulum chaperone glucose-regulated protein 170 enhances tumor immunity to a poorly immunogenic melanoma. J Immunol. 2006 Aug 1;177(3):1543-51. doi: 10.4049/jimmunol.177.3.1543. PMID: 16849461.
9. Dai W, Zong WX. Glutamine synthetase: a tumor suppressor in hepatocellular carcinoma? J Mol Cell Biol. 2023 Jun 1;15(1):mjad007. doi: 10.1093/jmcb/mjad007. PMID: 36737414; PMCID: PMC10251431.
10. Kim GW, Lee DH, Jeon YH, et al. Glutamine Synthetase as a Therapeutic Target for Cancer Treatment. Int J Mol Sci. 2021 Feb 8;22(4):1701. doi: 10.3390/ijms22041701. PMID: 33567690; PMCID: PMC7915753.
11. Dai W, Shen J, Yan J, et al. Glutamine synthetase limits β-catenin-mutated liver cancer growth by maintaining nitrogen homeostasis and suppressing mTORC1. J Clin Invest. 2022 Dec 15;132(24):e161408. doi: 10.1172/JCI161408. PMID: 36256480; PMCID: PMC9754002.
12. Hill M, Russo S, Olivera D, et al. The intracellular cation channel TMEM176B as a dual immunoregulator. Front Cell Dev Biol. 2022 Oct 20;10:1038429. doi: 10.3389/fcell.2022.1038429. PMID: 36340035; PMCID: PMC9630633.
13. Kim HD, Jung S, Lim HY, et al. Regorafenib plus nivolumab in unresectable hepatocellular carcinoma: the phase 2 RENOBATE trial. Nat Med. 2024 Mar;30(3):699-707. doi: 10.1038/s41591-024-02824-y. Epub 2024 Feb 19. PMID: 38374347; PMCID: PMC10957471.
14. Tojjari A, Saeed A, Singh M, et al. A Comprehensive Review on Cancer Vaccines and Vaccine Strategies in Hepatocellular Carcinoma. Vaccines (Basel). 2023 Aug 12;11(8):1357. doi: 10.3390/vaccines11081357. PMID: 37631925; PMCID: PMC10459477.
15. Zhou Y, Wei Y, Tian X, et al. Cancer vaccines: current status and future directions. J Hematol Oncol. 2025 Feb 17;18(1):18. doi: 10.1186/s13045-025-01670-w. PMID: 39962549; PMCID: PMC11834487.
16. Charneau J, Suzuki T, Shimomura M, et al. Peptide-Based Vaccines for Hepatocellular Carcinoma: A Review of Recent Advances. J Hepatocell Carcinoma. 2021 Sep 2;8:1035-1054. doi: 10.2147/JHC.S291558. PMID: 34513746; PMCID: PMC8424432.
17. Cancer Vaccine development for Hepatocellular Carcinoma. https://cordis.europa.eu/project/id/602893/reporting. 2024.
18. Jeng LB, Liao LY, Shih FY, et al. Dendritic-Cell-Vaccine-Based Immunotherapy for Hepatocellular Carcinoma: Clinical Trials and Recent Preclinical Studies. Cancers (Basel). 2022 Sep 8;14(18):4380. doi: 10.3390/cancers14184380. PMID: 36139542; PMCID: PMC9497058.
19. Yuan Y, Sun W, Xie J, et al. RNA nanotherapeutics for hepatocellular carcinoma treatment. Theranostics. 2025 Jan 1;15(3):965-992. doi: 10.7150/thno.102964. PMID: 39776807; PMCID: PMC11700867.

20. Cancer Treatment Vaccines. https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/cancer-treatment-vaccines. 2019.
21. Dunn GP. Cancer Vaccines: Preventive, Therapeutic, Personalized. https://www.cancerresearch.org/treatment-types/cancer-vaccines.
22. Tojjari A, Saeed A, Singh M, et al. A Comprehensive Review on Cancer Vaccines and Vaccine Strategies in Hepatocellular Carcinoma. Vaccines (Basel). 2023 Aug 12;11(8):1357. doi: 10.3390/vaccines11081357. PMID: 37631925; PMCID: PMC10459477.
23. Wen J, Wen K, Tao M, et al. Integrated analysis reveals an immune evasion prognostic signature for predicting the overall survival in patients with hepatocellular carcinoma. Cancer Cell Int. 2025 Mar 18;25(1):101. doi: 10.1186/s12935-025-03743-9. PMID: 40102844; PMCID: PMC11916977.
24. Shen KY, Zhu Y, Xie SZ, et al. Immunosuppressive tumor microenvironment and immunotherapy of hepatocellular carcinoma: current status and prospectives. J Hematol Oncol. 2024 Apr 29;17(1):25. doi: 10.1186/s13045-024-01549-2. PMID: 38679698; PMCID: PMC11057182.
25. Chen P, Chen D, Bu D, et al. Dominant neoantigen verification in hepatocellular carcinoma by a single-plasmid system coexpressing patient HLA and antigen. J Immunother Cancer. 2023 Apr;11(4):e006334. doi: 10.1136/jitc-2022-006334. PMID: 37076248; PMCID: PMC10124323.
26. Zheng X, Yang L, Shen X, et al. Targeting Gsk3a reverses immune evasion to enhance immunotherapy in hepatocellular carcinoma. J Immunother Cancer. 2024 Aug 21;12(8):e009642. doi: 10.1136/jitc-2024-009642. PMID: 39174053; PMCID: PMC11340705.
27. Löffler MW, Gori S, Izzo F, et al. Phase I/II Multicenter Trial of a Novel Therapeutic Cancer Vaccine, HepaVac-101, for Hepatocellular Carcinoma. Clin Cancer Res. 2022 Jun 13;28(12):2555-2566. doi: 10.1158/1078-0432.CCR-21-4424. PMID: 35421231.
28. Yarchoan M, Gane EJ, Marron TU, et al. Personalized neoantigen vaccine and pembrolizumab in advanced hepatocellular carcinoma: a phase 1/2 trial. Nat Med. 2024 Apr;30(4):1044-1053. doi: 10.1038/s41591-024-02894-y. Epub 2024 Apr 7. PMID: 38584166; PMCID: PMC11031401.
29. Lei W, Zhou K, Lei Y, et al. Cancer vaccines: platforms and current progress. Mol Biomed. 2025 Jan 10;6(1):3. doi: 10.1186/s43556-024-00241-8. PMID: 39789208; PMCID: PMC11717780.
30. Shariati A, Khani P, Nasri F, et al. mRNA cancer vaccines from bench to bedside: a new era in cancer immunotherapy. Biomark Res. 2024 Dec 18;12(1):157. doi: 10.1186/s40364-024-00692-9. PMID: 39696625; PMCID: PMC11656831.
31. Personalized Cancer Vaccine: Targeting Tumors More Precisely. https://biologyinsights.com/personalized-cancer-vaccine-targeting-tumors-more-precisely/. 2025.
32. Kumar A, Dixit S, Srinivasan K, et al. Personalized cancer vaccine design using AI-powered technologies. Front Immunol. 2024 Nov 8;15:1357217. doi: 10.3389/fimmu.2024.1357217. PMID: 39582860; PMCID: PMC11581883.
33. Ahmed S, Mazhar MS, Shabbir MF. Neoantigen-Based Cancer Vaccines: Current Innovations, Challenges and Future Directions in Personalized Immunotherapy. Cancer Immunol Connect. 2024;1(Article ID: 0001). doi: 10.69709/CIConnect.2024.194763.
34. How Vaccines are Developed and Approved for Use. https://www.cdc.gov/vaccines/basics/how-developed-approved.html. 2024.
35. How Vaccines are Made Safe and Effective. https://www.sabin.org/resources/how-vaccines-are-made-safe-and-effective/. 2024.
36. Clinical evaluation of new vaccines - Scientific guideline. https://www.ema.europa.eu/en/clinical-evaluation-new-vaccines-scientific-guideline. 2023.
37. Malesu VK. Advancing vaccine adjuvants: exploring cutting-edge platforms for improved immunization. https://www.news-medical.net/news/20230721/Advancing-vaccine-adjuvants-exploring-cutting-edge-plat-

forms-for-improved-immunization.aspx. 2023.
38. Lensch V, Johnson JA, Kiessling LL. Glycoconjugate vaccines: platforms and adjuvants for directed immunity. Glycobiology. 2024 Sep 30;34(11):cwae092. doi: 10.1093/glycob/cwae092. PMID: 39593193; PMCID: PMC11604072.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat.)

KLCA-TLCA Joint Symposium

Innovating and Expanding Surgical Horizons for Hepatocellular Carcinoma in the Immunotherapy Era

Chairs:

Kyung Sik Kim (Yonsei Univ.)
Yi-Hsiang Huang (National Yang Ming Chiao Tung Univ., Taiwan)

Gi Hong Choi

Yonsei University

Self Introduction

Prof. Gi Hong Choi earned his medical degree from the Yonsei University College of Medicine, Seoul, Korea in 1998. Since Mar. 2019, he is a professor in the Department of Surgery, Yonsei University College of Medicine. Throughout his academic career, he focused on surgical treatment of primary and metastatic liver cancer, hilar cholangiocarcinoma and living donor hepatectomy. Especially, he is interested in minimally invasive liver surgery including laparoscopy and robotic surgery. He has published approximately 190 publications in international peer-reviewed scientific journals.

Research Interests

- Minimally Invasive Liver Resection (Laparoscopic and Robotic Surgery)
- Surgical Treatment for Primary and Metastatic Liver Cancer
- Surgical Treatment of Hilar Cholangiocarcinoma

Representative Publications

1. Choi M, Han DH, Kim KS, Choi JS, Kim BK, Kim SU, Seong J, Kim DY, Choi GH (co-corresponding author). Is liver resection still required for patients who have predictive factors for complete pathologic necrosis after downstaging treatments of locally advanced hepatocellular carcinoma? Eur J Surg Oncol. 2024. (Online ahead of print)
2. Kim NR, Han DH, Joo DJ, Lee JG, Kim DG, Kim MS, Choi JS, Choi GH (corresponding author). Propensity Score-matched Donor and Recipient Outcomes: Robotic Versus Laparoscopic Donor Right Hepatectomy. Transplantation 2024 (Online ahead of print)
3. Kim NR, Bae H, Hwang HS, Han DH, Kim KS, Choi JS, Park MS, Choi GH (co-corresponding author). Preoperative Prediction of Microvascular Invasion with Gadoxetic Acid-Enhanced Magnetic Resonance Imaging in Patients with Single Hepatocellular Carcinoma: The Implication of Surgical Decision on the Extent of Liver Resection. Liver Cancer. 2023;13:181-192.
4. Hwang HS, Yoo JE, Han DH, Choi JS, Lee JG, Joo DJ, Kim MS, Kim SI, Choi GH (co-corresponding author), Park YN. Circulating Cancer Stem Cells Expressing EpCAM/CD90 in Hepatocellular Carcinoma: A Pilot Study for Predicting Tumor Recurrence after Living Donor Liver Transplantation. Gut Liver 2022 May 15;16(3):443-455.
5. Rho SY, Lee JG, Joo DJ, Kim MS, Kim SI, Han DH, Choi JS, Choi GH (corresponding author). Outcomes of Robotic Living Donor Right Hepatectomy From 52 Consecutive Cases: Comparison With Open and Laparoscopy-assisted Donor Hepatectomy. Ann Surg 2022 Feb 1;275(2):e433-e442
6. Navarro JG, Kang I, Rho SY, Choi GH (corresponding author), Han DH, Kim KS, Choi JS. Major Laparoscopic Versus Open Resection for Hepatocellular Carcinoma: A Propensity Score-Matched Analysis Based on Surgeon's Learning Curve. Ann Surg Oncol 2021 Jan;28(1):447-458.
7. Kang I, Jang M, Lee JG, Han DH, Joo DJ, Kim KS, Kim MS, Choi JS, Kim SI, Park YN, Choi GH (co-corresponding author). Subclassification of Microscopic Vascular Invasion in Hepatocellular Carcinoma. Ann Surg 2021 Dec;274(6):e1170-e1178.

KLCA-TLCA Joint Symposium | DAY 3: May 31 (Sat.) | ROOM 2 [3F]

Surgical Innovations for Advanced Hepatocellular Carcinoma in the Immunotherapy Era

Gi Hong Choi *Yonsei University*

Recent advances in systemic therapies have significantly increased long-term outcomes for advanced hepatocellular carcinoma (HCC). Due to the improved treatment efficacy and response rate of the molecular targeted therapy and immunotherapy can lead to tumor downstaging and consequently provide patients with initially unresectable HCC with opportunities for surgical resection.

Even though the resectability of HCC has been assessed based on the presence of tumor thrombosis, intrahepatic metastatic lesions and extrahepatic spread, there has been no universal consensus on the resectability. As the experience of conversion therapy from effective systemic treatments has accumulated, the status of technically resectable of HCC can be further classified from the oncologic standpoint. Recently, the Japanese group introduced three classifications for oncologic resectability in HCC based on consensus statement from the expert panel. The first one is oncologic resectable status (Single or multinodular: 2-3 nodules, each≤3cm, Vp0-1, Vv0-1, B0-1) in which surgery also may offer better survival outcomes than other treatments. The second one is borderline resectable 1 status (Multinodular: 3-5 nodules, each≤5cm or Vp2-3, Vv2, B2-3 or localized extrahepatic spread) in which surgery as a part of multidisciplinary treatment may offer survival benefit. The third one is borderline resectable 2 status (Mutlinodular:>5 nodules, any each>5cm or Vp4, Vv3, B4 or extrahepatic spread) in which the efficacy of surgery is uncertain and the indication for surgery should be determined carefully under the standard multidisciplinary treatment. Even though this classification has some area of discussion, it is expected to guide clinical management in patients with advanced HCC. In HCC patients with borderline resectable 2, systemic treatments should be designed to induce the maximal tumor response and combined approach by locoregional treatments would be better than systemic treatment alone.

Conversion surgery after systemic treatment for advanced HCC is in its infancy. In this lecture, I'd like to review studies about conversion surgery and suggest future perspectives.

Ming-Chin Yu

Chang Gung Medical Foundation, Taiwan

Self Introduction

Prof. Yu graduated from Taipei medical university and got his PhD degree at the institute of clinical medical sciences of Chang Gung university. He has worked at Linkou Chang Gung Memorial Hospital and New Taipei Municipal Tucheng Hospital for 30 years and he focused on surgical oncology treatments and basic research.

He has HPB surgery experience of more than 1,200 patients and was also annotated as a tutor for HPB robotic surgery at Taiwan Surgical Society of Gastroenterology and TAES.

Clinical research includes analysis of clinical factors of liver cancer, such as liver tumor rupture and bleeding, lymph node metastasis (1.23%), alkaline phosphatase (J Gastrointest Surg. 2011 Aug and J Pers Med. 2022 Mar 23;12(4) :518. J Surg Oncol. 2016). The chemotaxis of Sox4 in liver cancer (Chemotaxis), the Vault RNA 2-1 (VTRNA2-1, also known as nc886), chromosomal variation (Sorafenib) is related to the target drug of liver cancer (Biomedicines. 2022 Sep 14; 10(9): 2277), VETC and vascular invasion (Cancers 2022 Nov 3;14(21):5428.)

Research Interests

HPB Surgery, Tumor Oncology

Representative Publications

1. Recurrence and Poor Prognosis Following Resection of Small Hepatitis B-Related Hepatocellular Carcinoma Lesions Are Associated with Aberrant Tumor Expression Profiles of Glypican 3 and Osteopontin. Ann Surg Oncol. 2012 Jul;19 Suppl 3: S455-463.
2. Alkaline Phosphatase: Does it have a Role in Predicting Hepatocellular Carcinoma Recurrence? J Gastrointest Surg. 2011 Aug;15(8):1440-9.
3. Prediction of early-stage hepatocellular carcinoma using OncoScan chromosomal copy number aberration data. World Journal of Gastroenterology. 2018;23(44):7818-7829.
4. SOX4 activates CXCL12 in hepatocellular carcinoma cells to modulate endothelial cell migration andangiogenesis in vivo. Oncogene. 2020 Jun;39(24):4695-4710.
5. Hypermethylation of the VTRNA2-1 promoter in hepatocellular carcinoma as a prognostic factor: Tumor Marker Prognostic Study. Int J Surg. 2020 Jul;79:282-289.

KLCA-TLCA Joint Symposium | DAY 3: May 31 (Sat.) | ROOM 2 [3F]

Advancing Liver Surgery in the Immunotherapy Era: The Taiwanese Experience

Ming-Chin Yu *Chang Gung Medical Foundation, Taiwan*

HCC is the fourth leading cause of cancer-related mortality worldwide and an advanced stage or aggressive tumor pathology is associated with poor prognosis. For unresectable HCC, the combination of atezolizumab plus bevacizumab as the first systemic therapy proved superior overall survival (OS) to sorafenib in the IMBrave150 Trial, and the combination of durvalumab and tremelimumab showed better outcome in the HIMALAYA Trial, with a median survival of 16 months and 25% of the patients living beyond 4 years. The current interesting issue is the combinations of systemic therapy with embolic or radiation-based therapies in intermediate-stage HCC, and (neo)adjuvant therapy with surgical therapies in early-stage disease. In real world practice, both the Lenvatinib and pembrolizumab and the AtezoBev groups had comparable OS and PFS outcome in our institute. The real-world experience revealed that good liver functional reserve and continuing 2L therapy made better outcome after the failure of first-line Atezo-Bev treatment.

The Taiwan Liver Cancer Association (TLCA) and the Gastroenterological Society of Taiwan developed and updated the guidelines for HCC management in 2020. In clinical practice, we follow these guidelines and the reimbursement policy of the government. Currently, the IMbrave050 trial is the first phase 3 study of adjuvant treatment for HCC with positive results in short-term outcome. Therefore, conversion surgery has been proposed as a strategy for patients with response to targeted therapy/ immunotherapy. However, longer follow-up for both recurrence-free and overall survival is still not satisfactory.

It was still no clear definition of the standard protocol of conversion surgery for unresectable HCC or advanced HCC. There were 10% HCC patients who had the chance to have surgical resection and all had underwent major hepatectomies. The surgical outcome is good, and the short-term result inspire us that immunotherapy should be considered as a consequent treatment protocol.

References

1. Chen CT, Feng YH, Yen CJ, Chen SC, Lin YT, Lu LC, et al. Prognosis and treatment pattern of advanced hepatocellular carcinoma after failure of first-line atezolizumab and bevacizumab treatment. Hepatol Int. 2022;16(5):1199-207.
2. Hsu YC, Lin PT, Teng W, Hsieh YC, Chen WT, Su CW, et al. Comparing Lenvatinib/Pembrolizumab with Atezoli-

zumab/Bevacizumab in Unresectable Hepatocellular Carcinoma: A Real-World Experience with Propensity Score Matching Analysis. Cancers (Basel). 2024;16(20).
3. Lee CK, Yoo C, Hong JY, Park SJ, Kim JW, Tai DWM, et al. Real-World Study of Systemic Treatment after First-Line Atezolizumab plus Bevacizumab for Hepatocellular Carcinoma in Asia-Pacific Countries. Liver Cancer. 2025;14(2):127-41.
4. Lee SW, Lee TY, Yang SS, Huang YJ, Peng YC. The Impact of Sequential Therapies after First-Line Systemic Therapies in Unresectable Hepatocellular Carcinoma. J Clin Med. 2024;13(9).
5. Lee SW, Yang SS, Lien HC, Peng YC, Ko CW, Lee TY. Efficacy of Lenvatinib and Sorafenib in the Real-World First-Line Treatment of Advanced-Stage Hepatocellular Carcinoma in a Taiwanese Population. J Clin Med. 2022;11(5).
6. Qin S, Chen M, Cheng AL, Kaseb AO, Kudo M, Lee HC, et al. Atezolizumab plus bevacizumab versus active surveillance in patients with resected or ablated high-risk hepatocellular carcinoma (IMbrave050): a randomised, open-label, multicentre, phase 3 trial. Lancet. 2023;402(10415):1835-47.
7. Shao YY, Feng YH, Yen CJ, Yang TS, Shen YC, Chao Y, et al. Bevacizumab and atezolizumab as first-line therapy for advanced hepatocellular carcinoma: A Taiwanese subgroup analysis on efficacy and safety. J Formos Med Assoc. 2022;121(12):2430-7.
8. Shen YC, Liu TH, Nicholas A, Soyama A, Yuan CT, Chen TC, et al. Clinical Outcomes and Histologic Findings of Patients With Hepatocellular Carcinoma With Durable Partial Response or Durable Stable Disease After Receiving Atezolizumab Plus Bevacizumab. J Clin Oncol. 2024;42(34):4060-70.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Yun Bin Lee

Seoul National University

Self Introduction

Prof. Yun Bin Lee is a Professor at the Department of Internal Medicine, Seoul National University Hospital. She graduated from Seoul National University College of Medicine in 2006 and completed her internship, residency, and fellowship at the Department of Internal Medicine at Seoul National University Hospital, receiving her diploma in Internal Medicine in 2018.

Since 2014, she has been taking on a number of roles in the Korean Association for the Study of the Liver and the Korean Liver Cancer Association. She is also serving as the Director of Academic Affairs of the Korean Radioembolization Association.

Research Interests

Prof. Yun Bin Lee is conducting translational and clinical research, including big data-based studies. In the clinical research domain, her team focuses on identifying risk factors for hepatocellular carcinoma development in patients with chronic liver diseases. In translational research, her current interest lies in regenerative medicine using stem cells. Her laboratory investigates the mechanisms of mitochondrial dysfunction and the therapeutic potential of various mesenchymal stem cells in metabolic dysfunction-associated steatotic liver disease (MASLD).

In addition, she is actively involved in investigator-initiated clinical trials—such as the SOLID trial and the DETECT trial—evaluating novel combinations of immunotherapy and locoregional treatments for unresectable hepatocellular carcinoma.

Representative Publications

1. A phase 1/2a trial of yttrium-90 radioembolization in combination with durvalumab for locally advanced unresectable hepatocellular carcinoma. Clin Cancer Res. 2023;29(18):3650-3658. (first author)
2. Association between daily aspirin therapy and risk of hepatocellular carcinoma according to metabolic risk factor burden in non-cirrhotic patients with chronic hepatitis B. Aliment Pharmacol Ther. 2023;58(7):704-714. (first & corresponding author)
3. Aspirin Use and Risk of Hepatocellular Carcinoma in Patients With Chronic Hepatitis B With or Without Cirrhosis. Hepatology. 2022;76:492-501. (first & corresponding author)
4. Association of Metabolic Risk Factors With Risks of Cancer and All-Cause Mortality in Patients With Chronic Hepatitis B. Hepatology. 2021;73:2266-2277. (first & corresponding author)
5. Association of Chronic Hepatitis B Infection and Antiviral Treatment with the Development of the Extrahepatic Malignancies: A Nationwide Cohort Study. J Clin Oncol. 2022;40:3394-3405 (contributing author)

Combining Immunotherapy with Local Treatments: New Directions for Hepatocellular Carcinoma Management in Korea

Yun Bin Lee *Seoul National University*

Introduction

Hepatocellular carcinoma (HCC) is a major public health burden in Korea, with most patients diagnosed at intermediate or advanced stages. The introduction of immune checkpoint inhibitors (ICIs), particularly the combination of atezolizumab and bevacizumab, has revolutionized systemic therapy for unresectable HCC.[1] However, locoregional therapies such as transarterial chemoembolization (TACE), transarterial radioembolization (TARE), and ablation continue to be widely used and have retained a pivotal role in the Korean clinical setting.[2] There is growing interest in combining these modalities to harness potential synergistic effects and improve outcomes.

Scientific Rationale

Locoregional therapies may enhance antitumor immunity by inducing immunogenic cell death, releasing tumor-associated antigens, and promoting local inflammation.[3] These changes in the tumor microenvironment can prime the immune system, potentially amplifying the effects of ICIs.[4,5] In addition, anti-angiogenic agents like bevacizumab may reduce immunosuppressive signaling and normalize tumor vasculature, further facilitating T-cell infiltration.[6] Preclinical and translational studies support this immunologic synergy and provide a compelling rationale for combination strategies.[7,8]

Clinical Strategies and Korean Experience

In Korea, real-world data and institutional experience have driven the integration of ICIs with locoregional therapy. A multicenter retrospective study comparing atezolizumab–bevacizumab and TACE plus radiotherapy in HCC patients with portal vein tumor thrombosis demonstrated that the immunotherapy combination was associated with significantly better overall survival (median OS, 14.9 vs. 12.2 months; P=0.021) and higher objective response rates (ORR; 43.5% vs. 26.5%) compared to the locoregional therapy group.[8] These results suggest that combining ICIs with or even in place of traditional locoregional therapies may offer superior outcomes in select advanced HCC populations in Korea.

TARE has also been actively investigated as a partner to immunotherapy. Notably, our research team at Seoul National University Hospital conducted the SOLID trial, a phase I/IIa prospective study evaluating

the combination of Y90-radioembolization and durvalumab in patients with locally advanced unresectable HCC without extrahepatic spread.[9] Among the 24 enrolled patients, the median time to progression was 15.2 months, and the ORR was 83.3% per modified RECIST. Importantly, no treatment-related serious adverse events were reported, underscoring the safety and feasibility of this approach. The SOLID trial was the first to evaluate this combination and supports further exploration of radioembolization as an immunologic primer in HCC.

Additional prospective trials are ongoing in Korea. A phase II study (NCT05301842) is assessing concurrent TARE with durvalumab and tremelimumab. In addition, our institution has recently initiated the DETECT trial (Durvalumab and Tremelimumab with Concurrent TACE for Unresectable HCC), a phase I/IIa, single-arm investigator-initiated study assessing the safety and efficacy of concurrent TACE with tremelimumab and durvalumab in patients with unresectable HCC. This trial aims to evaluate PFS as the primary endpoint and includes 24 patients with intermediate or advanced HCC, including those with limited extrahepatic disease. The study is expected to generate pivotal data to support immune-locoregional synergy in real-world Korean patients. These efforts reflect a growing consensus in Korea that integrating ICIs with locoregional therapy is both practical and potentially impactful in improving patient outcomes.

Challenges and Future Directions

Despite encouraging data, several challenges remain. Optimal sequencing and timing of combination therapies are yet to be established. Response assessment is complicated by post-treatment inflammation, necessitating careful interpretation with mRECIST or immune-specific criteria. Furthermore, validated biomarkers to guide treatment selection are lacking. Incorporating precision medicine approaches—such as radiomics, genetic profiling, and immune markers—may refine patient selection and enhance outcomes. The role of multidisciplinary care is increasingly important, especially in balancing oncologic efficacy with hepatic functional reserve. The high cost of combination therapy and the need for careful patient selection further underscore the importance of real-world evidence and health policy support.

Conclusions

Combining immunotherapy with locoregional therapies represents a promising paradigm shift in HCC treatment in Korea. Building on strong clinical rationale, emerging real-world evidence, and institutional research such as the SOLID trial, these strategies offer new hope for patients with intermediate and advanced-stage HCC. Further prospective, biomarker-driven studies are essential to optimize this approach and establish it as a new standard in clinical practice.

References

1. Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-905.
2. Korean Liver Cancer A, National Cancer Center K. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. Clin Mol Hepatol 2022;28:583-705.
3. Duffy AG, Greten TF. Immunological off-target effects of standard treatments in gastrointestinal cancers. Ann Oncol 2014;25:24-32.
4. Chew V, Lee YH, Pan L, et al. Immune activation underlies a sustained clinical response to Yttrium-90 radioembolisation in hepatocellular carcinoma. Gut 2019;68:335-46.
5. Berz AM, Santana JG, Iseke S, et al. Impact of Chemoembolic Regimen on Immune Cell Recruitment and Immune Checkpoint Marker Expression following Transcatheter Arterial Chemoembolization in a VX2 Rabbit Liver Tumor Model. J Vasc Interv Radiol 2022;33:764-74 e4.
6. Boucher Y, Kumar AS, Posada JM, et al. Bevacizumab improves tumor infiltration of mature dendritic cells and effector T-cells in triple-negative breast cancer patients. NPJ Precis Oncol 2021;5:62.
7. Greten TF, Mauda-Havakuk M, Heinrich B, Korangy F, Wood BJ. Combined locoregional-immunotherapy for liver cancer. J Hepatol 2019;70:999-1007.
8. Rimassa L, Finn RS, Sangro B. Combination immunotherapy for hepatocellular carcinoma. Journal of hepatology 2023;79:506-15.
9. Lee YB, Nam JY, Cho EJ, et al. A Phase I/IIa Trial of Yttrium-90 Radioembolization in Combination with Durvalumab for Locally Advanced Unresectable Hepatocellular Carcinoma. Clin Cancer Res 2023;29:3650-8.

Chien-Hung Chen

National Taiwan University, Taiwan

Self Introduction

Dr. Chien-Hung Chen graduated from National Taiwan University. He completed his residency and fellowship training in gastroenterology at National Taiwan University Hospital (NTUH). He later earned a Ph.D. from the same university. Following his fellowship, he joined the medical staff at NTUH, serving at the main campus, Yunlin Branch, and the Cancer Center. He currently holds the position of Vice Superintendent at the National Taiwan University Cancer Center.

Research Interests

Clinical Studies in HCC and Hepatic Immunology

Representative Publications

1. Hsu YC, Wu MC, Weng MT, Lee YT, Chou HC, Lee HS, Wang LF, Sheu JC, Chen CH*. Ethanol inhibits the growth and metastasis of hepatocellular carcinoma by inducing immunogenic cell death. J Immunother Cancer 2025 Feb;13(2):e010472.
2. Lee RC, Liang PC, Liang HL, Chen YF, Yu CY, Cheng PN, Hung CF, Hsia CY, Lai HC, Ho MC, Cheng YF, Liu YS, Chao Y*, Chen CH*. Multicenter evaluation of the safety and efficacy of selective internal radiation therapy with yttrium-90 resin microspheres in Taiwan: data from the RESIN registry. J Gastroenterol Hepatol 2024 Jul;39(7):1318-1327.
3. Liu YS, Chang PY, Liang PC, Ou MC, Hwang JI, Chen CH*. Safety and Efficacy of Drug-Eluting Beads Trans-Arterial Chemoembolization for Hepatocellular Carcinoma in Taiwan (SERENADE-T). J Hepatocell Carcinoma. 2022 Aug 15;9:811-821.
4. Liao SH, Chen CL, Hsu CY, Chien KL, Kao JH, Chen PJ, Chen TH, Chen CH*. Long-term effectiveness of population-wide multifaceted interventions for hepatocellular carcinoma in Taiwan. J Hepatol 2021 Jul;75(1):132-141.
5. Liao SH, Su TH, Jeng YM, Liang PC, Chen DS, Chen CH*, Kao JH*. Clinical Manifestations and Outcomes of Patients with Sarcomatoid Hepatocellular Carcinoma. Hepatology 2019 Jan;69(1):209-221.

Immune Checkpoint Inhibitors and Biomarker Discovery: Tailoring Treatment for Hepatocellular Carcinoma

Chien-Hung Chen *National Taiwan University, Taiwan*

Immune checkpoint inhibitors (ICIs), either in combination with TKI or as dual ICIs, have been the treatment of choice for unresectable HCC. Despite these advances, the overall tumor response rate to ICIs remains modest. Moreover, ICIs are associated with substantial immune-related adverse events, which can range from mild to life-threatening. Thus, there are urgently needs to identify reliable biomarkers that can predict patients most likely to respond to therapy and minimize unnecessary toxicity.

Several biomarkers have been proposed for ICIs in HCC, including PD-L1 expression, tumor mutational burden (TMB), microsatellite instability (MSI) and mismatch repair deficiency (dMMR), gene expression signatures, inflammatory cytokines, tumor-infiltrating lymphocytes (TILs), Wnt/ β-catenin signaling pathway mutations, neutrophil-to-lymphocyte ratio (NLR) and gut microbiome. Additionally, composite biomarkers that integrate these molecular and immunologic features with radiomic signatures or histopathological characteristics have been explored in an effort to improve predictive power.

While these biomarkers have shown promise in other tumor types, there are no validated biomarkers for ICIs in HCC. Several factors may account for this limitation. One of the primary challenges is that HCC arises in diverse etiologic backgrounds—such as hepatitis B or C infection, alcohol-related liver disease, or nonalcoholic steatohepatitis. The tumor heterogeneity adds an additional layer of complexity.

To develop a clinically useful biomarkers, prospective studies that enroll more homogeneous patient populations, for example defined by etiology, may help clarify biomarker–response relationships. Spatial omics and machine learning might help us identifying clinically useful biomarkers for tailoring Treatment for HCC.

References

1. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol 2025;82(2):315-374.
2. Kudo M. Treatment Decision-Making in Unresectable Hepatocellular Carcinoma: Importance of Understanding the Different Response Patterns between IO plus Anti-VEGF and IO plus IO Regimens. Liver Cancer 2025;14(2):119-12.
3. Childs A, Aidoo-Micah G, Maini MK, Meyer T. Immunotherapy for hepatocellular carcinoma. JHEP Rep 2024;6(10):10113.

4. Chew V, Chuang CH, Hsu C. Translational research on drug development and biomarker discovery for hepatocellular carcinoma. J Biomed Sci. 2024;31(1):22.
5. Prelaj A, Miskovic V, Zanitti M, Trovo F, Genova C, Viscardi G, Rebuzzi SE, Mazzeo L, Provenzano L, Kosta S, Favali M, Spagnoletti A, Castelo-Branco L, Dolezal J, Pearson AT, Lo Russo G, Proto C, Ganzinelli M, Giani C, Ambrosini E, Turajlic S, Au L, Koopman M, Delaloge S, Kather JN, de Braud F, Garassino MC, Pentheroudakis G, Spencer C, Pedrocchi ALG. Artificial intelligence for predictive biomarker discovery in immuno-oncology: a systematic review. Ann Oncol. 2024;35(1):29-65.
6. Greten TF, Villanueva A, Korangy F, Ruf B, Yarchoan M, Ma L, Ruppin E, Wang XW. Biomarkers for immunotherapy of hepatocellular carcinoma. Nat Rev Clin Oncol. 2023 Nov;20(11):780-79.
7. Lehrich BM, Zhang J, Monga SP, Dhanasekaran R. Battle of the biopsies: Role of tissue and liquid biopsy in hepatocellular carcinoma. J Hepatol 2024;80(3):515-530.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

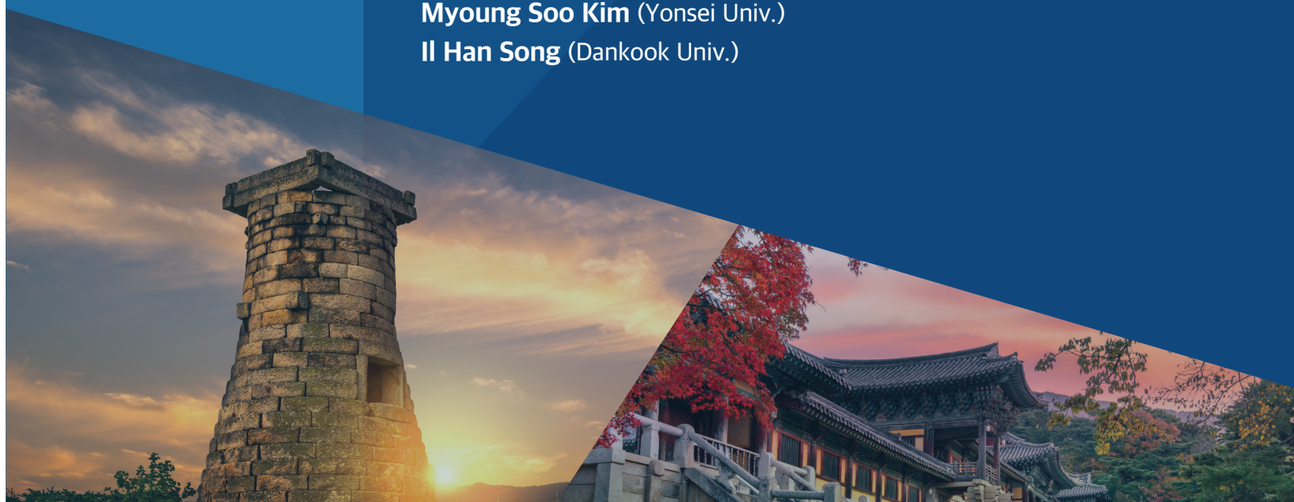
DAY 3: May 31 (Sat.)

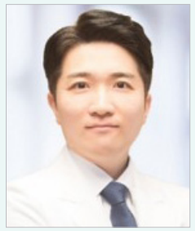
KLTS Symposium 1

Living Donor Liver Transplantation-Based Protocol for Hepatocellular Carcinoma: Intention-to-Treat Approach with Pre-Transplant Therapy

Chairs:

Myoung Soo Kim (Yonsei Univ.)
Il Han Song (Dankook Univ.)





Moon Haeng Hur

Seoul National University

Self Introduction

Education

2018.02 M.D., College of Medicine, Seoul National University
2024.02 Ph,D., College of Medicine, Seoul National University

Work Experiences

2019.03-2022.02 Residency, Department of Internal Medicine, Seoul National University Hospital
2022.03-2023.07 Fellowship, Department of Gastroenterology, Seoul National University Hospital
2023.08-Present Assistant Professor, Department of Gastroenterology, Seoul National University Hospital

Research Interests

Artificial Intelligence Modeling, Chronic Hepatitis B, Hepatocellular Carcinoma

Representative Publications

1. Hur MH, Yip TC, Kim SU, Lee HW, Lee HA, Lee HC, Wong GL, Wong VW, Park JY, Ahn SH, Kim BK, Kim HY, Seo YS, Shin H, Park J, Ko Y, Park Y, Lee YB, Yu SJ, Lee SH, Kim YJ, Yoon JH, Lee JH. A machine learning model to predict liver-related outcomes after the functional cure of chronic hepatitis B. J Hepatol. 2025 Feb;82(2):235-244.
2. Shin H, Hur MH, Song BG, Park SY, Kim GA, Choi G, Nam JY, Kim MA, Park Y, Ko Y, Park J, Lee HA, Chung SW, Choi NR, Park MK, Lee YB, Sinn DH, Kim SU, Kim HY, Kim JM, Park SJ, Lee HC, Lee DH, Chung JW, Kim YJ, Yoon JH, Lee JH. AI model using CT-based imaging biomarkers to predict hepatocellular carcinoma in patients with chronic hepatitis B. J Hepatol. 2024 Dec 20:S0168-8278(24)02784-3. Epub ahead of print (Co-first author).
3. Hur MH, Park MK, Yip TC, Chen CH, Lee HC, Choi WM, Kim SU, Lim YS, Park SY, Wong GL, Sinn DH, Jin YJ, Kim SE, Peng CY, Shin HP, Chen CY, Kim HY, Lee HA, Seo YS, Jun DW, Yoon EL, Sohn JH, Ahn SB, Shim JJ, Jeong SW, Cho YK, Kim HS, Jang MJ, Kim YJ, Yoon JH, Lee JH. Personalized Antiviral Drug Selection in Patients With Chronic Hepatitis B Using a Machine Learning Model: A Multinational Study. Am J Gastroenterol. 2023 Nov 1;118(11):1963-1972.
4. Hur MH, Lee DH, Lee JH, Kim MS, Park J, Shin H, Chung SW, Cho HJ, Park MK, Jang H, Lee YB, Yu SJ, Lee SH, Jung YJ, Kim YJ, Yoon JH. Extrahepatic malignancies and antiviral drugs for chronic hepatitis B: A nationwide cohort study. Clin Mol Hepatol. 2024 Jul;30(3):500-514.
5. Hur MH, Cho Y, Kim DY, Lee JS, Kim GM, Kim HC, Sinn DH, Hyun D, Lee HA, Seo YS, Lee IJ, Park JW, Kim YJ. Transarterial radioembolization versus tyrosine kinase inhibitor in hepatocellular carcinoma with portal vein thrombosis. Clin Mol Hepatol. 2023 Jul;29(3):763-778.

Definition and Current Status of Bridging, Neoadjuvant, Downstaging, and Conversion Therapies

Moon Haeng Hur *Seoul National University*

Liver transplantation (LT) remains the optimal curative treatment for early-stage hepatocellular carcinoma (HCC) and underlying cirrhosis.[1] Surgical resection is also a primary curative option for patients with preserved liver function.[2] However, many patients are not eligible for these treatments at diagnosis due to tumor size, location, or other factors. In these situations, preoperative therapies play a crucial role in improving the chances of curative treatment. These strategies include bridging, neoadjuvant, downstaging, and conversion therapy.

1. Bridging Therapy

Bridging therapy is defined as treatment applied to HCC patients who are within accepted transplant criteria while they are on the waiting list for LT.[3] The primary goal is to prevent tumor progression and reduce the risk of patients being removed from the transplant list due to disease advancement. It acts as a “bridge” until a suitable donor organ becomes available. Bridging therapy is typically considered for patients meeting the Milan criteria with an expected waiting time of six months or longer. Common bridging therapies include transarterial chemoembolization (TACE), radiofrequency ablation (RFA), microwave ablation (MWA), percutaneous ethanol injection (PEI), selective internal radiation therapy (SIRT), and stereotactic body radiotherapy (SBRT). Studies suggest that bridging therapy can reduce the dropout rate for patients meeting Milan criteria to 0-10%.[3]

2. Neoadjuvant Therapy

Neoadjuvant therapy encompasses any treatment given before surgery (resection or transplantation) for HCC.[4] It aims to improve surgical outcomes by reducing tumor size, downstaging the disease, treating potential micrometastases, and increasing the likelihood of R0 resection. Neoadjuvant therapy can include locoregional treatments as well as systemic therapies such as targeted agents (e.g., sorafenib, lenvatinib) and immunotherapies (e.g., atezolizumab plus bevacizumab, nivolumab, pembrolizumab). The choice of neoadjuvant therapy depends on the patient’s liver function, tumor characteristics, and treatment goals.

3. Downstaging Therapy

Downstaging therapy is a specific type of neoadjuvant therapy aimed at reducing the tumor burden in patients who initially exceed liver transplant criteria (e.g., Milan criteria) so that they can meet the criteria and become eligible for LT. This is typically achieved through locoregional therapies such as TACE and TARE. The United Network for Organ Sharing (UNOS) downstaging protocol is a widely used guideline that includes criteria for patient selection and defines successful downstaging. Studies have shown that long-term survival rates for patients undergoing LT after successful downstaging can be comparable to those who initially met Milan criteria.[5]

4. Conversion Therapy

Conversion therapy is a treatment strategy for patients with initially unresectable HCC, aiming to convert the tumor to a resectable state, thereby offering the potential for curative surgery.[6] Unresectability can be due to factors such as tumor size, location, vascular invasion, insufficient future liver remnant, or the patient's overall condition. Conversion therapy often involves a combination of locoregional therapies and systemic therapies. The goal is to achieve a significant tumor response, allowing for subsequent surgical resection. Studies have reported promising long-term survival rates in patients who undergo successful conversion therapy followed by surgery.

Conclusion

Bridging, neoadjuvant, downstaging, and conversion therapies represent crucial strategies in the management of HCC. Bridging therapy maintains transplant eligibility, downstaging aims to achieve it, and conversion therapy strives to make initially unresectable tumors resectable. Neoadjuvant therapy encompasses a broader range of treatments used before surgery to improve outcomes. The increasing use of systemic therapies, particularly targeted agents and immunotherapies, in the neoadjuvant and conversion settings highlights the evolving landscape of HCC treatment, offering hope for improved survival in patients who might not have been candidates for curative treatments in the past.

Reference

1. De Martin E, Berg T, Samuel D, et al. EASL Clinical Practice Guidelines on liver transplantation. J Hepatol. 2024;81(6):1040-1086.
2. Sangro B, Argemi J, Ronot M, et al. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol. 2024.
3. She WH, Cheung TT. Bridging and downstaging therapy in patients suffering from hepatocellular carcinoma waiting on the list of liver transplantation. Translational gastroenterology and hepatology. 2016;1:34.
4. Vogel A, Grant RC, Meyer T, Sapisochin G, O'Kane GM, Saborowski A. Adjuvant and neoadjuvant therapies for hepatocellular carcinoma. Hepatology. 2023:10.1097.
5. Tan DJH, Lim WH, Yong JN, et al. UNOS down-staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-analysis of 25 studies. Clin Gastroenterol Hepatol. 2023;21(6):1475-1484.
6. Matsuki R, Kogure M, Hasui N, Momose H, Suzuki Y, Sakamoto Y. Development of conversion therapy for advanced hepatocellular carcinoma. Hepatobiliary Surgery and Nutrition. 2023;12(3):453.

Dongho Hyun

Sungkyunkwan University

Self Introduction

Prof. Dongho Hyun is a Professor of the Department of Radiology, Sungkyunkwan University College of Medicine.

He graduated from Soonchunhyang University College of Medicine with his medical degree in 2003 and completed his internship and residency at the Department of Radiology at Asan Medical Center in 2011.

Since 2021, he has been taking a number of roles, including treasury secretary of KSIR (2021-2022), secretary of scientific committee of KSIR (2023-2024).

Research Interests

Transarterial Treatment of HCC, Portal Hypertension Intervention, Lymphatic Intervention

Representative Publications

1. Cha DI, Lee MW, Hyun D, Ahn SH, Jeong WK, Rhim H. Combined Transarterial Chemoembolization and Radiofrequency Ablation for Hepatocellular Carcinoma Infeasible for Ultrasound-Guided Percutaneous Radiofrequency Ablation: A Comparative Study with General Ultrasound-Guided Radiofrequency Ablation Outcomes. Cancers (Basel). 2023 Oct 28;15(21):5193. doi: 10.3390/cancers15215193. PMID: 37958370; PMCID: PMC10650828.
2. Kim H, Hyun D, Shin SW, Jeong G, Kim J, Cho JH, Lee HY, Jang Y. Factors Contributing to Successful Transvenous Retrograde Thoracic Duct Cannulation. J Vasc Interv Radiol. 2023 Feb;34(2):205-211. doi: 10.1016/j.jvir.2022.10.037. Epub 2022 Oct 29. PMID: 37190971.
3. Lee HN, Hyun D, Lee WH, Kim JG, Kim HJ. Modified Surgical Drain-Guided Percutaneous Catheter Drainage of Postoperative Fluid Collection in Inaccessible Locations. J Vasc Interv Radiol. 2022 Dec;33(12):1500-1506. doi:10.1016/j.jvir.2022.07.031. Epub 2022 Sep 7. PMID: 36084841.
4. Hyun D, Lee HY, Cho JH, Kim HK, Choi YS, Kim J, Zo JI, Shim YM. Pragmatic role of noncontrast magnetic resonance lymphangiography in postoperative chylothorax or cervical chylous leakage as a diagnostic and preprocedural planning tool. Eur Radiol. 2022 Apr;32(4):2149-2157. doi: 10.1007/s00330-021-08342-6. Epub 2021 Oct 26. PMID: 34698929.
5. Lee HN, Hyun D, Lee WH, Kim SS, Bae SH, Hwang JA, Ko SE. Ultrasound-Guided Deployment of a Plug-Based Vascular Closure Device in Femoral Arteries with Calcified Plaque or Stenosis. J Vasc Interv Radiol. 2021 Jun;32(6):802-806. doi:10.1016/j.jvir.2021.02.017. PMID: 34051988.

Pros and Cons of Repetitive Transarterial Chemoembolization or Other Locoregional Therapies Prior to Liver Transplantation

Dongho Hyun *Sungkyunkwan University*

As the criteria for liver transplantation (LT) has been expanding in patients with hepatocellular carcinoma (HCC), the role of various locoregional therapies (LRT) have caught physicians' eye. Although ablation and external beam radiation therapy play a role as downstaging (DS) or bridging to LT, transarterial treatment (transarterial chemoembolization [TACE] or 90Y radioembolization) is most frequently performed. Its efficacy has been proved through many retrospective and prospective studies over the last couple of decades. In terms of post-LT overall survival and recurrence-free survival, patients with DS achieve to the outcomes from patients who are initially within the Milan criteria (MC).

DS has several issues: the upper limits of tumor burden, goals of DS, and the optimal time-period between DS and LT. Since the introduction of MC in 1996, many institutions have introduced their own extended criteria to give a curative opportunity to patients in HCC beyond MC. BCLC B or C stage HCCs are often attempted to be downstaged and require repeated or combination treatment. While TACE can be performed repeatedly preserving liver function, several factors need to be considered when TACE is chosen for DS to LT.

My lecture deals with definition of and prognosticators of successful DS, impact of TACE on post-LT hepatic artery and bile duct complications, and immunologic changes in the recipient.

Dong Hyun Sinn

Sungkyunkwan University

Self Introduction

Prof. Dong Hyun Sinn is a professor of the Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine.

He graduated from Dankook University College of Medicine with his medical degree in 2001 and completed his internship and residency at the Department of Medicine at Samsung Medical Center, receiving his diploma in Internal Medicine in 2006.

Since 2014, he is working at the Samsung Medical Center, as an assistant professor (2014-2016), associate professor (2016-2022) and as a professor since 2023.

Research Interests

- Hepatocellular Carcinoma
- Liver Transplantation
- Liver Cirrhosis

Representative Publications

1. Kim JE, Sinn DH, Choi GS, Kim JM, Joh JW, Kang W, et al. Predictors and outcome of emergent Liver transplantation for patients with acute-on-chronic liver failure. Dig Liver Dis. 2021;53(8):1004-10.
2. Kim AY, Sinn DH, Jeong WK, Kim YK, Kang TW, Ha SY, et al. Hepatobiliary MRI as novel selection criteria in liver transplantation for hepatocellular carcinoma. J Hepatol. 2018;68(6):1144-52.

Practical Factors Considered in Immunotherapy Prior to Liver Transplantation

Dong Hyun Sinn *Sungkyunkwan University*

Liver transplantation (LT) is one of the most definitive and the most efficacious treatment option for HCC.[1] However, LT is a highly complex and challenging field of clinical practice.[2] Unlike in the setting of deceased donor LT (DDLT), living donor liver transplantation (LDLT) has another unique characteristic to consider. The timing of LT can be determined by transplantation team.[2] This gives unique opportunity to develop protocol for LDLT to offer LT at the most appropriate time. Immunotherapy has changed clinical practice for advance stage hepatocellular carcinoma (HCC).[2,3] In addition immunotherapy for HCC shown promising results in downstaging advanced HCC to become eligible for LT.[4,5] Now, immunotherapy are considered to enhance outcome of patients who are planned for LT. In this session, practical factors that need to be considered in immunotherapy prior to LT will be discussed.

References

1. Sequeira LM, Ozturk NB, Sierra L, Gurakar M, Toruner MD, Zheng M, et al. Hepatocellular Carcinoma and the Role of Liver Transplantation: An Update and Review. J Clin Transl Hepatol. 2025;13(4):327-38.
2. Kim DS, Yoon YI, Kim BK, Choudhury A, Kulkarni A, Park JY, et al. Asian Pacific Association for the Study of the Liver clinical practice guidelines on liver transplantation. Hepatol Int. 2024;18(2):299-383.
3. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. J Liver Cancer. 2023;23(1):1-120.
4. Hwang SY, Choi H, Jeon W, Kim RG. Multidisciplinary approaches to downstaging hepatocellular carcinoma: present and future. J Liver Cancer. 2024;24(2):171-7.
5. Kulkarni AV, Kumaraswamy P, Menon B, Sekaran A, Rambhatla A, Iyengar S, et al. Downstaging with atezolizumab-bevacizumab: a case series. J Liver Cancer. 2024;24(2):224-33.

Dong-Hwan Jung

University of Ulsan

Self Introduction

Education

Since 2018 Professor, Asan Medical Center, School of Medicine, Ulsan University

Professional Experience

Director of the Scientific Board (Liver), The Korean Association of hepato-Biliary-Pancreatic Surgery
Prev. Secretary General, The Korean Association of hepato-Biliary-Pancreatic Surgery
Director of Public Relations Board, The Korean Liver Transplantation Society.
Prev. Secretary General, The Korean Liver Transplantation Society
Director of The Treasury Board, The Korean Association of Liver Surgery.
Director of The Insurance Board, The Korean Society for Transplantation.

Research Interests

Liver Transplantation, Living Donor Hepatectomy, Post-Transplantation Patient Care, Hepatocellular Carcinoma, Laparoscopic Hepatectomy

Representative Publications

1. Incidence and Outcomes of Diaphragmatic Hernia After Living Donor Hepatectomy: The Significance of Bipolar Irrigated Sealer Use Transplantation. 2025 Mar 10. doi: 10.1097/TP.0000000000005362.
2. Feasibility of Pure Laparoscopic Donor Right Hepatectomy Compared to Open Donor Right Hepatectomy: A Large Single-Center Cohort Study Ann Surg. 2025 Jan 20. doi: 10.1097/SLA.0000000000006633.
3. Outcomes of highly urgent living donor liver transplantation in Korean national data HepatoBiliary Surg Nutr 2024 | https://dx.doi.org/10.21037/hbsn-24-30.
4. Mini-incision Right Hepatectomy for Living Donor Hepatectomy. Transplantation. 2023 Nov 1;107(11):2384-2393. doi: 10.1097/TP.0000000000004594. Epub 2023 Oct 21.PMID: 37314498.
5. Efficacy and safety of adhesion barrier in living-donor liver transplantation with right liver graft to prevent delayed gastric emptying. Liver Transpl. 2023 Apr 1;29(4):388-399. doi: 10.1097/LVT.0000000000000056. Epub 2023 Jan 3. PMID: 36809284.

Lessons for Developing Protocols Based on Real-World Data

Dong-Hwan Jung *University of Ulsan*

Introduction

LT has long been a definitive treatment for HCC, particularly in patients within Milan or UCSF criteria. In DDLT, organ scarcity and waitlist dropout necessitate bridging therapies like TACE or RFA. Conversely, LDLT provides flexibility in timing, potentially reducing the need for such interventions. Yet, questions remain on whether LRT or immunotherapy still holds value in LDLT.

Rationale for Pre-Transplant Therapies

Bridging and Downstaging in DDLT Pre-transplant LRT is used in DDLT to prevent tumor progression beyond transplant criteria during the waitlist period. Downstaging aims to make initially ineligible patients suitable for LT. Both strategies are linked to improved intention-to-treat survival and lower recurrence, particularly with significant tumor necrosis.[1-4,6]

LDLT: A Different Clinical Context LDLT minimizes waiting time, often less than four weeks, eliminating most dropout concerns.[5] Therefore, the relevance of routine LRT in LDLT is diminished. Instead, LRT's utility in LDLT may center around biological assessment or recurrence risk reduction.

Evidence for Locoregional Therapy Prior to LDLT

Clinical Outcomes Retrospective and prospective studies show that in LDLT, routine LRT does not significantly improve recurrence-free survival (RFS) or overall survival (OS), except when profound tumor necrosis is achieved.[5] Patients requiring downstaging from beyond UCSF criteria showed worse outcomes, indicating tumor biology's importance.

Pathological Response Complete pathological tumor necrosis correlates with improved post-transplant outcomes.[4-6] However, the short LDLT timeline limits LRT effectiveness in achieving this goal. Radiological assessments also poorly predict necrosis.

Guideline Perspectives International guidelines support selective LRT use in LDLT for high-risk cases or expected delays. Its routine use is not recommended in regions with short wait times.[3-5]

Immuno-Oncologic Therapy Prior to LT

Checkpoint Inhibitors in HCC ICIs like atezolizumab plus bevacizumab have shown efficacy in unresectable HCC.[7-10] Neoadjuvant immunotherapy aims to reduce tumor burden and evaluate biology.

Risks: Allograft Rejection Immunotherapy before LT poses a significant risk of immune-mediated graft rejection, with a rejection rate around 26%.[11,12] A washout period of at least three months reduces this risk. While survival may not differ significantly, rejection remains a serious concern.

Preliminary Efficacy Data Case reports show successful transplantation after neoadjuvant immunotherapy, some with complete pathological response.[8-10,13] Larger trials are needed to assess safety, efficacy, and timing.

LDLT vs. DDLT in Pre-LT Therapy Context

Waitlist Dropout and Bridging Bridging is essential in DDLT due to 10–30% dropout rates.[1-4,14] LDLT's rapid scheduling removes this need in most cases.

Oncologic Outcomes Recent studies show similar recurrence and survival rates between LDLT and DDLT when using strict criteria.[4-6] The benefits of LRT in LDLT appear limited to select high-risk or downstaged patients.

Immunotherapy Coordination LDLT allows better planning of ICI washout, potentially minimizing rejection. This advantage is not present in DDLT due to unpredictable organ availability.[11]

Tumor Biology and Individualized Decision-Making

Biological Insights Pre-LT therapy may help identify aggressive tumors. Poor LRT response could signal high recurrence risk, whereas complete necrosis may indicate favorable biology. However, LDLT's short timeline limits observation of response.[5]

Multidisciplinary Approach Therapy decisions should be individualized based on AFP levels, tumor characteristics, and patient status. A multidisciplinary team should assess risks and benefits.[4-5]

Conclusion

LDLT's ability to provide timely transplantation challenges the necessity of routine pre-LT LRT or immunotherapy. Current evidence suggests limited benefit of LRT unless profound necrosis is achieved. Immunotherapy shows promise but carries risks of rejection. Pre-LT therapy should be selectively applied, with decisions guided by tumor biology, patient factors, and multidisciplinary input.

References

1. Yao FY, Mehta N, Flemming J, et al. Downstaging of hepatocellular cancer before liver transplant: Long-term outcome compared to tumors within Milan criteria. Hepatology. 2015;61(6):1968-1977.
2. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2016 Annual Data Report: Liver. Am J Transplant. 2018;18 Suppl 1:172-253.
3. Takada Y, Ueda M, Sanefuji K, et al. Living donor liver transplantation for patients with hepatocellular carcinoma: Proposal of expanded criteria. Transplantation. 2008;86(7):1043-1052.
4. Park JH, Kim YK, Park MS, et al. Role of pretransplant locoregional treatment in hepatocellular carcinoma patients undergoing living donor liver transplantation. J Clin Med. 2024;13(22):6633.
5. Lee SG, Hwang S, Moon DB, et al. Expanded indication criteria of living donor liver transplantation for hepatocellular carcinoma at one institution: Validity and outcomes. Liver Transpl. 2010;16(8):930-938.
6. Shindoh J, Makuuchi M, Matsuyama Y, et al. Complete response of hepatocellular carcinoma to preoperative therapy: Predictive factors and long-term outcomes. Ann Surg. 2013;258(2):308-315.
7. Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. N Engl J Med. 2020;382(20):1894-1905.
8. Biondani G, Rossi G, Salvagni S, et al. Neoadjuvant immunotherapy before liver transplantation for HCC: Current landscape and future perspectives. Front Immunol. 2024;15:1355812.
9. Tabrizian P, Florman SS, Schwartz ME. PD-1 inhibition as a bridge to liver transplantation? Am J Transplant. 2021;21(11):3891-3896.
10. Wong CN, Chok KSH. Use of immune checkpoint inhibitors as bridging therapy to liver transplantation for hepatocellular carcinoma: A review. World J Hepatol. 2023;15(3):317-328.
11. Vithayathil M, Arora A, McCaughan G. Immune checkpoint inhibitors in liver transplantation: A systematic review. Transplant Rev. 2024;38(1):100720.
12. Tella SH, Kommalapati A, Rech KL, et al. Immune checkpoint inhibitors in organ transplant patients with cancer: A single-center experience and review of literature. J Immunother Cancer. 2021;9(8):e002990.
13. Han DH, Choi GH, Kim KS, et al. Pilot study of neoadjuvant nivolumab for resectable hepatocellular carcinoma. J Clin Med. 2024;13(11):3068.
14. Berry K, Ioannou GN. Serum alpha-fetoprotein level independently predicts hepatocellular carcinoma recurrence after liver transplantation. Clin Gastroenterol Hepatol. 2013;11(7):947-953.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

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DAY 3: May 31 (Sat.)

KLTS Symposium 2

Technical Hurdles in Living Donor Liver Transplantation

Chairs:

Dong-Sik Kim (Korea Univ.)
Unenbat Gurbadam (National Cancer Center, Mongolia)

Outflow Reconstruction Tips in Liver Transplant for Budd-Chiari Syndrome

Gyu-seong Choi *Sungkyunkwan University*

Kwang-Woong Lee

Seoul National University

Self Introduction

Prof. Lee graduated from Seoul National University. He has been with Samsung Medical Center and National Cancer Center, Korea as a hepatic and transplant surgeon. He has also been in Johns Hopkins University Hospital as a LDLT consultant. He is a professor of department of surgery, Seoul National University, Korea. He performed the first successful hepatocyte transplantation in Korea when he was in Samsung Medical Center.

He developed several innovative techniques to reduce biliary complications after liver transplantation such as high hilar dissection (HHD) and Tailored Telescopic Reconstruction (TTR) of bile duct. He also played an important role to change deceased donor allocation system in Korea (split liver transplantation regulation and Deceased donor allocation system based on MELD) by publishing several important papers analyzing Korean database. H has performed more than 150 cases of LDLT in Kazakhstan, Georgia and Myanmar since 2013. He performed most of living donors by laparoscopically since Dec. 2015 and performed the world first minimal invasive recipient surgery using Robot and/or laparoscopic approach.

He is currently the president of Korean Liver Transplantation Society and a secretary general of iLDLTG (international living donor liver transplantation group).

Research Interests

His research topics are related to the unmet needs in liver transplantation such as diagnostic or aggressive marker of HCC in liquid biopsy, hepatocyte or liver tumor organoids, microbiome research in liver transplantation, gene delivery into the graft, cancer stem cell, best immunosuppressant for HCC, GWAS so on.

Representative Publications

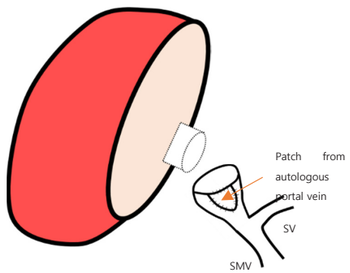
1. Total robot-assisted recipient's surgery in living donor liver transplantation: First step towards the future. Lee KW, Choi Y, Lee S, Hong SY, Suh S, Han ES, Hong SK, Yang SM, Yi NJ, Suh KS J Hepatobiliary Pancreat Sci. 2023 Mar 3. doi: 10.1002/jhbp.1327.
2. Laparoscopic donor and recipient hepatectomy followed by robot-assisted liver graft implantation in living donor liver transplantation. Lee KW, Choi Y, Hong SK, Lee S, Hong SY, Suh S, Han ES, Yi NJ, Suh KS. Am J Transplant. 2022 Apr;22(4):1230-1235. doi: 10.1111/ajt.16943. Epub 2022 Jan 11. PMID: 34971490
3. Shorter operation time and improved surgical outcomes in laparoscopic donor right hepatectomy compared with open donor right hepatectomy. Han ES, Lee KW, Suh KS, Yi NJ, Choi Y, Hong SK, Lee JM, Hong KP, Hong SY, Suh S. Surgery. 2021 Dec;170(6):1822-1829. doi: 10.1016/j.surg.2021.06.005. Epub 2021 Jul 10. PMID: 34256932
4. Donor wound satisfaction after living-donor liver transplantation in the era of pure laparoscopic donor hepatectomy. Lee JM, Shehta A, Lee KW, Hong SK, Cho JH, Yi NJ, Suh KS. Surg Endosc. 2021 May;35(5):2265-2272. doi: 10.1007/s00464-020-07640-2. Epub 2020 May 19. PMID: 32430524
5. Pure Laparoscopic Living Donor Hepatectomy for Donors With Right Portal Vein Anatomical Variations. Shehta A, Lee JM, Lee KW, Hong SK, Cho JH, Yi NJ, Suh KS. Liver Transpl. 2019 Sep;25(9):1445-1454. doi: 10.1002/lt.25582. Epub 2019 Jul 8. PMID: 31169982

Portal Vein Reconstruction in a Recipient with Atretic Portal Vein

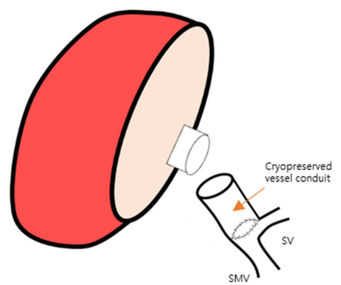
Kwang-Woong Lee *Seoul National University*

Atrophic portal vein with/without collaterals are difficult situation to manage. In this video presentation, I will introduce 3 ways to overcome this situation.

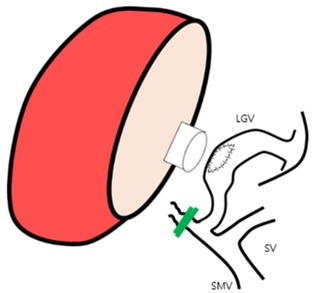
1. Patch venoplasty with autologus porat vein segment



2. Conduit formation using cryopreserved vessel



3. Left gastric varix as an inflow



Chul Soo Ahn

University of Ulsan

Self Introduction

Prof. ChulSoo Ahn is a Professor of the Department of Liver Transplantation and HBP Surgery, Asan Medical Center, College of Medicine, Ulsan University, since

He graduated from Hanyang University College of Medicine with his medical degree in 1990 and completed his internship and residency at the Department of Surgery at Asan Medical Center, receiving his diploma in General Surgery in 1999.

Research Interests

Liver Transplantation Robotic HBP Surgery

Representative Publications

1. Hepatic artery reconstruction in living donor liver transplantation. Balci D, Ahn CS. Curr Opin Organ Transplant. 2019 Oct;24(5):631-636.
2. Liver retransplantation for adult recipients. Hwang S, Ahn CS, Kim KH, Moon DB, Ha TY, Song GW, Jung DH, Park GC, Lee SG. Korean J Hepatobiliary Pancreat Surg. 2013 Feb;17(1):1-7.
3. Liver transplantation in Korea: past, present, and future. Lee SG, Moon DB, Hwang S, Ahn CS, Kim KH, Song GW, Jung DH, Ha TY, Park GC, Jung BH. Transplant Proc. 2015 Apr;47(3):705-8.
4. Mini-incision Right Hepatectomy for Living Donor Hepatectomy. Park JI, Jung DH, Moon DB, Ahn CS, Yoon YI, Kang WH, Na BG, Ha SM, Kim SH, Kim M, Kim SM, Yang G, Oh RK, Hwang S, Lee SG. Transplantation. 2023 Nov 1;107(11):2384-2393.
5. Toward 300 liver transplants a year. Lee SG, Hwang S, Kim KH, Ahn CS, Moon DB, Ha TY, Song KW, Chung DH. Surg Today. 2009;39(5):367-73.

KLTS Symposium 2 | DAY 3: May 31 (Sat.) | ROOM 3 [2F]

Difficult Arterial Reconstruction: Multiple Arteries or Size-Mismatched Situations

Chul Soo Ahn *University of Ulsan*

Arterial anastomosis in liver transplantation, especially in live donor liver transplantation(LDLT) is the most important procedure for graft and recipient's survival and long term outcome. But initial results of early experiences were very poor, then microscopic technique was applied to overcome the post-anastomosis failure. And it becomes the standard technique with very good results, less than 1 or 2 percent of arterial thrombosis. Microscope was designed in the late of 16th century, in 1960, it was applied to experimental animals and human with confidential results. And 1n 1992, first arterial anastomosis in LDLT was successfully performed.

Microscope provides sufficient magnification up to 10 folds for precise anastomosis. But this technique requires long learning curve. Now a days, as the accumulation of experiences, it is replaced with direct anastomosis under the surgical loopes with similar results. Hepatic arteries are very small, so its anastomosis should be strictly performed with general principles, such as, end-to-end anastomosis, tension-free approximation of both stump, good size-matching, needling through full thickness of arterial wall, avoid slip in of adventitia, etc. arterial anastomosis can be done with single interrupted suture technique or continuous suture technique. Under the microscope, interrupted suture is preferred in general.

Hepatic arterial anastomosis is more difficult compared to middle and large sized arterial anastomosis. In donor side, it is smaller, less than 3 mm. with thin and weak wall. Many grafts had multiple arterial stumps. In recipient side, most of arterial stumps were under the pathologic conditions, such as hypertrophy of artery, edematous or fragile intimal, intramural thrombosis, vascular spasm, direct injury during dissection or preexisting treatment(TACE) So careful evaluation of arterial anatomy during preparation is essential in donor and recipient too. And during recipient operation, hilar structure should be dissected very carefully to minimize arterial injury.

Multiple hepatic arteries are more frequent in left lobe grafts than right lobe grafts (45% vs 1%). Grafts which have triple arterial stumps anastomosed in 1% of left lobe grafts.

Anastomoses of all possible arterial stumps of graft are suggested with several reasons: it restores grafts original arterial supply, it is difficult to identify the dominant one, minor hepatic artery stump is usually located deeper than dominant stump, multiple anastomoses can be helpful when one stump is ac-

cidently thrombosed, patient stump may save the graft. Alternative arterial inflow in recipient side is needed if native hepatic arteries were no available for anastomosis. Various candidates were available, right gastroepiploic artery is most useful and applicable in most cases. About 35% of anastomoses are considered as difficult cases, size discrepancies, poor blood flow from stump, short stump, intimal damage or mural thrombosis, etc.

How many hepatic arteries may exist, how many injuries or obstacles is present, how difficult its techniques, all the anastomoses should be performed to save the grafts and patients. So every arterial anastomosis surgeon should be familiar with the careful and refined and meticulous anastomosis techniques.

Tae-Seok Kim

Keimyung University

Self Introduction

Education and Degrees

1996.3-2003.2 M.D., Chung-Ang University, School of Medicine
2007.3-2013.2 M.S., Sungkyunkwan University, School of Medicine

Positions

2003.3-2004.2 Intern, Chung-Ang University Medical Center, Seoul
2004.3-2008.2 Resident, Department of Surgery Samsung Medical Center
2008.5-2011.4 Public Health Doctor for Military Service
2011.5-2013.2 Fellowship, Division of Transplantation, Department of Surgery, Samsung Medical Center
2013.3-2014.2 Fellowship, Division of Hepatobiliary and Pancreatic surgery, Department of Surgery, The Catholic University of Korea, Uijeongbu St. Mary's Hospital
2014.3- Present Assistant Professor/Associate Professor, Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Keimyung University School of Medicine
2021.9-Present Director of Organ Transplantation Center

Membership

Korean Surgical Society
Korean Society of Laparoscopic and Endoscopic Surgeons
Korean Association of Hepato Biliary Pancreatic Surgery
The Korean Association for the Study of the Liver
The Korean Liver Cancer Study Group
The Korean Society for Transplantation
International Liver Transplantation Society
The Transplantation Society

KLTS Symposium 2 | DAY 3: May 31 (Sat.) | ROOM 3 [2F]

Various Bile Duct Anastomosis Methods for Multiple Duct Bile Situations

Tae-Seok Kim *Keimyung University*

Biliary reconstruction is a critical component of liver transplantation, and anatomical variations of the biliary tree—especially in living donor liver transplantation (LDLT)—frequently result in multiple bile duct orifices. In such cases, multiple bile duct anastomosis (MBDA) becomes necessary. This situation poses significant technical challenges and is associated with an increased risk of biliary complications, including leaks and strictures.

This presentation aims to explore practical surgical strategies for managing multiple bile duct openings during liver transplantation. The presentation will focus on intraoperative decision-making, refinement of surgical techniques, and complication prevention. Special attention will be given to how anatomic considerations influence surgical planning, and to technical approaches that improve outcomes.

When grafts have two or more bile duct orifices, reconstruction should be tailored according to donor-recipient anatomical alignment and the hilar length of the graft. Preoperative MRCP and intraoperative cholangiography play critical roles in defining ductal anatomy. Ductoplasty or bridging techniques may be utilized to reduce the number of anastomoses when feasible.

Duct-to-duct anastomosis remains the preferred method; however, in cases where the recipient's bile duct is narrow or misaligned, Roux-en-Y hepaticojejunostomy becomes necessary. Even in such cases, a single jejunal opening is preferred over multiple ones. Intraoperative ICG fluorescence cholangiography is a useful adjunct for confirming alignment and preventing bile leaks. Importantly, when there is high tension at the anastomosis or ductal caliber is narrow, biliary stenting should be actively considered as it can reduce the risk of early complications such as leakage and stricture.

Although MBDA has traditionally been associated with higher rates of biliary complications compared to single anastomosis, recent standardization of surgical techniques and increased experience have narrowed this gap. Through case-based video presentations, this lecture will share practical tips and real-world decision-making processes to support optimal outcomes in complex biliary reconstruction during liver transplantation.

Successful management of multiple bile duct anastomoses requires meticulous surgical planning, detailed anatomical assessment, and adaptation of technique to each clinical scenario. With appropriate use of ductoplasty, stenting, and intraoperative imaging, MBDA can be performed safely with favorable outcomes.

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LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

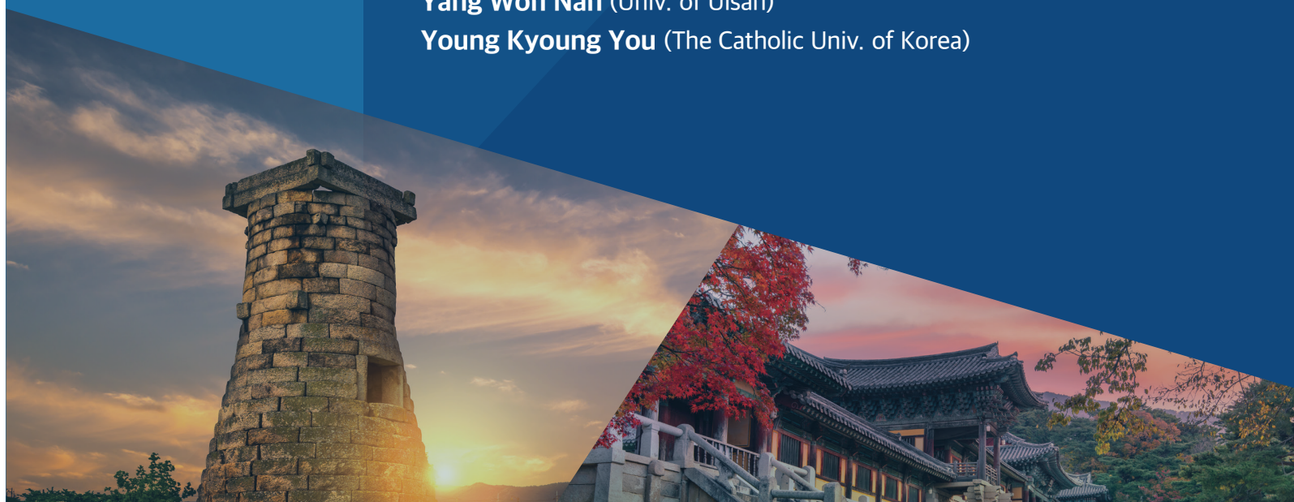
DAY 3: May 31 (Sat.)

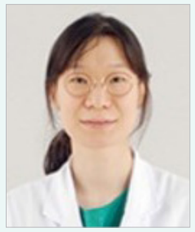
KLTS Symposium 3

Frontline Approaches in Deceased Donor Liver Transplantation: Optimizing Outcomes with Limited Liver Grafts

Chairs:

Yang Won Nah (Univ. of Ulsan)
Young Kyoung You (The Catholic Univ. of Korea)





Young-In Yoon

University of Ulsan

Self Introduction

Education

2002.03-2004.02 Premedical Course, Yonsei University School of Medicine, Wonju, Korea
2004.03-2008.02 Medical Course, Yonsei University School of Medicine, Wonju, Korea
2008.05-2009.02 Rotating Internship, Asan Medical Center,Ulsan University College of Medicine, Seoul, Korea
2009.03-2010.02 Resident Year 1, Department of Surgery, Asan Medical Center,Ulsan University College of Medicine, Seoul, Korea
2010.03-2011.02 Resident Year 2, Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea
2011.03-2012.02 Resident Year 3, Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea
2012.03-2013.02 Resident Year 4, Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea

Professional Experience

2013.2 Master Degree, Ulsan University College of Medicine, Seoul, Korea
2016.2 PhD, Ulsan University College of Medicine, Seoul, Korea
2013.3-2016.2 Clinical Fellow, Liver Transplantation and Hepato-Biliary Surgery, Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea
2016.3-2018.2 Clinical Assistant Professor, Liver Transplantation and Hepato-Biliary Surgery, Department of Surgery, Anam Hospital, Korea University School of Medicine, Seoul, Korea
2018.3-2023.2 Clinical Assistant Professor, Liver Transplantation and Hepato-Biliary Surgery, Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea

Representative Publications

1. Yang GH, Yoon YI, Hwang S, Kim KH, Ahn CS, Moon DB, Ha TY, Song GW, Jung DH, Park GC, Lee SG. Clinical significance and outcomes of adult living donor liver transplantation for acute liver failure: a retrospective cohort study based on 15-year single-center experience. Ann Surg Treat Res. 2024 Sep;107(3):167-177. doi: 10.4174/astr.2024.107.3.167. SCIE/IF 1.2.
2. Yoon YI, Kim KH, Hwang S, Ahn CS, Moon DB, Ha TY, Song GW, Lee SG. Outcomes of 6000 living donor liver transplantation procedures: a pioneering experience at ASAN Medical Center. Updates Surg. 2024 Apr 10. doi: 10.1007/s13304-024-01807-5. Online ahead of print. SCIE/IF 2.4.
3. Yoon YI, Lee SG, Hwang S, Kim KH, Ahn CS, Moon DB, Ha TY, Song GW, Jung DH, Park GC. Safety of right liver donation after improving steatosis through weight loss in living donors: a retrospective study. Hepatol Int. 2024 Mar 15. doi: 10.1007/s12072-024-10641-1. Online ahead of print. SCIE/IF 5.9.
4. Yoon YI, Moon DB, Lee SG, Ahn CS, Hwang S, Kim KH, Ha TY, Song GW, Jung DH, Park GC, Kim MJ. Evolution of the technique of renoportal anastomosis for patients with complete portal venous occlusion in living donor liver transplantation: a retrospective cohort study. Int J Surg. 2023 Jul 1;109(7):1953-1960. SCIE/IF 13.4.
5. Yoon YI, Lim JH, Lee SG, Kang PJ, Hwang GS, Ha SM, Do HY, Hong SK, Huh JW. Role of extracorporeal membrane oxygenation as a salvage therapy for liver transplant recipients in a high-volume transplant center. Liver Transpl. 2023 Jan 1;29(1):67-79. doi: 10.1002/lt.26567. SCIE/IF 6.112.

Current Status and Challenges of the Liver Allocation System for Deceased Donors in Korea

Young-In Yoon *University of Ulsan*

In Korea, the change in the liver allocation system to the Model for End-Stage Liver Disease (MELD) score was implemented on June 1, 2016. A report published in 2017 evaluated this system only for a 4-month period before and after the change. Due to the short study duration, the report was limited in assessing the real impact of the new system. This study aims to assess the long-term appropriateness of the MELD-based allocation system by comparing clinical outcomes over the 3 years before and 5 years after the policy change.

Following the introduction of the MELD-based system, the median waiting time for liver transplant recipients decreased from 21 days to 14 days, and the probability of receiving a transplant within 7 days increased from 27.9% to 36.6%. However, the 30-day post-transplant survival rate decreased significantly (93.9% vs. 89.8%, $p<0.001$), while no significant differences were observed by gender or blood type.

An analysis of 7,444 patients registered exclusively for deceased donor liver transplantation (DDLT) revealed statistically significant increases in transplant rates within 7, 30, 90, and 180 days in the post-MELD era. However, a comparative analysis of the pre- and post-MELD periods (excluding the transition year) showed that the increase in transplant rates was most pronounced within the first 7 days. Subgroup analysis by blood type indicated that type AB still had a higher transplant probability compared to other blood types.

Regional differences in transplant probabilities were also noted. In the pre-MELD system, transplantation rates at 30 days were highest in Region 1, followed by Regions 3 and 2, with the gap widening over time. In the post-MELD era, while the order of regional transplant rates remained similar (1 > 3 > 2 after 14 days), the disparity between Regions 1 and 3 narrowed. Nonetheless, the low transplant probability for DDLT in Region 2 remained unchanged. Pre-transplant mortality rates increased significantly, rising from 1.2% to 2.2% within 7 days, and this increase became more pronounced after 90 days.

Although the MELD system has positively impacted early transplantation probability, reduced waiting times, and improved regional distribution equity, the observed increase in pre-transplant mortality raises concerns. Further analysis is required to determine whether this increase is attributable to the severity of patients on the waiting list or the inherent limitations of the MELD scoring system in reflecting clinical severity. Future multi-institutional studies will be essential to validate the appropriateness of the MELD system and address potential limitations.

Do Seon Song

The Catholic University of Korea

Self Introduction

Education

1997.03-2003.02 Bachelor's Degree, The Catholic University of Korea
2010.03-2016.03 Doctor's Degree, The Catholic University of Korea

Training

2003.03-2004.02 Intern, Catholic Medical Center
2004.03-2008.02 Resident of Internal Medicine, Catholic Medical Center

Work

2011.05-2013.02 Fellow, Seoul. St. Mary Hospital
2013.03-2014.02 Fellow, St. Vincent's Hospital
2014.03-2017.02 Clinical Assistant Professor, St. Vincent's Hospital
2017.03-2022.02 Assistant Professor, St. Vincent's Hospital
2022.03-Present Associate Professor, St. Vincent's Hospital

Research Interests

Portal Hypertension, HCC, MASLD, Alcoholic Liver Disease

Representative Publications

1. Dynamic analysis of acute deterioration in chronic liver disease patients using modified quick sequential organ failure assessment. Clin Mol Hepatol 2024; 30: 388-405
2. Association between serum TNF-α and sarcopenia in liver cirrhosis. Han JW, Kim DI, Nam HC, Chang UI, Yang JM, Song DS. Clin Mol Hepatol 2022; 28: 219-231
3. Effect of exercise-based interventions in nonalcoholic fatty liver disease: A systematic review with meta-analysis. Nam H, Yoo JJ, Cho Y, Kang SH, Ahn SB, Lee HW, Jun DW, Song DS, Choi M. Dig Liver Dis. 2023 Sep;55(9):1178-1186
4. Change in skeletal muscle mass is associated with hepatic steatosis in nonalcoholic fatty liver disease. Jo IH, Song DS, Chang UI, Yang JM Sci Rep. 2023 Apr 28;13(1):6920.
5. Improving the Prediction of Relapse After Nucleos(t)ide Analogue Discontinuation in Patients with Chronic Hepatitis B. Song DS, Jang JW, Yoo SH, Kwon JH, Nam SW, Bae SH, Choi JY, Yoon SK Clin Infect Dis. 2021 Aug 16;73(4):e892-e903

KLTS Symposium 3 | DAY 3: May 31 (Sat.) | ROOM 3 [2F]

Patient Selection and Timing of Referral for Liver Transplantation in Acute Alcoholic Hepatitis

Do Seon Song *The Catholic University of Korea*

Severe alcohol-associated hepatitis (AH) is a rapidly progressive and often fatal manifestation of alcohol-associated liver disease, particularly in patients who do not respond to corticosteroid therapy. Although corticosteroids are the current standard of care, their survival benefit is restricted to a MELD-defined therapeutic window—most pronounced between MELD scores of 25 and 39, and absent beyond MELD 51. In patients with poor response to medical therapy and high predicted mortality, early liver transplantation (LT) has emerged as a potentially life-saving option.

Candidate selection for early LT in AH requires a multifaceted evaluation that incorporates both clinical indicators and psychosocial factors. Medically, the absence of significant comorbidities, nonresponse to corticosteroids, and absence of alternative treatment options form the foundation for urgency. Equally important, the risk of post-transplant alcohol relapse must be rigorously assessed, as it directly influences long-term graft and patient outcomes.

Structured psychosocial evaluations—using tools such as the SALT score or SIPAT—are increasingly employed to identify individuals with a low risk of relapse. Key considerations include patient insight, engagement in addiction treatment, family support, and absence of active psychiatric illness. Rather than relying solely on a fixed period of abstinence, recent evidence supports individualized risk stratification to guide decision-making in this context.

This review will outline current evidence and expert guidance on selecting appropriate candidates for early LT in AH, emphasizing the importance of integrating disease severity, timing of intervention, and relapse risk assessment. By applying this comprehensive framework, clinicians can better navigate the ethical and clinical challenges inherent in transplanting patients with active or recent alcohol use disorders.

Young Chul Yoon

The Catholic University of Korea

Self Introduction

Prof. Young Chul Yoon is a board certified hepato-biliary-pancreas surgeon and surgical oncologist. Dr. Yoon received his medical degree (2001) at Catholic University College of Medicine, Seoul, Korea. Presently, Dr. Yoon is director of hepato-biliary-pancreas surgery division and liver transplantation, Department of Surgery at the Incheon St. Mary's Hospital and the chief of Transplantation Center.

His clinical interest is in the treatment of hepato-biliary-pancreas cancers with an emphasis in conducting clinical trials as an active investigator. Dr. Yoon has authored about 20 published articles in international journals.

Professional Experience

2023.1-2023.12	Academic Director of the Korean Liver Transplantation Society
2020.1-Present	Academic Director of Gyeongin Association of The Korean Association of Hepato-Biliary-Pancreatic Surgery
2021.3-Present	Speciality Examination Director of The Korean Association of Hepato-Biliary-Pancreatic Surgery
2021.7-2022.6	Public Relation Director of The Korean Liver Cancer Association
2022.7-Present	Editor of Korean Journal of Hepato-Biliary-Pancreatic Surgery
2025.3-Present	Education Committee Chair of the Korean Liver Transplantation Society
2025.3-Present	Information Committee Chair of Korean Association of Liver Surgery

Research Interests

HBP Surgery and Liver Transplantation

Representative Publications

1. Biliary Internal Stents and Biliary Complications in Adult Liver Transplantation. Young Chul Yoon, Kambiz Etesami, Navpreet Kaur, Juliet Emamaullee, Jim Kim, Shannon Zielsdorf, Aaron Ahearn, Linda Sher, Yuri Genyk, Yong Kyong Kwon, Transpl Proc. 2021 Jan-Feb;53(1):171-176
2. Ultrasound Guided Intraoperative Liver Radiofrequency Ablation by Surgeons. Yoon YC, J Surg Ultrasound 2018; 5: 39-44
3. Clinical analysis of recurrent hepatocellular carcinoma after living donor liver transplantation. Yoon YC, Hong TH, You YK, Kim DG., Clin Transplant 2013 Mar-Apr; 27(2)
4. Liver regeneration and factors influencing liver regeneration in donor and recipients of adult living donor liver transplantation using right lobe graft. Yoon YC, Park JH, Hong TH, You YK, Kim DG., J Korean Soc Transplant 2011 Jun;25(2)
5. Hepatic artery protection using a polyglycolic acid sheet during pancreaticoduodenectomy: A multicenter study. Jun Suh Lee, Young Chul Yoon , Tae Ho Hong , Yoo-Seok Yoon , Sung Eun Park, J Hepatobiliary Pancreat Sci. 2023 Oct 4

Perioperative Challenges and Solutions for Patients with Chronic Liver Disease Undergoing Deceased Donor Liver Transplantation

Young Chul Yoon *The Catholic University of Korea*

In Korea, due to the extreme shortage of deceased organ donors, patients undergoing deceased donor liver transplantation (DDLT) often present with exceptionally high MELD scores and severely compromised general health. These patients frequently suffer from profound metabolic derangements and hemodynamic instability, placing them at high risk for multi-organ dysfunction. As a result, the perioperative management of such patients is complex and demands a multidisciplinary, evidence-based approach.

One of the major perioperative challenges is hemodynamic instability, which may arise from low preload, impaired cardiac function, or profound vasodilation. Management strategies must be tailored to individual hemodynamic profiles and include the use of vasopressors such as norepinephrine and vasopressin, fluid restriction, and close hemodynamic monitoring through invasive or minimally invasive techniques

Coagulopathy in patients with advanced liver disease represents another significant challenge, as the delicate balance between bleeding and thrombosis can be easily disrupted. Traditional coagulation tests often fail to reflect true hemostatic capacity. Management should focus on correcting fibrinogen deficits, using antifibrinolytic agents where appropriate, and minimizing unnecessary transfusions.

Pulmonary complications such as hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PoPH) also pose significant perioperative risks. PoPH, in particular, can lead to right ventricular failure during or after transplantation and requires preoperative optimization, careful volume control during surgery, and the potential use of pulmonary vasodilators. In refractory cases, combined liver and lung transplantation may be necessary.

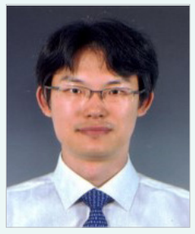
Hepatic encephalopathy is commonly observed in high-MELD patients awaiting DDLT and can affect post-transplant cognitive recovery. Preoperative management should include lactulose and rifaximin, nutritional optimization, oral care, physical activity, and caregiver support. Although cognitive function often improves after transplantation, deficits may persist in some patients and should be monitored long-term.

Hepatorenal syndrome (HRS) is a functional form of renal failure with high pre-transplant morbidity and

mortality. Its management relies on vasoconstrictors such as terlipressin or norepinephrine combined with albumin, cautious fluid resuscitation, and renal replacement therapy in selected cases. During surgery, preserving renal perfusion and avoiding nephrotoxic agents are crucial for postoperative renal recovery.

Infection remains the leading cause of early mortality following DDLT. High-MELD patients are often immunocompromised even before receiving immunosuppression, making them particularly vulnerable. Preventive strategies include careful donor screening, pre- and postoperative infection surveillance, and targeted antimicrobial therapy, especially in the face of rising multidrug-resistant organisms.

In conclusion, the perioperative management of chronic liver disease patients undergoing DDLT involves anticipating and addressing a wide range of organ-specific challenges. Optimizing care across hemodynamic, coagulation, pulmonary, renal, neurologic, and infectious domains is essential to improving outcomes in this high-risk population.



YoungRok Choi

Seoul National University

Self Introduction

Education

1999-2003	Busan National University College of Medicine,
2007-2012	M.S., College of Medicine, Seoul National University
2014-Present	Ph.D. candidate, College of Medicine, Seoul National University

Training

2003.03-2004.02	Internship, Busan National University Hospital, Busan, Korea
2004.03-2008.02	Residentship in Department of Surgery Seoul National University Hospital, Seoul, Korea

Research Interests

Graft DSA in Liver Transplantation, Bile Exome Excretion after Liver Transplantation, Bile Duct Ischemia

Representative Publications

1. Long-term outcomes of liver transplantation using grafts from donors with active hepatitis B virus replication: a multi-center cohort study, Annals of Surgical Treatment and Research 104 (4), 183
2. Total robot-assisted recipient's surgery in living donor liver transplantation: First step towards the future, J hepatobiliary pancreas science, https://doi.org/10.1002/jhbp.1327
3. Changes in Awareness Toward Minor's Organ Donation Through Structured Information; Survey, Transplant Int https://doi.org/10.3389/ti.2023.10795
4. Long - term outcomes of laparoscopic versus open liver resection for intrahepatic combined hepatocellular - cholangiocarcinoma with propensity score matching, Annals of Gastroenterological Surgery 6 (4), 562-568
5. Changes in Indices of Steatosis and Fibrosis in Liver Grafts of Living Donors After Weight Reduction, Front. Surg. 2022;9: 827526

Predicting Futile Outcomes in Deceased Donor Liver Transplantation: Focus on Acute-on-Chronic Liver Failure

YoungRok Choi *Seoul National University*

Acute-on-chronic liver failure (ACLF) presents one of the toughest challenges in liver transplantation. These patients typically show rapid health decline, multiple organ failure, and extremely high short-term death rates. While liver transplantation offers the only cure, not everyone benefits from it—especially patients whose critical illness has advanced beyond meaningful recovery. Identifying these "futile" cases is crucial, particularly given the shortage of donor organs.

My talk will examine how to assess futility in deceased donor liver transplantation for ACLF patients, highlighting evidence-based risk assessment and practical decision-making approaches.

I'll first discuss the limitations of traditional scoring systems like MELD and MELD-Na. While essential for organ allocation, these scores often underestimate death risk in ACLF because they don't account for non-liver organ failures and widespread inflammation.

Next, I'll cover the CLIF-C ACLF score—developed by European researchers—as a more accurate tool for predicting short-term mortality in these patients. Multiple studies show it outperforms MELD in predicting 28-day and 90-day mortality, particularly in intensive care settings. A score above 64 or 70 increasingly suggests futility, where expected survival after transplant remains extremely low despite best care.

I'll then introduce newer models specifically designed for ACLF patients. The TAM score uses just four variables (age ≥53, lactate ≥4 mmol/L, mechanical ventilation, and low white blood cell count) to clearly predict one-year survival in the most severe ACLF patients. In validation studies across multiple centers, a TAM score >2 was linked to less than 10% survival after transplant, effectively identifying cases with little chance of benefit.

Similarly, the SALT-M score, developed from a large international dataset, includes age, BMI, use of blood pressure medications, breathing failure, and diabetes to estimate one-year mortality after transplantation. This score has shown better predictive performance than older systems in high-risk patients. Both TAM and SALT-M provide transplant teams valuable tools for measuring risk and guiding patient selection, especially when time-sensitive decisions are needed.

In conclusion, while transplantation can save ACLF patients, we increasingly need to recognize when

the point of futility has been reached. By using validated scoring systems like CLIF-C ACLF, TAM, and SALT-M, alongside bedside evaluation of disease trajectory, physical condition, and infection, doctors can better identify patients most likely to benefit from transplant and avoid cases where outcomes are predictably poor. This approach ensures ethical organ use and improves overall transplant program success

THE LIVER WEEK 2025

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LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat.)

KASL Special Interest Group 5.
The KASL Study Group of Portal Hypertension

Advancing the Frontiers of Cirrhosis Care: Diagnostic and Therapeutic Insights

Chairs:

Young Seok Kim (Soonchunhyang Univ.)
Won Hyeok Choe (Konkuk Univ.)

Jae Yoon Jeong

Ewha Womans University

Self Introduction

Prof. Jae Yoon Jeong is a Clinical Professor of the Division of Gastroenterology and Hepatology, Department of Internal Medicine, Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine.

He graduated from Hanyang University College of Medicine with his medical degree in 2002 and completed his internship and residency at the Department of Internal Medicine at Hanyang University Medical center, receiving his diploma in Internal Medicine in 2007. From 2010 to 2012, he completed a fellowship in the Division of Gastroenterology and Hepatology, Department of Internal Medicine, at Hanyang University Guri Hospital, and in 2013, he earned his Ph.D. in Medicine from the Graduate School of Hanyang University.

Since 2012, he has worked at Daerim St. Mary's Hospital, Hanyang University Guri Hospital, and the National Medical Center. He has also served as a member of the Publication Committee of the Korean Liver Cancer Association (2016–2019), a member of the Research Committee of the Korean Association for the Study of the Liver (2020–2021), and a member of the External Affairs Committee of the Korean Association of Clinical Ultrasound (2023–present).

Research Interests

Cirrhosis and Portal Hypertension, Viral Hepatitis, Metabolic Dysfunction-associated Steatotic Liver Disease

Representative Publications

1. Temporal Dynamics and Treatment Outcomes of Hepatitis C Virus/Human Immunodeficiency Virus Coinfection: A Multicenter Retrospective Study from South Korea. Gut Liver. 2025. Accept. (First author)
2. The chronological changes in the seroprevalence of anti-hepatitis A virus IgG from 2005 to 2019: Experience at four centers in the capital area of South Korea. Medicine (Baltimore). 2022;101:e31639. (Corresponding author)
3. Changing Features of Liver Injury in COVID-19 Patients: Impact of Infection with the SARS-CoV-2 Delta (B.1.617.2) Variants. Infect Chemother. 2022;54:744-756. (Corresponding author)
4. Clinical Characteristics and Treatment Outcomes of Patients with Hepatitis C Virus and Human Immunodeficiency Virus Coinfection: Experience at a Single Center in Korea. J Korean Med Sci. 2021;36(46):e308. doi: 10.3346/jkms.2021.36.e308. (Corresponding author)
5. Computed Tomography-Determined Body Composition Abnormalities Usefully Predict Long-term Mortality in Patients with Liver Cirrhosis. J Comput Assist Tomogr. 2021;45(5):684-690. (Corresponding author)

KASL Special Interest Group 5. | DAY 3: May 31 (Sat.) | ROOM 4 [2F]

Optimal Management Strategies for Non-Selective Beta-Blockers in Cirrhosis

Jae Yoon Jeong *Ewha Womans University*

As hepatic fibrosis progresses, it leads to the development of portal hypertension. When the hepatic venous pressure gradient (HVPG) exceeds 10 mmHg—defining clinically significant portal hypertension (CSPH)—there is a substantial risk of variceal formation and hepatic decompensation. Notably, once HVPG reaches or exceeds 16 mmHg, the risk of mortality increases significantly. Since the initial demonstration in the early 1980s of propranolol's efficacy in reducing the risk of recurrent variceal bleeding, non-selective beta-blockers (NSBBs) have been established as the cornerstone of care for both primary and secondary prophylaxis of variceal bleeding in patients with cirrhosis, primarily due to their portal pressure-lowering effects.

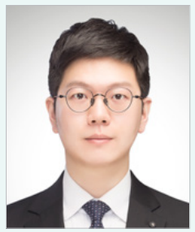
Beyond bleeding prevention, NSBBs have also demonstrated efficacy in preventing the progression to decompensation in patients with advanced chronic liver disease and CSPH. While the benefits of NSBBs in decompensated cirrhosis are less well established than in compensated cirrhosis, they may still offer protective effects by reducing the risk of further decompensation. However, in patients with advanced decompensated cirrhosis, particularly those with refractory ascites, NSBB therapy may exacerbate circulatory dysfunction and increase the risk of mortality, thereby proving harmful rather than beneficial.

Recently, increasing attention has been directed toward carvedilol, a beta-blocker that not only inhibits beta-1 and beta-2 receptors but also exerts alpha-1 adrenergic blockade. Emerging evidence suggests that carvedilol may be superior to classical NSBBs in reducing portal hypertension.

In this lecture, we will review recent studies and emerging evidence surrounding the optimal management strategies for NSBBs use in cirrhosis.

References

1. Baveno VII - Renewing consensus in portal hypertension. de Franchis R, et al. Hepatol. 2022;76:959-974.
2. Preventing the progression of cirrhosis to decompensation and death. illanueva C, et al. Nat Rev Gastroenterol Hepatol. 2025;22:265-280.
3. Screening and management of portal hypertension and varices in cirrhosis: Expert perspectives. Brown RS Jr, et al. Hepatol Commun. 2025;9:e0682.
4. Carvedilol vs. propranolol for the prevention of decompensation and mortality in patients with compensated and decompensated cirrhosis. Fortea JI, et al. J Hepatol. 2024:S0168-8278(24)02772-7.



Hyunwoo Oh

Sungkyunkwan University

Self Introduction

Prof. Hyunwoo Oh is a Clinical Assistant Professor of the Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine.

He graduated from Hanyang University College of Medicine with his medical degree in 2011 and completed his internship and residency at the Department of Internal Medicine at Hanyang University Medical center. And he received his Doctoral degree in Medicine in 2024 at Seoul National University.

Since 2022, he has been taking a role as a member of Informatics and Public Relations committee of the Korean Association of the Study of the Liver.

Research Interests

Metabolic Dysfunction-Associated Steatotic Liver Disease, Portal Hypertension, Hepatocellular Carcinoma

Advances in Non-Invasive Methods for Detecting Clinically Significant Portal Hypertension

Hyunwoo Oh *Sungkyunkwan University*

Introduction

Clinically significant portal hypertension (CSPH) is defined as a hepatic venous pressure gradient (HVPG) of ≥10 mmHg, a threshold above which complications such as esophageal varices, ascites, and hepatic encephalopathy become more likely. The Baveno VII workshop, entitled "Personalized Care for Portal Hypertension" has provided refined consensus criteria using non-invasive tools for CSPH diagnosis in patients with compensated advanced chronic liver disease (cACLD), aiming to simplify and personalize clinical decision-making.

The gold standard for assessing portal pressure remains HVPG, but this invasive procedure is limited to expert centers. As a result, efforts have intensified to identify non-invasive tests (NITs) that can stratify risk, guide screening for varices, and direct therapeutic decisions.

Recent Advances in Non-Invasive Assessment

1) Blood-Based Biomarkers

Recent studies have highlighted the utility of simple blood tests in identifying patients with cACLD and stratifying CSPH risk. For instance, FIB-4 ≥1.75 correlates well with liver stiffness measurements (LSM ≥10 kPa), while the VITRO score (von Willebrand factor to platelet ratio) demonstrates potential for CSPH stratification. These tools offer high accessibility and have demonstrated competitive predictive accuracy in large cohorts.

2) Ultrasound-Based Techniques

Liver stiffness measurement (LSM) and spleen stiffness measurement (SSM) via vibration-controlled transient elastography (VCTE) have emerged as core tools. Notably, SSM at 100 Hz was validated in recent studies, including Yoo et al., who demonstrated a strong correlation between SSM and HVPG ($r=0.486$, $p<0.001$) and identified 38.9 kPa as an optimal cut-off for detecting varices needing treatment and CSPH. Baveno VII now recommends SSM cut-offs (<21 kPa to exclude CSPH, >50 kPa to confirm CSPH) in viral etiologies.

Multiparametric ultrasound (including B-mode, Doppler, and contrast-enhanced techniques) offers de-

tailed structural and hemodynamic insights. These include liver surface nodularity, portal vein diameter, spleen size, and blood flow velocity assessments.

3) CT-Based Assessments

Recent data demonstrate that spleen volume measured via enhanced CT correlates linearly with HVPG (r=0.364), enabling the development of the "S-HVPG" score, which achieved an AUC of 0.803 for identifying severe PH (≥16 mmHg). This method combines spleen volume with serum albumin and age to enhance diagnostic accuracy.

4) Artificial Intelligence (AI)-Driven Models

Machine learning and radiomics are increasingly integrated into CSPH assessment. AI-based models analyzing TE, CT, and laboratory data have shown improved prediction of CSPH by identifying image-based features or composite scores that exceed human diagnostic capabilities. Radiomics-based vascularomics and spleen-liver texture analysis are particularly promising.

Conclusion

CSPH remains a critical clinical landmark in advanced liver disease. While HVPG is the reference standard, non-invasive alternatives have substantially advanced. The incorporation of spleen stiffness and blood-based markers, imaging volumetrics, and AI-driven models are redefining diagnostic strategies. The Baveno VII consensus continues to guide these developments with rule-of-five liver stiffness thresholds (10–15–20–25 kPa), platelet-based cutoffs, and gray-zone refinements. Future prospective validations and integration of multimodal data platforms are anticipated to further refine patient stratification and therapeutic planning.

References

1. Brol MJ, et al. Non-invasive Assessment of Clinically Significant Portal Hypertension. Curr Hepatol Rep. 2023;22:206–215. https://doi.org/10.1007/s11901-023-00609-4.
2. Brown RS, et al. Screening and Management of Portal Hypertension and Varices in Cirrhosis. Hepatology Comm. 2025;9:e0682. https://doi.org/10.1097/HC9.0000000000000682.
3. Chen X, et al. CT-Derived Spleen Volume Accurately Diagnoses Severe PH. Sci Rep. 2025;15:16850. https://doi.org/10.1038/s41598-025-02143-3.
4. Du Z, et al. Artificial Intelligence for the Noninvasive Diagnosis of CSPH. EngMed. 2025;2:100069. https://doi.org/10.1016/j.engmed.2025.100069.
5. Jachs M, et al. Spleen Stiffness at 100 Hz for CSPH Diagnosis. Lancet Gastroenterol Hepatol. 2024;9:1111–1120. https://doi.org/10.1016/S2468-1253(24)00234-6.
6. Semmler G, et al. Simple Blood Tests to Diagnose cACLD and Stratify CSPH Risk. Hepatology. 2024;80:887–900. https://doi.org/10.1097/HEP.0000000000000829.
7. Möller K, et al. Noninvasive Multiparametric Ultrasound in PH. Portal Hypertens & Cirrhosis. 2025;4:44–65. https://doi.org/10.1002/poh2.70002.
8. Liu C, et al. A Combined Model of Spleen Stiffness and Baveno VII Criteria. Portal Hypertens & Cirrhosis. 2025;4:4–12. https://doi.org/10.1002/poh2.70004.
9. Mendizabal M, et al. Evolving Portal Hypertension through Baveno VII Recommendations. Ann Hepatol. 2024;29:101180. https://doi.org/10.1016/j.aohep.2023.101180.
10. Yoo JJ, et al. Enhancing CSPH Risk Prediction with SSM at 100-Hz. Sci Rep. 2024;14:13674. https://doi.org/10.1038/s41598-024-63848-5.
11. Franchis R, et al. Baveno VII – Renewing Consensus in Portal Hypertension. J Hepatol. 2022;76:959–974. https://doi.org/10.1016/j.jhep.2021.12.022.

Sung Hwan Yoo

Yonsei University

Self Introduction

Prof. Sung Hwan Yoo is a clinical assistant professor of the Department of internal medicine, Yonsei University College of Medicine.

He graduated from Yonsei University College of Medicine with his medical degree in 2014 and completed his internship and residency at the Department of Interal medicine at Gangnam Severance Hospital, receiving his diploma in Internal medicine 2020.

Since 2023, he has been taking a number of roles, including a regular member of the Korean Association of the Study of the Liver, the Korea Liver Cancer Association. Since 2024, Prof. Yoo has been a roles as an member of Viral Hepatitis Research Group.

Research Interests

- Early Diagnosis of Hepatocelluar Carcinoma Using Liquid Biopsy
- Prognostic Analysis of Hepatitis B Virus Using HBcrAg

Representative Publications

1. Song W, Yoo SH, Jang J, Baik SJ, Lee BK, Lee HW, Park JS, Association between Sarcopenic Obesity Status and Nonalcoholic Fatty Liver Disease and Fibrosis. Gut Liver. 2023 Jan 15;17(1):130-138. doi: 10.5009/gnl220041. Epub 2022 Dec 6.
2. Hwang SY, Yoo SH et al. Baseline and on-treatment HBcrAg levels as predictors of HBeAg seroconversion in chronic hepatitis B patients treated with antivirals. J Viral Hepat. 2023 Jan;30(1):39-45. doi: 10.1111/jvh.13765. Epub 2022 Nov 11.
3. Yoo SH, Nahm JH, Lee WK, Lee HW, Chang HY, Lee JI. Loss of Krüppel-like factor-10 facilitates the development of chemical-induced liver cancer in mice Mol Med. 2023 Nov 9;29(1):156. doi: 10.1186/s10020-023-00751-1.
4. Yoo SH, Park JY, Lee HS, Lee HW, Lee JI. Risk of dementia in the elderly with non-alcoholic fatty liver disease: A nested case-control study in the Republic of Korea. Ann Acad Med Singap. 2023 Nov 29;52(11):570-579. doi: 10.47102/annals-acadmedsg.202379.
5. Ju MK, Yoo SH, Choi KH, Yoon DS, Lim JH. Selective hanging maneuver and rubber band retraction technique for pure laparoscopic donor right hepatectomy. Asian J Surg. 2024 Jan;47(1):354-359. doi: 10.1016/j.asjsur.2023.08.227. Epub 2023 Oct 6.

Updates in the Management of Acute Kidney Injury in Patients with Cirrhosis

Sung Hwan Yoo *Yonsei University*

Initial Management Strategies

The management of acute kidney injury (AKI) in cirrhosis follows the KDIGO consensus and specific cirrhosis guidelines, emphasizing nephrotoxin avoidance and fluid optimization. Fluid therapy should be carefully adjusted based on disease severity, urine output, and resuscitation phase. Assessment of volume status requires a combination of history, physical examination, vital signs, imaging, and dynamic measurements, although no single method is superior. Regular reassessment is crucial to prevent volume overload complications.

Fluid choice should be patient-specific: blood products for gastrointestinal bleeding, balanced crystalloids for volume depletion, and 20-25% albumin for spontaneous bacterial peritonitis (SBP) or hepatorenal syndrome-AKI (HRS-AKI). Although albumin is traditionally used to maintain oncotic pressure, its structural alterations in cirrhosis may reduce effectiveness. Conflicting RCTs suggest albumin improves short-term hemodynamics but not long-term renal outcomes compared to crystalloids.

Paracentesis and Intraperitoneal Pressure

The interaction between ascites, intra-abdominal pressure (IAP), and AKI is complex. Increased IAP due to tense ascites can impair renal function by reducing cardiac output. Paracentesis plus albumin can improve creatinine clearance, though large-volume paracentesis (LVP) may induce circulatory disturbances. Routine IAP measurement is not currently recommended, and systematic LVP without albumin remains controversial.

Renal Replacement Therapy (RRT)

RCTs do not support early RRT initiation in critically ill patients, but cirrhotic patients were underrepresented. RRT timing should be individualized, considering kidney and liver disease progression. Early RRT is advisable for patients with severe volume overload or persistent encephalopathy despite treatment. RRT should be used as a bridge to liver transplantation (LT) for eligible patients, while non-transplant candidates should have discussions about prognosis and therapy goals.

Transplantation Considerations

AKI episodes significantly impact short-term mortality in cirrhotic patients, warranting expedited transplant evaluation. Current US policies for simultaneous liver-kidney transplantation (SLKT) consider AKI duration (≤6 weeks with eGFR ≤25 ml/min) and chronic kidney disease (CKD) presence, but additional factors like AKI etiology and comorbidities are not included. Biomarkers may enhance SLKT decision-making. Isolated kidney transplantation is feasible for compensated cirrhosis patients without significant portal hypertension.

Transjugular Intrahepatic Portosystemic Shunt (TIPS) and Liver Support

TIPS has shown potential in improving glomerular filtration rate (GFR) in refractory ascites but has limited study as an HRS-AKI treatment. An ongoing RCT aims to clarify its role. Extracorporeal liver support methods like albumin dialysis and plasma exchange target systemic inflammation but lack AKI-specific efficacy.

HRS-AKI Specific Management

Terlipressin, preferably as a continuous infusion, is the first-line vasoconstrictor for HRS-AKI. Norepinephrine has similar efficacy, except in acute-on-chronic liver failure (ACLF), where terlipressin is superior. Norepinephrine requires ICU admission and central venous access, making terlipressin the preferred outpatient option. Midodrine and octreotide are less effective.

Guidelines recommend daily administration of 20-25% albumin (20-40 g/day), but optimal dosing and duration remain unclear. Albumin should be discontinued if pulmonary edema develops. Vasoconstrictors are most effective when initiated at serum creatinine (SCr) <2.25 mg/dL and achieving mean arterial pressure (MAP) increases ≥15 mmHg. If MAP rises without SCr improvement, alternative AKI causes should be considered.

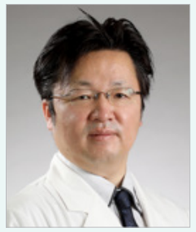
Patients receiving vasoconstrictors require monitoring for ischemic complications, which may necessitate dose reduction or conversion to continuous terlipressin infusion. Pulmonary edema risk is higher with terlipressin; careful fluid management, including temporary albumin suspension and diuretics, may allow continued vasoconstrictor therapy.

Transplant Considerations in HRS-AKI

HRS-AKI reversal lowers CKD and RRT risk post-LT but does not improve transplant-free survival. Vasoconstrictor therapy reduces SCr, lowering MELD scores and potentially delaying transplant priority in high-MELD regions. Some countries counteract this by maintaining peak SCr values for allocation purposes or assigning extra points to treated patients. Future policy revisions should ensure fair transplant allocation as new treatments and prognostic markers emerge.

References

1. Mitra KN, John AK, Lui Forni et al. Acute kidney injury in patients with cirrhosis: Acute Disease Quality Initiative (ADQI) and International Club of Ascites (ICA) joint multidisciplinary consensus meeting. J Hepatol. 2024 Jul;81(1):163-183. doi: 10.1016/j.jhep.2024.03.031. Epub 2024 Mar 26
2. Stevn LF, Florence Wong, Joseph Ahn et al. AGA Clinical Practice Update on the Evaluation and Management of Acute Kidney Injury in Patients With Cirrhosis: Expert Review. Clin Gastroenterol Hepatol. 2022 Dec;20(12):2707-2716. doi: 10.1016/j.cgh.2022.08.033.
3. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69(2):406–460. https://doi.org/10.1016/j.jhep.2018.03.024.
4. Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American association for the study of liver diseases. Hepatology 2021;74(2):1014–1048. https://doi.org/ 10.1002/hep.31884.
5. Singh V, De A, Mehtani R, et al. Asia-Pacific association for study of liver guidelines on management of ascites in liver disease. Hepatol Int 2023;17(4):792–826. https://doi.org/10.1007/s12072-023-10536-7.



Masahito Shimizui

Gifu University, Japan

Self Introduction

Education

1995	Gifu University School of Medicine, Gifu (Japan). M.D.
2001	Gifu University Graduate School of Medicine, Gifu (Japan). Ph.D.
2002-2005	Postdoctoral Fellow, Columbia University Medical Center, New York, USA.
2013-2015	Associate Professor, Department of Gastroenterology, Gifu Univ. Sch. Med., Gifu, Japan.
2015-Present	Professor, Department of Gastroenterology, Gifu Univ. Sch. Med., Gifu, Japan.

Professional Organizations and Societies

Japanese Society of Internal Medicine, Japanese Society of Gastroenterology (JSG), Japanese Society for the Study of the Liver (JSH), American Association for the Study of Liver Diseases (AASLD)

Research Interests

- Pathobiology and Treatment of Acute and Chronic Liver Failure
- Nutritional Pharmacotherapy of Liver Cirrhosis
- Cancer Chemoprevention Using Retinoid and Natural Compounds

Representative Publications

1. Hanai T, Shimizu M, et al. Alcohol-associated liver disease increases the risk of muscle loss and mortality in patients with cirrhosis. J Gastroenterol. 2024 Oct 59(10):932-940.
2. Hanai T, Shimizu M, et al. Nutritional counseling improves mortality and prevents hepatic encephalopathy in patients with alcohol-associated liver disease. Hepatol Res. 2024 Nov 54(11):1089-1098.
3. Miwa T, Shimizu M, et al. Usefulness of the Global Leadership Initiative on Malnutrition criteria to predict sarcopenia and mortality in patients with chronic liver disease. Hepatol Res. 2022 Nov 52(11):928-936.
4. Miwa T, Shimizu M, et al. Survival benefit of l-carnitine supplementation in patients with cirrhosis. JPEN J Parenter Enteral Nutr. 2022 Aug;46(6):1326-1334.
5. Hanai T, Shimizu M, et al. Hanai T, Shimizu M, et al. Usefulness of nutritional therapy recommended in the Japanese Society of Gastroenterology/Japan Society of Hepatology evidence-based clinical practice guidelines for liver cirrhosis 2020. J Gastroenterol. 2021 Oct 56(10):928-937.

KASL Special Interest Group 5. | DAY 3: May 31 (Sat.) | ROOM 4 [2F]

Optimizing Nutrition in Cirrhosis: Recent Advances and Clinical Implications

Masahito Shimizu *Gifu University, Japan*

Cirrhotic patients with reduced hepatic functional reserve are associated with several nutritional/metabolic disorders. In particular, protein-energy malnutrition (PEM) is strongly associated with poorer prognosis and quality of life (QOL) in cirrhotic patients. The progression of cirrhosis is often accompanied by abnormal glucose metabolism, including hyperinsulinemia, which contributes to the development of hepatocellular carcinoma (HCC). In addition, sarcopenia, a syndrome characterized by reduced skeletal muscle mass and strength often seen in cirrhotic patients, is predictive of patient prognosis and mortality.

In cirrhosis, a decrease in branched-chain amino acids (BCAA) is commonly observed and is strongly associated with the onset of complications such as hepatic encephalopathy and acute kidney injury.[1,2] BCAA supplementation in PEM increases serum albumin levels and improves QOL and survival in cirrhotic patients. BCAA supplementation is also effective in improving hepatic encephalopathy. In particular, BCAA-enriched supplementation given as a late evening snack improves nutritional status and increases body protein content. The results of a randomized trial (LOTUS) showed that long-term administration of BCAA granules may improve event-free survival, serum albumin levels and QOL in cirrhotic patients.[3] Evidence-based Japanese clinical practice guidelines for liver cirrhosis 2020 recommend that BCAA should be administered to cirrhotic patients with PEM.[4,5]

BCAA plays an important role in maintaining and increasing skeletal muscle mass. Therefore, the decrease in BCAA in cirrhotic patients is closely related to the development of sarcopenia. In cirrhosis, the progression of PEM, the decrease in BCAA, the development of sarcopenia, and the onset of impaired glucose tolerance are observed as a series of pathological conditions. Japanese guidelines suggest that exercise and nutritional therapy as treatment for sarcopenia.[4,5]

In addition to malnutrition, hypernutrition worsens the prognosis of cirrhotic patients. Obesity and diabetes increase the risk of HCC and liver cirrhosis, and metabolic dysfunction associated steatotohepatitis (MASH) associated with obesity and lifestyle diseases is also on the rise. Patients with diabetes and MASH are also prone to sarcopenia. Interestingly, BCAA supplementation has been reported to inhibit liver carcinogenesis in obese cirrhotic patients.[6] BCAA may be a chemopreventive agent for HCC development, especially when the patients have metabolic disorders.

In conclusion, BCAA supplementation improves event-free survival, increases serum albumin levels, im-

proves QOL and at least suppresses obesity-related HCC in patients with cirrhosis. BCAA is a key agent in the overall management of cirrhosis.

References

1. Hanai T, Shimizu M, et al. Sarcopenia predicts minimal hepatic encephalopathy in patients with liver cirrhosis. Hepatol Res. 2017; 47: 1359-1367.
2. Miwa T, Shimizu M, et al. Acute kidney injury development is associated with mortality in Japanese patients with cirrhosis: impact of amino acid imbalance. J Gastroenterol. 2024; 59: 849-857.
3. Yoshiji H, Shimizu M, et al. Evidence-based clinical practice guidelines for Liver Cirrhosis 2020. J Gastroenterol. 2021; 56: 593-619.
4. Yoshiji H, Shimizu M, et al. Evidence-based clinical practice guidelines for Liver Cirrhosis 2020. Hepatol Res. 2021; 51: 725-749.
5. Muto Y, Sato S, et al. Effects of oral branched-chain amino acid granules on event-free survival in patients with liver cirrhosis. Clin Gastroenterol Hepatol. 2005; 3: 705-713.
6. Muto Y, Sato S, et al. Overweight and obesity increase the risk for liver cancer in patients with liver cirrhosis and long-term oral supplementation with branched-chain amino acid granules inhibits liver carcinogenesis in heavier patients with liver cirrhosis. Hepatol Res. 2006; 35: 204-214.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat.)

Data Science Camp 2

Artificial Intelligence in Hepatology

Chairs:

Jin-Woo Lee (Inha Univ.)
Kang Mo Kim (Univ. of Ulsan)

Seung Soo Lee

University of Ulsan

Self Introduction

Prof. Seung Soo Lee is a professor in the Department of Radiology at the University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea. He specializes in abdominal imaging, with a particular research focus on CT and MR imaging of the hepatobiliary system and quantitative image analysis.

He earned his M.D. from the University of Ulsan College of Medicine in 1997, followed by an M.S. and Ph.D. in Medical Sciences from the same institution. He completed his residency and clinical fellowship in radiology at Asan Medical Center and later served as a visiting scholar at the University of California San Diego.

An active member of the Korean Radiological Society and the Korean Society of Abdominal Radiology, he has contributed to academic research and peer review, serving as a reviewer for journals such as Radiology and the Korean Journal of Radiology. Since 2020, he has also been serving as the Director of International Liaison for the Korean Society of Abdominal Radiology.

Research Interests

Hepatobiliary Imaging, Quantitative Image Analysis

Representative Publications

1. Jeong B, Heo S, Lee SS, et al. Predicting post-hepatectomy liver failure in patients with hepatocellular carcinoma: nomograms based on deep learning analysis of gadoxetic acid-enhanced MRI. Eur Radiol. 2024 Nov 12. Online ahead of print
2. Heo S, Lee SS, Choi SH, et al. CT Rule-in and Rule-out Criteria for Clinically Significant Portal Hypertension in Chronic Liver Disease. Radiology. 2023 Oct;309(1):e231208.
3. Choi SJ, Lee SS, Jung KH, et al. Noncirrhotic Portal Hypertension after Trastuzumab Emtansine in HER2-positive Breast Cancer as Determined by Deep Learning-measured Spleen Volume at CT. Radiology. 2022 Dec;305(3):606-613.
4. Heo S, Lee SS, Kim SY, et al. Prediction of Decompensation and Death in Advanced Chronic Liver Disease Using Deep Learning Analysis of Gadoxetic Acid-Enhanced MRI. Korean J Radiol. 2022 Dec;23(12):1269-1280.
5. Kim DW, Ha J, Lee SS, et al. Population-based and Personalized Reference Intervals for Liver and Spleen Volumes in Healthy Individuals and Those with Viral Hepatitis. Radiology. 2021 Nov;301(2):339-347.

Hepatic Applications of Artificial Intelligence

Seung Soo Lee *University of Ulsan*

Introduction

Imaging plays a pivotal role in evaluating liver diseases, encompassing screening, surveillance, diagnosis, and prognostic assessment of both diffuse liver diseases and liver neoplasms. Traditionally, radiologic assessment has relied on the visual interpretation of images by radiologists. However, recent advancements in artificial intelligence (AI) and computer science have facilitated the automated analysis of radiologic images. Radiomics and deep learning enable diagnostic and predictive tasks by extracting high-dimensional, image-derived features. While conceptually similar, radiomics and deep learning differ in their technical processes. Radiomics employs classical machine learning techniques, requiring expert-defined features and pre-specified feature analysis methods. In contrast, deep learning utilizes representation learning, where the algorithm autonomously identifies the most relevant features for a given task without predefined feature engineering.[1,2] Recently, large language models (LLMs) have garnered attention for their potential applications in radiology.

Radiomics

Radiomics analysis involves multiple processes including image preprocessing, segmentation to define voxel of interest, radiomic feature extraction, feature selection, and building predictive or classification models. Radiomics features include morphologic (semantic) features, first-order histogram features, texture features, and high order features. Since radiomics features are redundant and highly correlated each other, feature selection is a crucial step. Feature selection can be performed as a separate process or along with modeling process. As conventional statistical method cannot effectively deal with high dimensional radiomics features, radiomics models are commonly built using regression analysis with regularization function or machine learning methods.[1,2] Radiomics is an effective method to summarize morphologic or texture features in objective and comprehensive way. Therefore, it has been utilized for liver fibrosis staging based on CT or MR imaging.[3] Based on an assumption that tumor phenotype may reflect its biologic behavior, radiomics has been investigated for prognostication of liver malignancies. Previous studies have demonstrated that radiomics allow for prediction of microvascular invasion in hepatocellular carcinoma (HCC), recurrence after local ablation or surgical resection of HCC, and post-op-

erative prognosis of intrahepatic cholangiocarcinoma.[1,2,4]

Deep Learning

Deep learning has gained attention as a method for automated analysis of medical images, and convolutional neural network (CNN) is the most widespread type of deep learning architecture in medical imaging analysis. Deep learning enabled automated abdominal organ segmentation on CT or MR images with a high accuracy,[5] which would be clinically used in near future. Automated liver and spleen segmentation have diverse clinical applications, including prediction of remnant liver volume prior to liver resection that is a major factor associated with post-operative morbidity. Deep learning algorithms for liver segmentation may be used for the automatic measurement of the quantitative metrics of the whole liver on CT or MR images such as proton density fat fraction. Other potential utilities may include risk assessment of chronic liver disease by using spleen volume which is known to be related with portal hypertension.[6]

Deep learning has also been applied to liver tumor segmentation, while the performance of these algorithms is not satisfactory, probably because of low lesion to liver contrast on CT or MR images. A few prior studies have demonstrated that deep learning is useful for assessing liver fibrosis based on ultrasound, CT, and MR images. Regarding the characterization of focal hepatic lesions, results of a few algorithms have been reported. However, all prior studies on the application of deep learning to liver lesion detection and characterization are considered preliminary, since these earlier reports focused mainly on the technical feasibility of deep learning and used data process not suitable for a real clinical workflow (e.g., decision based on image cropped by radiologists). Furthermore, deep learning has been used to improve CT and MR image quality. The specific applications include reducing respiratory motion artifacts on MR images, improving the quality of under-sampled MR images, and reducing the image noise of low-dose CT images.[1,2]

Large Language Model

LLMs have demonstrated remarkable capabilities in natural language processing and are now being explored for radiologic report management. Their applications in liver imaging include summarizing radiologic reports and generating structured reports from free-text narratives.[7] Recently, an LLM was tested for its ability to extract Liver Imaging Reporting and Data System (LI-RADS) major features and assign LI-RADS categories based on free-text reports, showing promising results.[8] The integration of LLMs with vision models (multimodal LLMs) is an emerging area of interest, with potential applications in automating radiologic report generation directly from imaging data.

Conclusions

Radiomics and deep learning are promising technologies that extend the capabilities of liver imaging beyond traditional visual assessment. These AI-driven approaches may provide additional information from images, which cannot be acquired by classic image analysis, and can facilitate labor-intensive tasks through automated image analysis. With ongoing advancements, the integration of AI into liver radiology has the potential to enhance diagnostic accuracy and clinical decision-making.

References

1. Park HJ, Park B, Lee SS. Radiomics and Deep Learning: Hepatic Applications. Korean J Radiol 2020;21:387-401
2. Sung YS, Park B, Park HJ, Lee SS. Radiomics and deep learning in liver diseases. J Gastroenterol Hepatol 2021;36:561-568
3. Park HJ, Lee SS, Park B, Yun J, Sung YS, Shim WH, et al. Radiomics Analysis of Gadoxetic Acid-enhanced MRI for Staging Liver Fibrosis. Radiology 2019;290:380-387
4. Wei J, Jiang H, Gu D, Niu M, Fu F, Han Y, et al. Radiomics in liver diseases: Current progress and future opportunities. Liver Int 2020;40:2050-2063
5. Ahn Y, Yoon JS, Lee SS, Suk HI, Son JH, Sung YS, et al. Deep Learning Algorithm for Automated Segmentation and Volume Measurement of the Liver and Spleen Using Portal Venous Phase Computed Tomography Images. Korean J Radiol 2020;21:987-997
6. Lee CM, Lee SS, Choi WM, Kim KM, Sung YS, Lee S, et al. An index based on deep learning-measured spleen volume on CT for the assessment of high-risk varix in B-viral compensated cirrhosis. Eur Radiol 2020
7. Bhayana R. Chatbots and Large Language Models in Radiology: A Practical Primer for Clinical and Research Applications. Radiology 2024;310:e232756
8. Gu K, Lee JH, Shin J, Hwang JA, Min JH, Jeong WK, et al. Using GPT-4 for LI-RADS feature extraction and categorization with multilingual free-text reports. Liver Int 2024;44:1578-1587

Beom Kyung Kim

Yonsei University

Self Introduction

Educational

1997-2003	Yonsei University College of Medicine, Seoul, Republic of Korea
2005-2007	Master Degree, Graduate School, Yonsei University College of Medicine, Seoul, Korea
2010-2013	Ph.D., Graduate School, Yonsei University College of Medicine, Seoul, Korea

Summary of Training and Employment

2003.3-2004.2	Intern, Severance Hospital, Yonsei University Health System, Seoul, Korea
2004.3-2008.2	Resident, Department of Internal Medicine, Severance Hospital, Yonsei University Health System, Seoul, Korea
2008.4-2011.4	Military Service as a Doctor
2011.5-2013.2	Fellow (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
2013.3-2018.2	Contract Employment Doctor (Division of Gastroenterology), Severance Hospital, Yonsei University Health System / Assistant Clinical Professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
2018.3-2020.2	Assistant Professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
2020.3-2023.2	Associate Professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
2021.8-2022.7	Visiting Scholar at the NAFLD Research Lab, University of California San Diego, La Jolla, CA, USA
2023.3-Present	Professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Research Interests

Viral Hepatitis, Liver Cirrhosis, and Liver Cancer, Epidemiology of Liver Disease, Pharmacoeconomics in Liver Disease

Representative Publications

1. Kim DS, Kim BK, Lee JS, Lee HW, Park JY, Kim DY, Ahn SH, Pyrsopoulos N, Kim SU. Noninvasive risk assessment of hepatic decompensation in patients with hepatitis B virus-related liver cirrhosis. J Gastroenterol Hepatol. 2023 Aug;38(8):1372-1380. doi: 10.1111/jgh.16210. Epub 2023 May 15.
2. Kim BK. How to deliver palliative care for patients with management in decompensated cirrhosis. Hepatobiliary Surg Nutr. 2023 Aug 1;12(4):576-579
3. Kim BK, Ahn SH. Prediction model of hepatitis B virus-related hepatocellular carcinoma in patients receiving antiviral therapy. J Formos Med Assoc. 2023 Jun 15:S0929-6646(23)00198-5. doi: 10.1016/j.jfma.2023.05.029. Online ahead of print.
4. Kim BK, Bergstrom J, Loomba R, Tamaki N, Izumi N, Nakajima A, Idilman R, Gumussoy M, Oz DK, Erden A, Truong E, Yang JD, Noureddin M, Allen AM, Loomba R, Ajmera V. Magnetic resonance Elastography-Based prediction model for hepatic decompensation in NAFLD; a Multi-Center cohort study. Hepatology. 2023 May 22. doi: 10.1097/HEP.0000000000000470. Online ahead of print.

Artificial Intelligence for Clinical Prediction

Beom Kyung Kim *Yonsei University*

Artificial intelligence (AI) has emerged as a transformative tool in the field of hepatology, offering unprecedented opportunities to enhance clinical prediction across the entire spectrum of liver diseases. Leveraging vast datasets—including electronic health records, laboratory parameters, radiologic and histologic imaging, and multi-omics data—AI models have demonstrated superior performance in predicting key clinical outcomes such as liver fibrosis progression, hepatic decompensation, hepatocellular carcinoma (HCC) development, and post-transplant survival. Machine learning algorithms, including ensemble methods and gradient boosting machines, as well as deep learning frameworks such as convolutional neural networks and recurrent neural networks, are increasingly being employed to capture complex, non-linear relationships among clinical variables that are often missed by traditional statistical models.

In particular, AI-based prediction models have shown considerable promise in detecting advanced fibrosis in patients with metabolic dysfunction-associated steatotic liver disease (MASLD), assessing the risk of esophageal variceal bleeding in cirrhosis, and forecasting HCC occurrence in at-risk populations. Imaging-based AI, especially when applied to ultrasound, CT, and MRI data, enables the automated extraction of radiomic features for early lesion characterization. Natural language processing (NLP) applied to clinical notes further allows for real-time risk stratification in hospital settings. Compared to conventional scores like MELD, Child-Pugh, and FIB-4, AI models offer improved discrimination and calibration, particularly when updated continuously with real-world data.

Despite these advancements, several critical limitations impede the routine clinical implementation of AI in hepatology. One major concern is the generalizability of models, many of which are developed using retrospective, single-center datasets that lack demographic diversity. Additionally, most high-performing models function as "black boxes," limiting their interpretability and hindering physician acceptance in real-time clinical decision-making. The quality and completeness of clinical datasets also remain a significant challenge, with missing values, unstructured data, and inconsistent coding posing threats to model robustness and reproducibility. Moreover, algorithmic bias—often reflecting underlying inequities in healthcare delivery—may exacerbate disparities in liver disease management if not properly addressed. Regulatory frameworks for AI in medicine are still evolving, and few AI models in hepatology have undergone prospective, multi-center validation or received regulatory approval.

Moving forward, collaborative efforts involving clinicians, data scientists, and regulatory bodies are essential to ensure that AI tools are transparent, reproducible, and ethically sound. When thoughtfully developed and responsibly integrated, AI has the potential to reshape the future of liver disease care—enabling earlier diagnosis, dynamic risk prediction, and more personalized treatment strategies.

Jong Chul Ye

KAIST

Self Introduction

Prof. Jong Chul Ye is a Professor at the Kim Jaechul Graduate School of Artificial Intelligence (AI) of Korea Advanced Institute of Science and Technology (KAIST), Korea. He received his B.Sc. and M.Sc. degrees from Seoul National University, Korea, and his PhD from Purdue University.

Before joining KAIST, he worked at Philips Research and GE Global Research in New York. He has served as an associate editor of IEEE Trans. on Image Processing, IEEE Computational Imaging, IEEE Trans. on Medical Imaging and a Senior Editor of IEEE Signal Processing and an editorial board member for Magnetic Resonance in Medicine. He is an IEEE Fellow, was the Chair of IEEE SPS Computational Imaging TC, and IEEE EMBS Distinguished Lecturer. He is the Fellow of the Korean Academy of Science and Technology, and National Academy of Medicine in Korea, and was the President of the Korean Society for Artificial Intelligence in Medicine. He received various awards including Merck Fellow Award, and Choi Suk-Jung Award- one of the most prestigious awards for mathematicians in Korea. His research interest is in generative AI for biomedical imaging and computer vision.

Research Interests

Machine Learning for Healthcare, Generative AI, Computer Vision

Representative Publications

1. Yujin Oh, Sangjoon Park, Hwa Kyung Byun, Yeona Cho, Ik Jae Lee, Jin Sung Kim, and Jong Chul Ye, "LLM-driven Multimodal Target Volume Contouring in Radiation Oncology", Nature Communications 15 (1), 9186,2024.
2. Chang, J., Ye, J.C. Bidirectional generation of structure and properties through a single molecular foundation model. Nat Commun 15, 2323 (2024).
3. Lee, C., Song, G., Kim, H. et al. Deep learning based on parameterized physical forward model for adaptive holographic imaging with unpaired data. Nat Mach Intell 5, 35–45 (2023).
4. Sangjoon Park, Gwanghyun Kim, Yujin Oh, Joon Beom Seo, Sang Min Lee, Jin Hwan Kim, Sungjun Moon, Jae-Kwang Lim, Chang Min Park, Jong Chul Ye, Self-evolving vision transformer for chest X-ray diagnosis through knowledge distillation. Nat Commun 13, 3848 (2022)
5. Park, H., Na, M., Kim, B. et al. Deep learning enables reference-free isotropic super-resolution for volumetric fluorescence microscopy. Nat Commun 13, 3297 (2022).

Imaging Reconstruction by Artificial Intelligence Models

Jong Chul Ye *KAIST*

The field of image reconstruction has undergone a significant transformation with the rise of generative models, particularly diffusion models. These models have demonstrated a remarkable ability to solve ill-posed inverse problems by serving as expressive data priors, enabling the recovery of high-fidelity images even from incomplete, noisy, or undersampled measurements. This generative approach departs from traditional optimization or heuristic-based techniques, shifting the focus toward probabilistic modeling and data-driven synthesis. As a result, diffusion-based inverse solvers have become central to a wide range of applications, including medical imaging.

Despite their impressive success in 2D image restoration, key challenges remain, particularly when extending to higher-dimensional problems and addressing ambiguity in measurement interpretation. One major limitation lies in the difficulty of scaling diffusion models to 3D data due to the curse of dimensionality and the high computational cost of training 3D models from scratch. To address this, recent research has explored strategies that reuse existing 2D diffusion models in novel ways. For example, by deploying two pre-trained 2D models along perpendicular planes and modeling the 3D data distribution as a product of 2D conditional distributions, it is possible to reconstruct volumetric data while avoiding the need for training large-scale 3D networks. This cross-view guidance enables the effective use of 2D generative priors for 3D tasks, opening a path toward efficient 3D reconstruction in practice.

Another critical issue in inverse problems is the inherent ambiguity of the solutions, where multiple plausible reconstructions may exist for the same measurement. Inspired by human visual perception—which often resolves such ambiguities through context, expectation, or bias—emerging methods now incorporate semantic guidance into the reconstruction process. One such approach leverages text prompts to inject prior knowledge or perceptual cues into the generative pipeline. Specifically, during the reverse diffusion process, text-based conditioning guides the model toward solutions that align with semantically meaningful interpretations. This is further refined through techniques such as null-text optimization, which adaptively adjusts the influence of text guidance to reflect dynamic confidence in the reconstruction process.

Building on these ideas, new unified frameworks have been proposed that combine multiple innova-

tions in diffusion modeling. A notable example is DreamSampler, which integrates score distillation—a technique for capturing the gradient flow of diffusion priors—with guided reverse sampling, to balance realism and data fidelity in a principled manner. These hybrid strategies represent a new wave of generative inverse solvers that are not only accurate and robust, but also interpretable and controllable.

In this talk, we survey these recent advancements and present our contributions to the field. Through comprehensive experiments across various inverse problems, we demonstrate that integrating spatial priors, semantic cues, and hybrid generative mechanisms significantly enhances the performance of AI-driven reconstruction systems. These developments mark a promising direction toward general-purpose inverse solvers that can adapt across modalities, dimensions, and application domains.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat.)

KASL Symposium 4

Integrative Approaches to Alcohol-Related Hepatic Disorders

Chairs:

Dominique Damais-Thabut (Sorbonne Univ., France)
Sang Gyune Kim (Soonchunhyang Univ.)

Young Chang

Soonchunhyang University

Self Introduction

Prof. Young Chang is an Assistant Professor of the Department of Internal Medicine, Soonchunhyang University College of Medicine.

She graduated from Seoul National University College of Medicine with her medical degree in 2011 and completed his internship and residency at the Department of Internal Medicine at Seoul National University Hospital, receiving his diploma in Internal Medicine in 2021.

She has been involved in a number of committees, and currently in Scientific Committee and Research Committee of the Korean Association of the Study of the Liver (2023-present), Publication Committee and Primary Liver Cancer Registry Committee of the Korean Liver Cancer Association (2023-present).

Sex and Gender Differences in Alcohol-Associated Liver Disease

Young Chang *Soonchunhyang University*

Alcohol-associated liver disease (ALD) demonstrates marked differences between sexes and genders in epidemiology, pathophysiology, and clinical outcomes, with increasing vulnerability of women. Over the past two decades, the prevalence of alcohol use disorder (AUD) and ALD among women has risen significantly, narrowing the historical gender gap in these conditions.[1] Notably, women tend to develop ALD at a younger age and with less cumulative alcohol exposure than men, and they often experience more severe disease progression.[2] This phenomenon is attributed to a complex interplay of biological and sociocultural factors.

Epidemiological studies indicate that while men still account for the majority of ALD cases globally, the incidence and mortality rates among women are increasing at a faster pace, particularly in high-income countries.[3] Women are at a 50–100% higher risk of developing cirrhosis and suffering liver-related mortality compared to men who consume similar amounts of alcohol.[4] This increased susceptibility is observed across the entire spectrum of ALD, from simple steatosis to advanced stages like alcoholic hepatitis and hepatocellular carcinoma.[5]

The underlying biological mechanisms for these sex differences are multifactorial. Women have lower gastric alcohol dehydrogenase activity, leading to higher systemic alcohol exposure for a given intake.[6] Estrogen appears to exacerbate liver injury by promoting oxidative stress and enhancing pro-inflammatory cytokine production.[7] Additionally, emerging research on the gut-liver axis suggests that sex-specific differences in gut microbiota composition may influence the degree of endotoxin-mediated liver injury, further contributing to the disparity in disease progression.[8]

Clinically, women with alcoholic hepatitis tend to present at a younger age and with higher rates of complications such as ascites, hepatic encephalopathy, and hepatorenal syndrome compared to their male counterparts.[9] While in-hospital mortality rates are similar between sexes, women experience higher rates of readmission and composite mortality within six months post-discharge.[10] These findings point to a more aggressive disease course and greater healthcare burden among women with ALD.

Sociocultural factors also play a significant role. Women with AUD and ALD often face unique psychosocial stressors and mental health comorbidities, which may accelerate disease progression and hinder engagement with treatment.[11] Furthermore, women remain underrepresented in clinical trials for

ALD, resulting in a lack of robust sex-specific evidence to guide therapy.[12] Barriers to seeking help for alcohol-related problems are also more pronounced among women, underscoring the need for gender-sensitive approaches in both prevention and management.

In summary, recent academic literature underscores the urgent necessity for gender-informed strategies in the prevention, early detection, and treatment of ALD. Future research should prioritize understanding the molecular and psychosocial drivers of these disparities and developing tailored interventions that address the unique needs of women affected by alcohol-associated liver disease.

References

1. Grant BF, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry. 2015;72(8):757-766.
2. Erol A, Karpyak VM. Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. Drug Alcohol Depend. 2015;156:1-13.
3. Tapper EB, Parikh ND. Mortality due to cirrhosis and liver cancer in the United States, 1999-2016: observational study. BMJ. 2018;362:k2817.
4. Becker U, et al. Prediction of risk of liver disease by alcohol intake, sex, and age: a prospective population study. Hepatology. 1996;23(5):1025-1029.
5. Liangpunsakul S, Haber P, McCaughan GW. Alcoholic liver disease in Asia, Europe, and North America. Gastroenterology. 2016;150(8):1786-1797.
6. Baraona E, et al. Gender differences in pharmacokinetics of alcohol. Alcohol Clin Exp Res. 2001;25(4):502-507.
7. Wang Y, et al. Sex differences in alcohol-induced liver injury: Estrogen and oxidative stress. Am J Physiol Gastrointest Liver Physiol. 2022;323(2):G149-G158.
8. Bajaj JS, et al. Gut microbiota and the gut-liver axis in alcoholic liver disease. J Hepatol. 2022;76(4):1013-1026.
9. Shah ND, et al. Sex differences in alcoholic hepatitis: Clinical characteristics and outcomes. Hepatology. 2023;77(1):123-134.
10. Tapper EB, et al. Six-month outcomes in patients hospitalized with alcoholic hepatitis: A nationwide cohort study. J Hepatol. 2023;78(2):340-347.
11. Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. Clin Psychol Rev. 2004;24(8):981-1010.
12. Thursz MR, et al. Clinical trials in alcoholic hepatitis: Challenges and opportunities. J Hepatol. 2019;70(2):418-426.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

Barjesh Chander Sharma

Govind Ballabh Pant Hospital, India

Research Experience

Senior Resident (Hepatology)	2 years
DM Resident (Gastroenterology)	3 years
Senior Research Associate (Gastroenterology)	1 year
Assistant Professor (Gastroenterology)	3 years
Associate Professor (Gastroenterology)	5 years
Professor (Gastroenterology)	11 years
Professor (Hepatology)	2 years
Director-Professor	2 years

Research Interests

Chronic Liver Disease, Hepatic Encephalopathy, Portal Hypertension, Acute Cholangitis

Representative Publications

1. Jain A, Sharma BC, Mahajan B, Srivastava S, Kumar A, Sachdeva S, Sonika U, Dalal A. L-ornithine L-aspartate in acute treatment of severe hepatic encephalopathy: A double-blind randomized controlled trial. Hepatology 2022.
2. Sidhu SS, Sharma BC, Goyal O, Kishore H, Kaur N. L-ornithine L-aspartate in bouts of overt hepatic encephalopathy. Hepatology 2017.
3. Sharma BC, Maharshi S. Prevention of recurrence of hepatic encephalopathy. Clin Liver Dis 2015.
4. Maharshi S, Sharma BC, Srivastava S, Jindal A. Randomized controlled trial of lactulose versus rifaximin for prophylaxis of hepatic encephalopathy in patients with acute variceal bleed. Gut 2014.
5. Sharma BC, Sharma P, Lunia MK, Srivastava S, Goyal R, Sarin SK. A randomized double-blind controlled trial comparing rifaximin plus lactulose with lactulose alone in treatment of overt hepatic encephalopathy. Am J Gastroenterol 2013.
6. Sharma BC, Sharma P, Agrawal A, Sarin SK. Secondary prophylaxis of hepatic encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. Gastroenterology 2009.

Altered Mental Status in Alcoholic Cirrhosis: Etiologies other than Hepatic Encephalopathy

Barjesh Chander Sharma *Govind Ballabh Pant Hospital, India*

Hepatic Encephalopathy is defined as a spectrum of neuropsychiatric abnormalities seen in patients with liver dysfunction after exclusion of other known brain diseases. This definition does not take into account all the potential causes of altered mental status in patients with cirrhosis. Altered mentation may be impaired because of common clinical events besides HE.

Altered mental status is defined as having any of the followings : impaired cognition, diminished attention, reduced awareness, and/or altered level of consciousness and not all patients of cirrhosis with altered mental status are HE. These changes may be gradual or sudden in onset, fluctuating or sustained with an acute or chronic duration. Altered mental status has been reported to be present in 4% to 10% of patients, and mental status abnormalities are particularly common in older patients (up to 40%) and alcohol related liver disease. These neurological disorders in patients with alcohol related liver disease are usually overlooked resulting in delay in diagnosis, initiating appropriate treatment and referral to neurologists leading to increased risk of morbidity and mortality. In some of these neurological manifestations, early diagnosis and treatment can lead to full recovery. Patients with alcohol related liver disease can suffer from altered mental status due to central nervous system involvement like hepatic encephalopathy, acute alcohol intoxication, alcohol withdrawal syndrome, Wernicke encephalopathy, Korsakoff syndrome, cerebellar degeneration and dementia. Other causes of altered mental status in patients with chronic alcohol consumption can be uremic encephalopathy, raised intracranial pressure, meningitis and encephalitis. The abnormalities of central nervous system functions in patients with alcohol related liver disease can be due to chronic alcohol consumption related nutritional deficiencies affecting brain. In addition there are functional and structural central nervous system abnormalities secondary to porto-systemic shunting in cirrhosis.

There are bidirectional communications between normal brain and gut in which neurons, glial cells, neurotransmitters, neuro-trophic factors, vagal nerves, and receptors are in homeostatic conditions via the immune system. Alcohol consumption disrupts the homeostatic conditions causing neuroinflammation. Alcohol transforms resting microglia to the activated stage which induces transcription factors, leading to increase in levels of proinflammatory cytokines and decrease in anti-inflammatory cytokines.

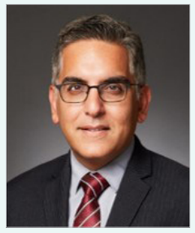
In a retrospective study on 1218 patients with cirrhosis, 29% had altered mental status. The most com-

mon cause of altered mental status was HE accounting for half of patients followed by sepsis or infection as the next most common cause whereas remaining had metabolic or structural etiologies. The overall mortality among patients of cirrhosis presenting with altered mental status was significantly higher than in those with normal mental status. Patients with HE, metabolic derangements and drug or toxin ingestion had significantly better outcomes than those with structural lesions or sepsis/infections. Structural lesions of brain in cirrhosis with altered mental status are uncommon and have focal neurological deficits like aphasia, facial nerve palsy, hemiplegia, seizures and decortication. There is 24% increase in life long risk of strokes in cirrhosis including ischemic strokes, intracranial heamorrhage and sub-arachnoid heamorrhage with associated higher mortality as compared to cirrhosis without strokes. CT head is recommended in patients with history of trauma or focal neurological deficits on clinical examination. Other causes of altered mental status in cirrhosis include non-convulsive status epilepticus and dementia. Acute HE with focal neurological signs have been reported in 25% of typical HE patents having transient asymmetry of neurological signs. Focal neurological signs observed in HE may be hemiplegia, hemiparesis, hemiagnosia and monoplegia and the CT scan showed cortical atrophy without structural lesion.

To summarise one-third of patients with cirrhosis are admitted with altered mental status. The common causes of altered mental status are hepatic encephalopathy, infections and metabolic disorders with higher mortality than in patients with normal mental status. Mortality is higher in cirrhotics with structural lesions of brain or infections or combination of causes of altered mental status. At admission cirrhotics with altered mental status, causes other than HE should be ruled out.

References

1. Nath P, Anand AC. Extrahepatic manifestations in alcoholic liver disease. J Clin and Exptl Hepatol 2022; 12 (5): 1371-83.
2. Khan MA, Chang SL. Alcohol and the brain–gut axis: the involvement of microglia and enteric glia in the process of neuro-enteric inflammation. Cells 2023; 12 (20): 2475.
3. Rahimi RS, Elliott AC, Rockey DC. Altered mental status in cirrhosis: etiologies and outcomes. Journal Investigative Medicine 2013; 61 (4): 695-700.
4. Rahimi RS, Rockey DC. Overuse of head computed tomography in cirrhosis with altered mental status. Am J Medical Sciences 2016; 351 (5): 459-66.
5. Bajaj JS, Silvey SG, Rogal S, O'Leary JG, Patton H, Morgan TR, Kanagalingam G, Gentili A, Godschalk M, Patel N. Undiagnosed cirrhosis and hepatic encephalopathy in a national cohort of veterans with dementia. JAMA Network Open 2024; 7 (1): e2353965-.
6. Hanna A, Gill I, Imam Z, Halalau A, Jamil LH. Low yield of head CT in cirrhotic patients presenting with hepatic encephalopathy. BMJ Open Gastroenterology 2021; 8 (1):e000609.
7. Bajaj JS, Gentili A, Wade JB, Godschalk M. Specific challenges in geriatric cirrhosis and hepatic encephalopathy. Clin Gastroenterol Hepatol 2022; 20 (8): S 20-9.
8. Nguyen A, Butt MA, Upadhyay S, Sheikh AB, Shekhar R. Non-convulsive status epilepticus in hepatic encephalopathy: a case series and review of the literature. Eur J Case Reports Intern Med 2022; 9 (2): 003179.



Sumeet Asrani

Baylor University, USA

Self Introduction

Dr. Sumeet Asrani, MD, MSc is the Chief of Hepatology and Liver Transplantation at the Baylor Simmons Transplant Institute in Dallas and Fort Worth. He received his medical degree from Baylor College of Medicine in Houston. He did his internship and residency at Washington University School of Medicine in St. Louis, MO. He went on to complete fellowships in gastroenterology, hepatology and transplant hepatology at the Mayo Clinic in Rochester, Minnesota before joining the transplant hepatology team at Baylor University Medical Center in 2013.

He has published over 200 peer reviewed publications and has mentored more than 35 trainees to help advance their medical careers. He previously served as an associate editor for the American Journal of Transplantation (AJT) and as an associate editor for Liver Transplantation (LT). He is actively involved in national and international collaborations to improve care for patients with liver disease and authored AASLD guidelines on non-invasive liver disease assessment and acute on chronic liver failure.

Research Interests

Alcohol Associated Liver Disease, Kidney Dysfunction and Cirrhosis, Liver Transplantation Predictive Models, Critically Ill Cirrhosis

Representative Publications

1. Burden of liver diseases in the world
2. Development of quality measures in cirrhosis by the Practice Metrics Committee of the American Association for the Study of Liver Diseases
3. Reducing the global burden of alcohol - associated liver disease: a blueprint for action
4. Meeting report: the Dallas consensus conference on liver transplantation for alcohol associated hepatitis
5. AASLD Practice Guidance on Acute-on-chronic liver failure and the management of critically ill patients with cirrhosis

KASL Symposium 4 | DAY 3: May 31 (Sat.) | ROOM 4 [2F]

Emerging Regimens Competing with Glucocorticoids for Severe Alcoholic Hepatitis

Sumeet Asrani *Baylor University, USA*

Steroids remain the main stay of treatment for alcohol associated hepatitis and still has a limited roles with regards to improvement in short term mortality. Over the years there have been several other agents that also have been studied.

Select cases: In select cases, antibiotics and/or n-acetylcysteine may play a role.

Did not improve outcomes: TNF as well as IL1 blockade have not shown improvement in outcomes in patients with AH Agents include Anakinra + zinc, Canakinumab, Ethanercept (TNFa) and Infliximab.

New agent: Larsucosterol with our without steroids may play a role in select patients with AH, but further study is planned.

Other modalities: Fecal microbiota transplantation as well as G-CSF administration has been studied

Other treatments to consider in AH is early liver transplantation. After admission for AH, linkage is needed for treatment comorbid obesity, diabetes as well as linking for care for the alcohol use disorder.

References

Shiffman et al. Larsucosterol for the Treatment of Alcohol-Associated Hepatitis. NEJM Evid 2025

Seong Hee Kang

Korea University

Self Introduction

Educational

Bachelor, Korea University, College of Medicine
Master's Degree of Medicine, Korea University, Graduate School of Medicine
Doctor's Degree of Medicine, Korea University, Graduate School of Medicine

Professional Experience

Associate Professor, Korea University College of Medicine

Research Interests

Nonalcoholic Fatty Liver Disease, Alcoholic Hepatitis, Portal Hypertension, Hepatocellular Carcinoma

Representative Publications

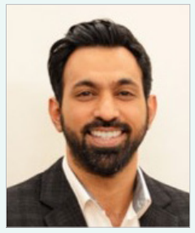
1. Outcome of Intermittent Thoracentesis versus Pigtail Catheter Drainage for Hepatic Hydrothorax, 2022.12.01
2. Long-Term Prediction Model for Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Receiving Antiviral Therapy: Based on Data from Korean Patients, 2022.11.01
3. Improved anti-fibrotic effects by combined treatments of simvastatin and NS-398 in experimental liver fibrosis models, 2022.07.01
4. Autoimmune Hepatitis Following Vaccination for SARS-Cov-2 in Korea: Coincidence or Autoimmunity?, 2022.04.01
5. Association between chronic hepatitis B infection and COVID-19 outcomes: a Korean nationwide cohort study, 2021.10.01
6. KASL clinical practice guidelines: Management of nonalcoholic fatty liver disease, 2021.07.01
7. From nonalcoholic fatty liver disease to metabolic-associated fatty liver disease: Big wave or ripple?, 2021.04.01
8. The longitudinal outcomes of applying non-selective beta-blockers in portal hypertension: real-world multicenter study, 2021.04.01

KASL Symposium 4 | DAY 3: May 31 (Sat.) | ROOM 4 [2F]

Multidisciplinary Approaches to Treat Alcohol-Associated Liver Disease

Seong Hee Kang *Korea University*

Alcohol-associated liver disease (ALD) is a leading cause of liver-related morbidity and mortality and has become the most common indication for liver transplantation in the United States. ALD spans from steatosis and alcoholic hepatitis to cirrhosis and liver failure. It is a leading cause of liver-related death globally and is rooted in alcohol use disorder (AUD). As such, effective management requires both hepatologic and psychiatric care. ALD is fundamentally driven by AUD, a chronic and often stigmatized condition frequently accompanied by psychiatric comorbidities. Although effective pharmacologic and behavioral treatments for AUD exist, most patients with ALD and AUD do not receive them. This review outlines the importance of integrating AUD treatment into ALD care, including the role of screening, alcohol withdrawal management, and relapse prevention strategies. We discuss pharmacologic options such as naltrexone and acamprosate, as well as psychosocial interventions like cognitive behavioral therapy and motivational enhancement therapy. We also explore multidisciplinary transplant models and structured scoring systems to assess relapse risk. Co-located and collaborative care models are emerging as effective strategies to improve outcomes, reduce relapse, and address the complex needs of this population.



Shashwat Sarin

Max Hospital, India

Self Introduction

Dr. Sarin did his M.Ch. in HPB Surgery and Liver Transplantation from the Institute of Liver and Biliary Sciences. He then trained as a Clinical Fellow in Istanbul (2019–2020) under Prof. Yaman Tokat. From 2020–2022, as Assistant Professor at Mahatma Gandhi University, Jaipur, India he started the liver transplant program and grew it to be the largest program in the state. He subsequently worked at Dr Rela Insitute and Medical Center, Chennai (2022–2023) and trained in robotic living-donor liver transplant. Since September 2023, he serves as Senior Consultant at Max Hospital Saket, India's highest-volume liver center. (>450 liver trasplants annually)

Research Interests

Living Donor Liver Transplant, Minimally Invasive and Robotic Donor Hepatectomy,
Ischemia Reperfusion Injury, Biomarkers in Acute Cellular Rejection, Gal Bladder Cancer

Representative Publications

1. Practices in the Management of Incidental Gallbladder Cancer South Asian JCancer 2023;00(00)., Peeyush Varshney, Anand Nagar, Shashwat Sarin, Krishnavardhan Venkatatelikicherla, Maunil Tomar, R.P. Choubey, Ajay Sharma, V.K. Kapoor
2. Pancreas-preserving limited duodenal resection: Minimizing morbidity without compromising oncological adequacy Ann Hepatobiliary Pancreat Surg. 2022 May 31; 26(2): 149–158.
3. Ajay Sharma, Anand Nagar, Peeyush Varshney, Maunil Tomar, Shashwat Sarin, Rajendra Prasad Choubey, and V. K. Kapoor
4. Neutrophil Lymphocyte Ratio can Preempt Development of Sepsis After Adult Living Donor Liver Transplantation, Journal of Clinical and Experimental Hepatology, Nov 21, S Sarin, Viniyendra Pamecha, Piyush K.Sinha
5. Technical Advancements in Living Donor Liver Transplant., Surg. Gastroenterol. Oncol. 2021;26(1):61-75., S Sarin, Ramazan Dönmez, Yaman Tokat
6. Impact of Human Leukocyte Antigen compatibility on outcomes of living donor liver transplantation: Experience from a tertiary care centre., Transpl Infect Dis 2021 May., S. Mittal, P Sinha, S Sarin, A Rastogi, V Pamecha, N Trehanpati

Specific Management of Portal Hypertension before and after Liver Transplantation

Shashwat Sarin *Max Hospital, India*

1. Introduction

Portal hypertension (PHT) is present in virtually all adults with end-stage liver disease awaiting transplantation. Its complications—variceal bleeding, ascites, hyponatremia, hepatorenal syndrome, portal vein thrombosis, and hypersplenism—significantly increase peri-operative risk and can compromise graft function. A multidisciplinary, phased approach to PHT management optimizes patient status before surgery, enhances intraoperative safety, and reduces post - transplant complications such as small - for - size syndrome.

2. Pre-Transplant Management

2.1 Variceal Bleeding

- Non-selective β-blockers (NSBBs)
  - o Reduce portal pressure and bleeding risk, but may blunt sympathetic compensation.
  - o Discontinue 3–5 days prior to transplant to avoid intraoperative hypotension and renal hypoperfusion.
- Endoscopic variceal ligation (EVL)
  - o Effective for acute bleed control.
  - o Avoid elective EVL within 2 weeks of surgery to prevent post - banding ulcer complications.

2.2 Ascites & Paracentesis

- Assessment & Drainage
  - o Grade ascites (tense, moderate, mild) and screen for spontaneous bacterial peritonitis (SBP).
  - o Large - volume paracentesis before transplant reduces abdominal wall tension, facilitating exposure.
- Preventing Paracentesis - Induced Circulatory Dysfunction (PICD)
  - o Administer intravenous albumin (6–8 g per litre of fluid removed), or albumin + terlipressin/midodrine.

2.3 Hyponatremia

- Definition & Risks

- Serum Na□ < 135 mmol/L; severe if < 125. Associated with increased cerebral edema and post-op complications.

- Correction Strategy
  - Fluid restriction (1–1.5 L/day), hypertonic saline for sNa□ < 110 mmol/L or severe symptoms.
  - Albumin infusion and vasopressin antagonists (e.g., tolvaptan) as adjuncts.
  - Strict monitoring: check sNa□ every 4–6 h; limit rise to ≤ 8 mmol/L per 24 h.

2.4 Hepatorenal Syndrome (HRS)

- Diagnosis
  - HRS-AKI: rapid rise in creatinine (≥ 0.3 mg/dL in 48 h or ≥ 50% to ≥ 1.5 mg/dL) after excluding other causes and failing an albumin challenge (1 g/kg for 2 days).

- Treatment
  - Albumin: 1 g/kg day 1, then 20–40 g/day.
  - Vasoconstrictors:
    - Terlipressin (0.5–1 mg IV q4–6 h), first-line.
    - Norepinephrine (0.5–3 μg/kg/min) in ICU for refractory cases.
    - Midodrine + Octreotide if terlipressin unavailable.
  - Early CRRT or TIPS in selected candidates.

2.5 Portal Vein Thrombosis (PVT)

- Anticoagulation
  - Indicated in all liver transplant candidates with PVT.
  - Start with LMWH, transition to VKA or DOAC.
  - Continue until recanalization (mean 5–6 months); two-thirds recanalize within 3–6 months.
  - Discontinue 24 h before surgery.

2.6 Hypersplenism

- When to Treat
  - Symptomatic cytopenias (platelets < 60 × 10□/L, refractory anemia/neutropenia) or massive splenomegaly causing discomfort.

- Interventions
  - Partial splenic embolization (60–70% infarction).
  - Splenectomy for definitive correction.
  - Schedule 2–4 weeks pre-transplant; vaccinate against encapsulated organisms if splenectomy planned.

3. Intraoperative Strategies

- Early Portocaval Shunt
  - Rapid portal decompression during hepatectomy.

- Graft Inflow Modulation
  - Splenic Artery Ligation (SAL): reduces portal pressure by ~ 25–40%; simple and effective first line.
  - Target portal pressure < 15 mmHg and portal flow < 250 mL/min/100 g to prevent small-for-size syndrome.

4. Post-Transplant Considerations

- Technical Causes of Persistent PHT
  - Outflow obstruction (hepatic vein or caval)
  - New/persistent PVT.

- Small for Size syndrome – portal hyperperfusion

- Management
  - Prompt imaging and interventional correction of stenosis or thrombosis.
  - Medical Management – pharmacological methods to reduce portal hyperperfusion
  - Failure – interventional radiology and surgical methods consider delayed or staged inflow modulation.

5. Take-Home Message

A systematic, staged approach—encompassing medical therapy, radiologic interventions, and surgical techniques—is essential to minimize

Selected references

1. de Franchis R, Primignani M. Management of portal hypertension. Clin Liver Dis. 2017;21(3):555–584.
2. Garcia-Tsao G, et al. Portal hypertension and varices: Consensus Care Recommendations. Hepatology. 2022;76:456–473.
3. Biggins SW, Kim WR, et al. Incorporating serum sodium into MELD. Gastroenterology. 2006;130:1652–1660.
4. Angeli P, et al. Diagnosis and management of HRS in cirrhosis. J Hepatol. 2019;71(2):406–422.
5. Nery F, et al. Vaptans in cirrhotic hyponatremia: Efficacy and safety. Hepatology. 2020;72(1):105–116.
6. Senzolo M, et al. Partial splenic embolization in portal hypertension. Dig Liver Dis. 2012;44(6):454–459.
7. Senzolo M, et al. Role of anticoagulation in PVT management. Eur J Gastroenterol Hepatol. 2017;29(5):568–575.

THE A Big Welcome to the Liver Festival in Gyeongju, Korea!
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DAY 3: May 31 (Sat.)

KASL Special Interest Group 6.
The KASL Alcohol-Related Problem Study Group

KASL-BATL Joint Session: Alcohol and Environmental Cues in Liver Disease

Chairs:

Yoon Mee Yang (Kangwon National Univ.)
Wonhyo Seo (Ewha Womans Univ.)

Won-Il Jeong

KAIST

Self Introduction

Education

1992.03-1999.02 Doctor of Veterinary Medicine (D.V.M), College of Veterinary Medicine, Kyungpook National University, Daegu, Korea
1999.03-2001.02 M.S., Department of Pathology, College of Veterinary Medicine, Kyungpook National University, Daegu, Korea
2001.03-2004.02 Ph.D., Department of Pathology, College of Veterinary Medicine, Kyungpook National University, Daegu, Korea

Career

2004.03-2005.02 Post-Doc of the Brain Korea 21 Project in 2003, Kyungpook National University, Daegu, Korea
2005.02-2008.11 Visiting Fellow, NIAAA/National Institutes of Health, Bethesda, MD, U.S.A.
2008.12-2012.08 Assistant professor, KAIST, Daejeon, Korea.
2012.09-2019.08 Associate professor, KAIST, Daejeon, Korea
2019.09-Present: Professor, KAIST, Daejeon, Korea

Research Interests

Alcohol-Associated Liver Disease (ALD), Steatotic Liver Disease (SLD), Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Liver Fibrosis, Hepatocellular Carcinoma, Liver Immunology, Liver Neurology

Representative Publications

1. CX3CR1+ macrophages interact with HSCs to promote HCC through CD8+ T-cell suppression.Hepatology. 2024.
2. Body Temperature-Responsive, Stiffness-Varying and Non-Reusable Intravenous Needle with On-Site Temperature Sensing for Improved Patient Care. Nature Biomedical Engineering, 2023.
3. xCT-mediated glutamate excretion in white adipocytes stimulates interferon-γ production by natural killer cells in obesity. Cell Reports, 2023.
4. Catecholamine induces Kupffer cell apoptosis via growth differentiation factor 15 in alcohol-associated liver disease. Experimental and Molecular Medicine, 2022.
5. Metabotropic glutamate receptor 5 in natural killer cells attenuates liver fibrosis by exerting cytotoxicity to activated stellate cells. Hepatology, 2021.
6. Mitochondrial double-stranded RNA in exosome promotes interleukin-17 production through toll-like receptor 3 in alcoholic liver injury. Hepatology, 2020.
7. Glutamate signaling in hepatic stellate cells drives alcoholic steatosis. Cell Metabolism, 2019.

Hepatic Glutamate Signaling Pathway in Alcohol-Associated Liver Disease

Won-Il Jeong *KAIST*

Traditionally, alcohol-related liver disease (ALD) is induced by multiple factors that occur during various metabolic processes of hepatocyte, diverse absorption of pathogen- or damage-associated molecular patterns (PAMS or DAMPs) from intestine, and delivery of free fatty acids and pro-inflammatory cytokines from adipose tissue. These factors cause fat accumulation in hepatocyte at early stage but continuous drinking promotes more serious diseases such as inflammation, fibrosis and even tumor. However, interestingly, our research team recently discovered the existence of glutamatergic signaling pathways in the liver and reported that ALD can be occurred by them.[1-3] Briefly, we have revealed that chronic alcohol consumption increases glutamate production especially by aldehyde dehydrogenase 4 family member A1 (ALDH4A1) enzyme in hepatocyte, and generated hepatic glutamate is stored within the hepatocytes, and then secreted through xCT or granules.[1] Simultaneously, metabotropic glutamate receptor 5 (mGluR5) is expressed in various non-parenchymal cells (NPCs) and exerts pathophysiological effects through interaction with secreted glutamate. In addition, released glutamate is mainly absorbed by hepatocytes and NPCs. Today, I would like to briefly introduce the roles of hepatic glutamate, as a hepatotransmitter,[4] in inducing alcohol-associated steatohepatitis (ASH).

Glutamate, a crucial player in hepatic amino acid metabolism, has been relatively unexplored in the development of alcohol-associated steatohepatitis (ASH). Our research reveals that chronic alcohol consumption induces the formation of hepatic glutamate vesicles, driven by the aryl hydrocarbon receptor-mediated expression of vesicular glutamate transporter 3 (VGLUT3). Simultaneously, alcohol-induced changes, including perivenous hepatocyte ballooning, microvilli loss, and mitochondrial Ca^{2+} accumulation, bring Kupffer cells (KCs) into close contact with ballooned hepatocytes. Additional binge drinking triggers the exocytosis of glutamate vesicles by altering intracellular Ca^{2+} level, consequently activating NADPH oxidase 2 (NOX2) through metabotropic glutamate receptor 5 (mGluR5) in KCs which induces ROS production and promotes ASH. Accordingly, genetic or pharmacological interference of mGluR5 and NOX2 in KCs attenuates ASH. In patients, plasma glutamate and VGLUT3 vesicles correlate with ASH development. Conclusively, our findings posit that hepatocytes and KCs form a pseudosynapse through which glutamatergic signaling may induce ASH.

References

1. Choi WM, Kim HH, Kim MH, Cinar R, Yi HS, Eun HS, Kim SH, et al. Glutamate Signaling in Hepatic Stellate Cells Drives Alcoholic Steatosis. Cell Metab 2019;30:877-889 e877.
2. Choi WM, Ryu T, Lee JH, Shim YR, Kim MH, Kim HH, Kim YE, et al. Metabotropic Glutamate Receptor 5 in Natural Killer Cells Attenuates Liver Fibrosis by Exerting Cytotoxicity to Activated Stellate Cells. Hepatology 2021;74:2170-2185.
3. Choi WM, Eun HS, Lee YS, Kim SJ, Kim MH, Lee JH, Shim YR, et al. Experimental Applications of in situ Liver Perfusion Machinery for the Study of Liver Disease. Mol Cells 2019;42:45-55.
4. Woo C, Jeong WI. Immunopathogenesis of liver fibrosis in steatotic liver disease. Clin Mol Hepatol 2024;30:299-302.

Chang Yeob Han

Jeonbuk National University

Self Introduction

Prof. Chang-Yeob Han is an Associate Professor at the School of Pharmacy, Jeonbuk National University.

He graduated from Chosun University College of Pharmacy with his pharmacy degree in 2006 and received his Ph.D. degree at Seoul National University College of Pharmacy in 2015. From 2017 to 2019, he worked as an Assistant Professor at Wonkwang University School of Medicine. Since 2020, he has been a faculty member at Jeonbuk National University.

He has taken roles and participates in several societies, including the Pharmaceutical Society of Korea and the Korean Association for the Study of the Liver.

Research Interests

- Cellular and Molecular Mechanisms for the Pathogenesis of Liver Diseases (MASLD, Fibrosis) and Metabolic Disorders (Obesity, Diabetes/IR)
- Role of Organ-to-Organ / Cell-to-Cell Crosstalk in Liver and Metabolic Diseases
- Regulation of Iron Homeostasis and Iron-Overload Diseases
- Pathophysiology of Organelles (ER, Mitochondria, Lipid Droplet, Peroxisome)
- Discovery of Novel Targets and Candidate Compounds for Metabolic Diseases

Representative Publications

1. Song MY*, Han CY*, Moon YJ, Lee JH, Bae EJ#, Park BH#. (2022) Sirt6 reprograms myofibers to oxidative type through CREB-dependent Sox6 suppression. Nat Commun. 13(1):1808. (*,#equal contribution).
2. Mao Y*, Han CY*, Hao L, Lee Y, Son JB, Choi H, Lee MR, Yang JD, Hong SK, Suh KS, Yu HC, Kim ND#, Bae EJ#, Park BH#. (2022) p21-activated kinase 4 inhibition protects against liver ischemia/reperfusion injury: Role of nuclear factor erythroid 2-related factor 2 phosphorylation. Hepatology. 76(2):345-356. (*,#equal contribution).
3. Han CY, Rho HS, Kim A, Kim TH, Jang K, Jun DW, Kim JW, Kim B, Kim SG. (2018) FXR Inhibits Endoplasmic Reticulum Stress-Induced NLRP3 Inflammasome in Hepatocytes and Ameliorates Liver Injury. Cell Rep. 24(11):2985-2999.
4. Han CY, Koo JH, Kim SH, Gardenghi S, Rivella S, Strnad P, Hwang SJ, Kim SG. (2016) Hepcidin inhibits Smad3 phosphorylation in hepatic stellate cells by impeding ferroportin-mediated regulation of Akt. Nat Commun. 7:13817.
5. Han CY, Lim SW, Koo JH, Kim W, Kim SG. (2016) PHLDA3 overexpression in hepatocytes by endoplasmic reticulum stress via IRE1–Xbp1s pathway expedites liver injury. Gut. 65(8):1377-88.

IRONing Out MASLD: Hepatocyte Messages to Adipose Tissue

Chang Yeob Han *Jeonbuk National University*

The global incidence of metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), has been steadily rising, making it a significant health concern. Despite its high prevalence and the increasing efforts to develop effective therapeutic strategies, current treatment options remain extremely limited, largely due to the disease's highly complex pathogenesis and heterogeneity. The strong epidemiological associations between MASLD and metabolic disorders imply a significant pathophysiological connection. Emerging evidence suggests that the liver also functions as an endocrine organ, secreting bioactive molecules, hepatokines, that facilitate inter-organ communication in metabolic regulation. The expression of various hepatokines is altered in metabolic disease conditions, exerting either beneficial or detrimental effects. However, despite their potential roles in the pathogenesis of metabolic disorders, the factors and stimuli responsible for specific hepatokine dysregulation remain poorly understood. Growing clinical evidence suggests that iron accumulation is a risk factor for MASLD and metabolic disorders, including type 2 diabetes. Although the liver is a major organ responsible for iron homeostasis, little is known about the roles of hepatocyte iron and its regulatory genes in systemic metabolic dysfunction. In this study, we aimed to address these knowledge gaps by investigating the mechanistic basis for the potential link between hepatic iron overload and metabolic dysfunction in MASLD.

References

1. Lazarus, J. V. et al. A global research priority agenda to advance public health responses to fatty liver disease. Journal of hepatology 79, 618-634, (2023).
2. Stefan, N., Yki-Järvinen, H. & Neuschwander-Tetri, B. A. Metabolic dysfunction-associated steatotic liver disease: heterogeneous pathomechanisms and effectiveness of metabolism-based treatment. The lancet. Diabetes & endocrinology 13, 134-148, (2025).
3. Stefan, N., Schick, F., Birkenfeld, A. L., Häring, H. U. & White, M. F. The role of hepatokines in NAFLD. Cell metabolism 35, 236-252, (2023).
4. Muckenthaler, M. U., Rivella, S., Hentze, M. W. & Galy, B. A Red Carpet for Iron Metabolism. Cell 168, 344-361, (2017).
5. Dongiovanni, P., Fracanzani, A. L., Fargion, S. & Valenti, L. Iron in fatty liver and in the metabolic syndrome: a promising therapeutic target. Journal of hepatology 55, 920-932, (2011).

Yong-Hyun Han

Kangwon National University

Self Introduction

Prof. Yong-Hyun Han is Assistant Professor of the College of Pharmacy at Kangwon National University and is currently member of Scientific Committee of the Korean Association for the Study of the Liver.

He graduated from Kangwon National University College of Pharmacy with his BS degree in 2011 and completed his PhD degree at the College of Pharmacy at Seoul National University in 2018.

Currently, he is Associate Editor of the Gut and Liver Journal (2024-).

Research Interests

- Identification of Roles of Liver Macrophage Heterogeneity in Liver Disease
- Novel Findings of Functional Endotoxin Neutralizer in Portal Vein such as Immune Cell, Lipid Metabolites and Microbiome
- Deciphering Roles of Adaptive Immunity System to Modulate Liver Pathology (B and T lymphocyte)
- Finding Drug Candidates Targeting NLRP3 Inflammasome

Representative Publications

1. Kim DH*, Choi G*, Song EB*, Lee H*, Kim J*, Jang YS, Park J, Chi S, Han J, Kim SM, Kim D, Bae SH, Lee HW, Park JY, Kang SG#, Cha SH#, Han YH#. Treatment of IL-18 binding protein biologics suppresses fibrotic progression in metabolic dysfunction-associated steatohepatitis. Cell Rep Med. (2025) Feb 15 [IF=11.7]
2. Kim DH, Lee KJ, Park J, Chi S, Han J, Bang Y, Kim SM, Kang SG#, Cha SH#, Han YH#. Disruption of IL-18 signaling via engineered IL-18BP biologics alleviates experimental cholestatic liver disease. Biomed Pharmacother. (2023) Nov;167:115587 [IF=6.9]
3. Han YH*, Onufer EJ, Huang LH, Sprung RW, Davidson WS, Czepielewski RS, Wohltmann M, Sorci-Thomas MG, Warner BW, Randolph GJ*. Enterically derived high-density lipoprotein restrains liver injury through the portal vein. Science, (2021) July 23;373:eabe6729 [IF=44.8]
4. Han YH, Shin KO, Khadka D, Kim JY, Kim HJ, Cho WJ, Cha JY, Lee YM, Lee BJ, Lee MO. A maresin 1/ROR α/12-lipoxygenase autoregulatory circuit prevents inflammation and progression of nonalcoholic steatohepatitis. J Clin Invest, (2019) Mar 11;130:1684-1698 [IF=13.3]
5. Han YH, Kim DK, Na TY, Ka NL, Choi HS, Lee MO. ROR α switches transcriptional mode of ERR γ that results in transcriptional repression of CYP2E1 under ethanol-exposure. Nucleic Acids Res, (2016) Feb 18;44:1095-1104 [IF=16.7]

Calibration of Gut-Liver Axis via Bile Acid and Neutrophils

Yong-Hyun Han *Kangwon National University*

The portal venous system serves as a critical passage for gut-derived microbes and metabolites entering into the liver, but its immune landscape remains largely unexplored. Here, we identify a distinct subset of CXCR4hi aged neutrophils enriched in the portal circulation with enhanced phagocytic capacity. Mechanistically, bile acid homeostasis orchestrates clustering of defensive neutrophil within ileal submucosal vasculature by promoting CXCL12-CXCR4 axis. Disruption of portal aged neutrophil accumulation enhances hepatic translocation of foreign substances, and accelerates progression liver fibrosis. In contrast, augmenting CXCR4-driven recruitment of aged neutrophils in portal venous system reinforces a pre-hepatic immune barrier and mitigates fibrotic progression. These findings uncover that bile acid-modulated trafficking of aged neutrophils at the gut–liver axis orchestrates immune surveillance and protects hepatic integrity. Additionally, this work uncovers a critical mechanism linking gut-derived toxins to liver immunity and fibrosis, emphasizing portal aged neutrophils as key sentinels in maintaining hepatic homeostasis.

Shuji Terai

Niigata University, Japan

Self Introduction

Prof. Terai graduated Yamaguchi University Medical school. He got Ph.D. degree at Yamaguchi University in 1997. After getting Ph.D., He joined LEC/NCI/NIH(USA) Postgraduate Training as Guest Researcher (Chief: Dr. Snorri S. Thorgeirsson) (1998-2000). During his stay in LEC/NCI, he cloned Helix-Loop-Helix transcriptional regulator, human homologue of Maid (HHM) gene. HHM regulates hepatic progenitor cell. Recently HHM is also found as a synexpression group-restricted regulator of TGF-beta signaling.

After come back to Yamaguchi University, Japan, Prof. Terai started a basic study to develop a cell therapy using bone marrow cell for liver cirrhosis. After getting the results of basic study which showed bone marrow cell therapy improved liver fibrosis and improved liver function, he got the proof of concept to develop an autologous bone marrow cell infusion therapy (ABMi) therapy for liver cirrhosis patients. He started the first clinical study from 2003. The effectiveness and safety of ABMi therapy was reported in Stem Cells 2006.

In January 2015, Prof. Terai was selected as a Chairman & Professor, Division of Gastroenterology & Hepatology, Graduate School of Medical and Dental Sciences, Now he is proceeding to develop next generative stem cell therapy using allogenic stem cell for liver cirrhosis. In September 2017, He started clinical trial allogenic MSC therapy for decompensated liver cirrhosis. This is the first clinical trial in Japan. From basic study, he found that infused mesenchymal stem cells act as "conducting cells", and the "working cells" are macrophages. Further analysis has revealed that extracellular vesicles (exosomes) secreted by mesenchymal stem cells make macrophages anti-inflammatory. Now Prof. Terai is analyzing MSC derived extracellular vesicle (EV) also. The Japanese Society for Regenerative Medicine has issued "Guidance for Clinical Application of Extracellular Vesicles" on April 30, 2024. Prof. Terai is a chairman of this guidance. The guidance will be used as a platform for the development of specific medical treatments using extracellular vesicles. Now Prof. Terai is an exosome and Gastro-Intestinal committee of ISCT (International Society for Cell and Gene Therapy). He also developed medaka fish to analyze MASH. From long experiment history, medaka is a suitable model fish for studying space also.

Research Interests

- Development of Stem Cell and Extracellular Vesicle (EV) Therapy for Liver Cirrhosis Patient.
- Analysis for the Cancer Stem Cell in HCC
- Analysis for the Mechanism of Liver Fibrosis (Liver Cirrhosis), Liver Steatosis (NASH)
- Development of Drug Screening System (Gene Therapy) for Liver Disease Using Medaka Fish System
- Microbiota, Extracellular Vesicle (EV)
- Neural Network Analysis

Representative Publications

1. Terai S, Asonuma M, Hoshino A, Kino-oka M, Ochiya T, Okada K, Sato Y, Takahashi Y, Tobita M, Tsuchiya A Guidance on the Clinical Application of Extracellular Vesicles. Regen Ther in press.
2. Maeda Y, Watanabe Y, Ishikawa N, Yoshida T, Kimura N, Abe H, Sakamaki A, Kamimura H, Yokoo T, Kamimura K, Tsuchiya A, Terai S. Platelet-rich plasma-derived extracellular vesicles improve liver cirrhosis in mice. Regen Ther. 2024 Nov 6;26:1048-1057. doi: 10.1016/j.reth.2024.10.010. PMID: 39569343; PMCID:PMC11576940.
3. Koyama K, Sakamaki A, Morita S, Nagayama I, Kudo M, Tanaka Y, Kimura N, Arao Y, Abe H, Kamimura K, Terai S. Maid gene dysfunction promotes hyperobesity via the reduction of adipose tissue inflammation in Mc4r gene-deficient mice. Sci Rep. 2024 Sep 10;14(1):21126. doi: 10.1038/s41598-024-72217-1. PMID: 39256539;PMCID: PMC11387655.
4. Hsiao YT, Yoshida Y, Okuda S, Abe M, Mizuno S, Takahashi S, Nakagami H, Morishita R, Kamimura K, Terai S, Aung TM, Li J, Furihata T, Tang JY, Walsh K,Ishigami A, Minamino T, Shimizu I. PCPE-1, a brown adipose tissue-derived cytokine, promotes obesity-induced liver fibrosis. EMBO J. 2024 Nov;43(21):4846-4869. doi: 10.1038/s44318-024-00196-0. Epub 2024 Aug 19. PMID: 39160276; PMCID: PMC11535236.

Diagnosis and Treatment of Liver Disease Using Extracellular Vesicles

Shuji Terai *Niigata University, Japan*

While conducting clinical trials using mesenchymal stromal cells for the treatment of cirrhosis, we have also discovered that extracellular vesicles secreted by mesenchymal stromal cells play a crucial role in the mechanism of action of these cells in improving liver fibrosis and inducing regeneration. Meanwhile, the Japanese Society for Regenerative Medicine (JSRM) has compiled and published "Guidance on clinical applications", emphasizing the importance of clinical applications based on the mode of action of extracellular vesicles, which is based on the quality evaluation of the heterogeneity and active component of extracellular vesicles, and is based on regenerative medicine products that have been developed in the past. We believe that extracellular vesicles will play a crucial role in the diagnosis and treatment of liver diseases in the future, and I will present our previous findings.

References

1. Terai S, Asonuma M, Hoshino A, Kino-Oka M, Ochiya T, Okada K, Sato Y, Takahashi Y, Tobita M, Tsuchiya A. Guidance on the clinical application of extracellular vesicles. Regen Ther. 2025 Mar 7;29:43-50. doi: 10.1016/j.reth.2025.02.008. PMID: 40124467; PMCID: PMC11930518.
2. Maeda Y, Watanabe Y, Ishikawa N, Yoshida T, Kimura N, Abe H, Sakamaki A, Kamimura H, Yokoo T, Kamimura K, Tsuchiya A, Terai S. Platelet-rich plasma-derived extracellular vesicles improve liver cirrhosis in mice. Regen Ther. 2024 Nov 6;26:1048-1057. doi: 10.1016/j.reth.2024.10.010. PMID: 39569343; PMCID: PMC11576940.
3. Kumagai M, Tsuchiya A, Yang Y, Takeda N, Natsui K, Natusi Y, Tomiyoshi K, Yamazaki F, Koseki Y, Shinchi H, Imawaka N, Ukekawa R, Nishibu T, Abe H, Sasaki T, Ueda K, Terai S. Fibulin-4 as a potential extracellular vesicle marker of fibrosis in patients with cirrhosis. FEBS Open Bio. 2024 Aug;14(8):1264-1276. doi: 10.1002/2211-5463.13842. Epub 2024 Jun 9. Erratum in: FEBS Open Bio. 2024 Nov;14(11):1927. doi: 10.1002/2211-5463.13885. PMID: 38853023; PMCID: PMC11301270.
4. Takeda N, Tsuchiya A, Mito M, Natsui K, Natusi Y, Koseki Y, Tomiyoshi K, Yamazaki F, Yoshida Y, Abe H, Sano M, Kido T, Yoshioka Y, Kikuta J, Itoh T, Nishimura K, Ishii M, Ochiya T, Miyajima A, Terai S. Analysis of distribution, collection, and confirmation of capacity dependency of small extracellular vesicles toward a therapy for liver cirrhosis. Inflamm Regen. 2023 Oct 9;43(1):48. doi: 10.1186/s41232-023-00299-x. PMID: 37814342; PMCID: PMC10561446.
5. Natsui K, Tsuchiya A, Imamiya R, Osada-Oka M, Ishii Y, Koseki Y, Takeda N, Tomiyoshi K, Yamazaki F, Yoshida Y, Ohashi R, Ling Y, Ueda K, Moritoki N, Sato K, Nakajima T, Hasegawa Y, Okuda S, Shibata S, Terai

S. Escherichia coli-derived outer-membrane vesicles induce immune activation and progression of cirrhosis in mice and humans. Liver Int. 2023 May;43(5):1126-1140. doi: 10.1111/liv.15539. Epub 2023 Mar 8. PMID: 36751961.

6. Tsuchiya A, Natsui K, Ishii Y, Koseki Y, Takeda N, Tomiyoshi K, Yamazaki F, Yoshida Y, Terai S. Small extracellular vesicles and liver diseases: From diagnosis to therapy. World J Hepatol. 2022 Jul 27;14(7):1307-1318. doi: 10.4254/wjh.v14.i7.1307. PMID: 36158910; PMCID: PMC9376785.
7. Tsuchiya A, Terai S, Horiguchi I, Homma Y, Saito A, Nakamura N, Sato Y, Ochiya T, Kino-Oka M; Working Group of Attitudes for Preparation and Treatment of Exosomes of Japanese Society of Regenerative Medicine. Basic points to consider regarding the preparation of extracellular vesicles and their clinical applications in Japan. Regen Ther. 2022 May 19;21:19-24. doi: 10.1016/j.reth.2022.05.003. PMID: 35619946; PMCID: PMC9127121.
8. Takeuchi S, Tsuchiya A, Iwasawa T, Nojiri S, Watanabe T, Ogawa M, Yoshida T, Fujiki K, Koui Y, Kido T, Yoshioka Y, Fujita M, Kikuta J, Itoh T, Takamura M, Shirahige K, Ishii M, Ochiya T, Miyajima A, Terai S. Small extracellular vesicles derived from interferon-γ pre-conditioned mesenchymal stromal cells effectively treat liver fibrosis. NPJ Regen Med. 2021 Mar 30;6(1):19. doi: 10.1038/s41536-021-00132-4. PMID: 33785758; PMCID: PMC8010072.
9. Watanabe Y, Tsuchiya A, Terai S. The development of mesenchymal stem cell therapy in the present, and the perspective of cell-free therapy in the future. Clin Mol Hepatol. 2021 Jan;27(1):70-80. doi: 10.3350/cmh.2020.0194. Epub 2020 Dec 3. PMID: 33317249; PMCID: PMC7820202.
10. Watanabe T, Tsuchiya A, Takeuchi S, Nojiri S, Yoshida T, Ogawa M, Itoh M, Takamura M, Suganami T, Ogawa Y, Terai S. Development of a non-alcoholic steatohepatitis model with rapid accumulation of fibrosis, and its treatment using mesenchymal stem cells and their small extracellular vesicles. Regen Ther. 2020 May 15;14:252-261. doi: 10.1016/j.reth.2020.03.012. PMID: 32455155; PMCID: PMC7232114.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri)

Plenary Presentation 1

Chairs:

Sung Su Yun (Yeungnam Univ.)
Mi-Sook Kim (Korea Cancer Center Hospital)
Yong-Han Paik (Sungkyunkwan Univ.)

PP 1-1

CXCR4$^+$ CD8$^+$ T Cells in Alcoholic Liver Disease: Enhanced Cytotoxicity and Associations with Liver Function Markers

Gil Won Lee[1], Kwon Yong Tak[2], Ji Won Han[1,2], Jeong Won Jang[1,2], Seung Kew Yoon[1,2], Pil Soo Sung[1,2]

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Aims: CXCR4 is a CXC chemokine receptor that mediates inflammatory responses and immune cell migration through interactions with chemokines. Although its potential involvement in the progression of alcoholic liver disease (ALD) has been proposed, direct evidence remains limited.

Methods: Single-cell RNA sequencing was performed to characterize the immune cell landscape in patients with alcoholic liver disease (ALD), while flow cytometry was utilized to examine the population distribution, activation states, and cytotoxic properties of CD4$^+$ and CD8$^+$ T cells.

Results: Single-cell RNA sequencing of immune cells revealed significant alterations in immune cell populations in patients with alcoholic liver disease (ALD) compared to healthy controls, including the downregulation of CD4$^+$ and CD8$^+$ T cells. FACS analysis confirmed that the CD8$^+$ T cell population was consistent with the RNA sequencing results, showing increased levels of activation and cytotoxicity. Pathway analysis of CD8$^+$ T cells identified CXCR4 as a key molecule associated with cytokine responses and the immune system. Furthermore, the CD8$^+$ T cell population within PBMCs was markedly elevated in patients with ALD. Although the precise mechanisms remain to be elucidated, an increase in CXCL12, the ligand for CXCR4, was observed in the ALD patient group. Additionally, CXCR4$^+$ CD8$^+$ T cells exhibited elevated levels of Granzyme B and Perforin. Importantly, significant correlations were identified between these findings and clinical parameters, including ALT, ALP, Albumin (Alb), and Total Bilirubin (TB).

Conclusions: In summary, we analyzed the immune cell composition of patients with ALD and identified a distinct CXCR4$^+$CD8$^+$ T cell population exhibiting high expression of Granzyme B and Perforin. Further studies are needed to clarify the role of these cells in immune responses to microbial pathogens and liver immunopathology.

Keywords: Alcoholic Liver Disease, C-X-C Chemokine Receptor Type 4 (CXCR4), CXCR4+ CD8 T Cell

PP 1-2

Adjuvant Cytokine-Induced Killer Cell Immunotherapy in Hepatocellular Carcinoma: 9-Year Extended Follow-up of a Randomized Controlled Trial and Post-Treatment Immune Cell Profiling

Hyunjae Shin[1], Youngsu Park[2], Byeong Geun Song,[3] Won-Mook Choi[4], Hyung Joon Han[4], Youngwoo Lee[6], TaeJin Song[5], Jong-Eun Yeon[6], YoungSuk Lim[4], Joon Hyeok Lee[3], Jae Woong Yoon[1], Gyung Sun Lim[1], Juyeon Kim[1], Yunmi Ko[1], Jeayeon Park[1], Moon Haeng Hur[1], Yun Bin Lee[1], Eun Ju Cho[1], Su Jong Yu[1], Yoon Jun Kim[1], Jung-Hwan Yoon[1], Jeong-Hoon Lee[1]

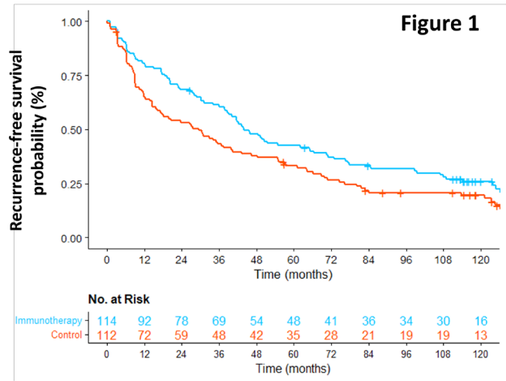
[1]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [2]Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Goyang, Republic of Korea; [3]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [5]Division of Hepatobiliopancreas and Transplant Surgery, Korea University Ansan Hospital, Ansan, Republic of Korea; [6]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Korea University Guro Hospital, Seoul, Republic of Korea

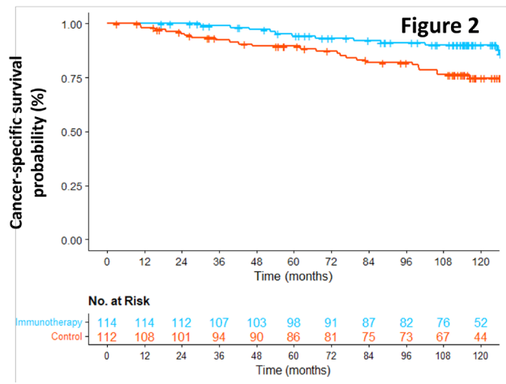
Aims: Notwithstanding the pressing need for adjuvant therapy for hepatocellular carcinoma (HCC), most adjuvant therapies, including atezolizumab/bevacizumab, have failed. Meanwhile, adjuvant immunotherapy utilizing autologous cytokine-induced killer (CIK) cells for HCC has demonstrated potential in improving recurrence-free survival (RFS) in a previously reported randomized controlled trial (RCT) and real-world data. However, the long-term effectiveness of CIK therapy beyond 5 years has not been unveiled. This study aimed to assess the longer-term outcomes of the RCT and elucidate the underlying mechanisms of sustained effects of CIK cell treatment.

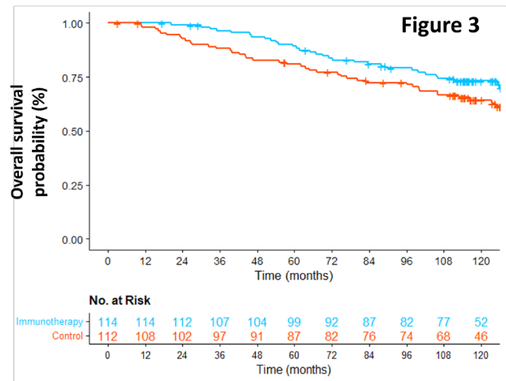
Methods: A long-term follow-up analysis was conducted on patients enrolled in the original RCT, which included 226 patients who underwent curative treatment for stage I or II HCC. Patients were randomly allocated to either the CIK group (n=114, 16 injections of 6.4×10^9 CIK cells over an 11-month period) or the control group (n=112). The follow-up period was extended to 9 years after the enrollment of the last patient. The primary endpoint was RFS, while secondary endpoints included cancer-specific survival (CSS) and overall survival (OS). Parallelly, a prospective study was conducted to investigate post-treatment changes of immune cells in peripheral blood of 19 patients, who received repeated transfer of CIK cells after curative treatment for HCC, using flow cytometry.

Results: In the extended follow-up of the RCT (median follow-up=116.1 months, interquartile range=77.5–130.5 months), the CIK group exhibited significantly prolonged RFS (median=44.0 vs. 30.0 months; hazard ratio [HR]=0.72, 95% confidence interval [CI]=0.54–0.97, ––P=0.033; Figure 1) and CSS (median=not reached; HR=0.49, 95% CI=0.25–0.95, P=0.036; Figure 2) compared to the control group. Adjuvant CIK cell therapy reduced the risk of overall death by 30%, although statistical significance was not reached (median=not reached; HR=0.70, 95% CI=0.44–1.11, P=0.13; Figure 3). Notably, the prolonged benefits of CIK therapy were observed beyond the initial treatment period, supporting its potential role in long-term disease control. A robust analysis of peripheral blood immune cells revealed that the CIK cell treatment tended to increase the frequencies of CD8$^+$ classical memory T cells (CD45RO+/CD45RA-; 28.9 ± 3.0% at baseline vs 41.3 ± 3.7% after repeated CIK cell transfer, P=0.03).

Conclusions: Adjuvant CIK cell treatment demonstrated significantly improved RFS and CSS in the prolonged follow-up of the RCT extending to 9 years in patients who received curative treatment for HCC. The CIK group also exhibited a consistent trend of improved OS. The increase in CD8$^+$ memory T cell populations might be linked to the sustained off-treatment anti-tumor efficacy of CIK cell treatment. These findings highlight the potential of CIK therapy as a durable immunotherapeutic strategy for HCC, warranting further investigation into its long-term effects and mechanisms of action.







Keywords: Hepatocellular Carcinoma, Adjuvant Immunotherapy, Cytokine-Induced Killer Cells, Recurrence-Free Survival

PP 1-3

Surgical Quality Assessment with Artificial Intelligence-Based Video Analysis for Laparoscopic Donor Right Hemihepatectomy: Usefulness of Round Ligament Fixation in Hilar Structure Dissection

Kanggil Park[1], Ji Su Kim[2], Su Hyung Park[3], Ahin Choi[1], Na Reum Kim[3], Gi Hong Choi[3], Jin Sub Choi[3], Namkug Kim[1], Dai Hoon Han[3]

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Aims: Laparoscopic donor right hemihepatectomy (LDRH) poses significant surgical challenges due to the complexity of liver parenchymal dissection while preserving key vascular and biliary structures. To optimize surgical efficiency, we developed a technique where the round ligament is fixed to the abdominal wall, allowing the assistant to retract only the gall bladder (RLFGT). This study evaluates the effectiveness of RLFGT compared to the conventional approach and explores artificial intelligence (AI)-based surgical video analysis for quality assessment.

Methods: A retrospective analysis was conducted on 77 patients who underwent LDRH by a single surgeon at Yonsei University Severance Hospital between April 2019 and February 2024. Outcomes from 21 patients who underwent the conventional method were compared with 56 RLFGT cases. Surgical video analysis was performed on 49 cases (15 conventional, 34 RLFGT), segmenting hilar dissection into six phases. Phase durations were compared, and AI-based recognition using Surgformer was evaluated against ground truth labels.

Results: While surgical outcomes showed no statistical differ-

ences, RLFGT significantly reduced times for hilum exposure (820.2 ± 199.62 vs. 584.26 ± 271.75 sec, *P*=0.004) and total hilar dissection (3352.73 ± 824.30 vs. 2683.71 ± 793.46 sec, *P*=0.010). AI phase recognition achieved high F1 scores for hilum exposure (95.33±1.08%), right hepatic artery (90.61± 1.96%), and portal vein (80.05±6.52%), demonstrating potential for surgical quality assessment.

Conclusions: RLFGT enhances surgical efficiency by reducing dissection time and unnecessary maneuvers. AI-based video analysis reliably identifies surgical phases, offering valuable insights for improving surgical quality.

Keywords: Laparosocpic Donor Hepatectomy, Artificial Intelligence Surgical Video Anaylsis, Surgical Quality Assessment

PP 1-4

Performance of Expanded Criteria for Liver Transplantation in Patients with Hepatocellular Carcinoma: A Network Meta-Analysis

Dongman Yoo[1], **Yeongseok Hwang**[1], Jihyun An[2], Ju Hyun Shim[1]

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Aims: Various expanded criteria (EC) for liver transplantation (LT) in patients with hepatocellular carcinoma (HCC) have been proposed to overcome the narrow boundary of the Milan criteria (MC). There were few studies directly comparing the performance of various EC. To investigate which EC predicts more favorable outcomes in terms of overall survival (OS) and disease-free survival (DFS), we conducted a network meta-analysis (NMA).

Methods: A database search was conducted on PubMed, EMBASE, and Cochrane Library to identify studies comparing OS and DFS between patients within the MC and those beyond the MC but within the EC. Specific survival data was extracted from Kaplan-Meier curve in each study. The effect size was assessed using the hazard ratio (HR), which was pooled in a random-effects network meta-analysis (NMA). The ranking for each EC was visualized via a composite line chart.

Results: Among 22,466 articles identified, 35 studies containing 45 pairwise comparisons were included in the NMA along with 8 different ECs. Regarding OS, UCSF (HR, 1.43; 95% CI, 1.19–1.71), Up-to-Seven (HR, 1.50; 95% CI, 1.15–1.97), and Hangzhou criteria (HR, 1.69; 95% CI, 1.11–2.57) were significantly inferior to the MC, and the MC had the highest rank probability of being best followed by Metroticket 2.0 model. Regarding DFS, UCSF (HR, 1.41; 95% CI, 1.20–1.66), Hangzhou (HR, 1.74; 95% CI, 1.46–2.08), Up-to-Seven criteria (HR, 2.18; 95% CI, 1.54–3.08), and AFP model (HR, 2.86; 95% CI, 1.06–7.72) were significantly inferior to the MC, and the MC had the highest rank probability of being best followed by Asan criteria.

Conclusions: This NMA found that several EC demonstrated comparable outcomes to the MC. The UCSF and Up-to-Seven criteria showed worse outcomes compared to other EC, which may be influenced by hepatitis C virus infection. Metroticket 2.0 model can be an alternative overcoming these discrepancies.

Keywords: Liver Transplantation, Liver Cancer, Network Meta-analysis

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat)

Plenary Presentation 2

Chairs:

June Sung Lee (Inje Univ.)
Si Hyun Bae (The Catholic Univ. of Korea)
Kwang-Woong Lee (Seoul National Univ.)

PP 2-1

Efficacy and Safety of Time-Restricted Eating in Metabolic Dysfunction-Associated Steatotic Liver Disease

Joo Hyun Oh[1], Eileen L. Yoon[2,3], Huiyul Park[4], Seungmin Lee[5], Ae Jeong Jo[6], Seon Cho[7], Eunjoo Kwon[7], Eun-Hee Nah[8], Jun Hyuk Lee[9], Jung Hwan Park[10], Sang Bong Ahn[1], Dae Won Jun[2,3]

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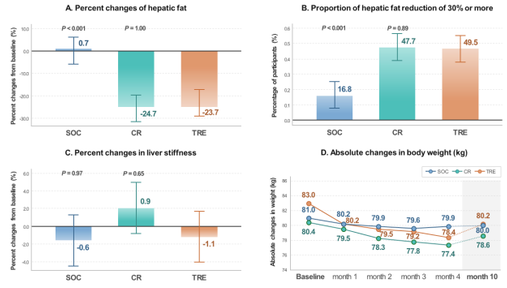
Aims: Time-restricted eating (TRE) may improve weight loss, insulin resistance, and body composition, key factors in the pathophysiology of metabolic dysfunction-associated steatotic liver disease (MASLD). However, evidence in patients with MASLD is limited. This study aimed to evaluate the potential benefits of TRE in patients with overweight or obese MASLD.

Methods: This 16-week randomized controlled trial included patients who were overweight or obese and had MASLD randomized into three groups in a 1:1:1 ratio: standard of care (SOC), calorie restriction (CR), and TRE. The primary endpoint was an improvement in hepatic steatosis, measured using magnetic resonance imaging proton density fat fraction. Changes in liver fibrosis, body composition, lipid profiles, glucose homeostasis, and sleep quality were also analysed. This study is registered at ClinicalTrals.gov, NCT05579158.

Results: Among the 337 participants randomized, 333 were included in the full analysis set (113 in SOC, 110 in CR, and 110 in TRE). After the 16-week intervention, hepatic steatosis significantly decreased in the TRE group (- 25.8%) than in the SOC group (0.7%, P<0.001), with no significant difference between TRE and CR (- 24.7%, P=1.00). The TRE group also showed greater reductions in body weight, waist circumference, and body fat mass compared to those of SOC, with similar changes between TRE and CR. No significant differences were observed between TRE and CR in liver stiffness, glucose homeostasis, or sleep quality. No serious adverse events were reported.

Conclusions: TRE effectively reduces hepatic steatosis in MASLD, with comparable benefits on weight loss, body composition, and metabolic parameters as CR. This approach may serve as a practical dietary strategy for MASLD management.

Keywords: Overweight/Obesity, Metabolic Dysfunction-Associated Steatotic Liver Disease, Calorie Restriction, Time-Restricted Eating



PP 2-2

Development of Glypican-3-Targeting CAR-NK Cells with IL-15 Secretion for Hepatocellular Carcinoma Treatment

Ji Young Kim[1], Minji Park[1], Hyeongbin Son[2], Yujung Jo[1], Soo Yun Lee[3], Gamin Han[1], Mijeong Lee[1], Hyun-Young Kim[4], Tae-Don Kim[3], Yeup Yoon[1,2,6], Duck Cho[1,2,4,7], Wonseok Kang[1,5,6]

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Aims: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality, accounting for 80% of liver cancers. Glypican-3 (GPC3) has emerged as a promising target for immunotherapy due to its selective expression on HCC cells. In this study, we aimed to engineer novel GPC3-targeting chimeric antigen receptor (CAR)-natural killer (NK) cells and evaluate their anti-tumor efficacy for HCC treatment.

Methods: We identified high-affinity GPC3-specific single-chain variable fragments (scFvs) using phage display technology. Using these scFVs, we developed CAR constructs incorporating a 4-1BB costimulatory domain and a CD3ζ signaling domain, with two variants additionally co-expressing IL-15 through an IRES element. The CAR constructs were stably transduced into NK92 cells and their cytotoxicity was evaluated against HCC cell lines with varying GPC3 expression. In vivo efficacy was assessed in a subcutaneous HCC xenograft model in NSG mice.

Results: GPC3 CAR-NK cells showed significant cytotoxicity against GPC3-positive HCC cell lines compared to untransduced NK cells, with minimal activity against GPC3-negative A549 cells. The IL-15 expressing CAR-NK cells secreted detectable IL-15 and demonstrated superior long-term survival under IL-2-deprived conditions, maintaining cell numbers through day 7 while non-IL-15 variants declined rapidly. In the xenograft model, intravenous administration of GPC3-IL15 CAR-NK cells significantly reduced tumor growth and improved overall survival compared to untransduced NK cells. Moreover, enhanced tumor-specific infiltration of GPC3 CAR-NK cells was observed compared to untransduced NK cells, as evidenced by flow cytometry and immunohistochemistry.

Conclusions: Our novel engineered GPC3-IL15 CAR-NK cells demonstrated enhanced tumor targeting capabilities and proved particularly effective in treating GPC3-positive HCC both in vitro and in vivo. The integration of IL-15 significantly improved NK cell persistence, while the GPC3-targeting scFv enabled enhanced tumor infiltration. These findings provide new insights into the development of cell-mediated therapies for HCC and warrant further investigation in clinical trials.

Keywords: Hepatocellular Carcinoma, Glypican-3, Chimeric Antigen Receptor, Natural Killer Cells

PP 2-3

A Novel Risk Prediction Model for Survival in Patients with Autoimmune Hepatitis: A Multicenter Cohort Study

Soon Kyu Lee[1], Jeong-Ju Yoo[2], U IM Chang[3], Ahlim Lee[3], Gwang Hyeon Choi[4], Ja Kyung Kim[5], Hye Yeon Chon[5], Seung Kak Shin[6], Kyung-Ah Kim[7], Hae Lim Lee[8], Ji-Won Park[9], Young-Joo Jin[10], Heechul Nam[11], Jung Hyun Kwon[1], Jung Hee Kim[12], Bo Hyun Kim[13], Hyung Joon Yim[14], Sook-Hyang Jeong[4]

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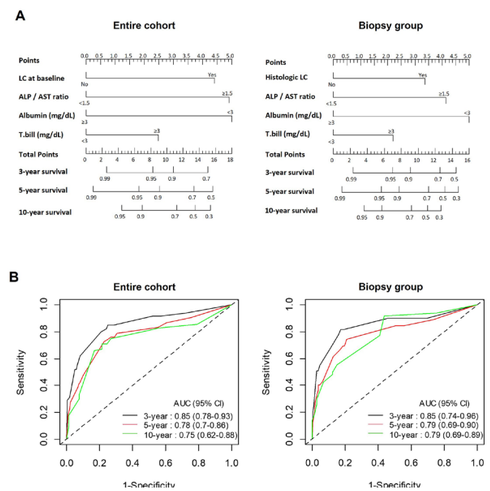
Aims: This study aimed to identify risk factors for survival in patients with autoimmune hepatitis (AIH) and develop a reliable risk prediction model using a multicenter cohort.

Methods: A total of 1,401 newly diagnosed AIH patients from 14 Korean centers (January 2010–December 2021) were included, of whom 1,133 (867 with liver histology, biopsy group) were analyzed. The primary outcome was identifying survival risk factors, including liver cirrhosis (LC). Secondary outcomes included the development and validation of a novel predictive model for survival.

Results: During a mean follow-up of 58.6 months, 69 patients died (19 with hepatitis and 50 with LC at baseline). Patients with LC or histologic cirrhosis had significantly lower survival (P<0.001). In multivariable Cox regression, LC at baseline (histologic LC in the biopsy group), a high ALP:AST ratio (≥1.5), low Albumin (<3.0 g/dL), and high Bilirubin (≥3.0 mg/dL) were identified as key survival predictors, forming the predictive model (LAAB model) (Figure A). This model demonstrated high predictive accuracy, with time-dependent AUROCs of 0.85, 0.78, and 0.75 for 3-, 5-, and 10-year survival (0.85, 0.79, and 0.75 in the biopsy group) (Figure B). When incorporating treatment response, non-response at 1, 6, and 12 months was also a significant survival predictor. However, adding response data did not significantly enhance the model's predictive power. Internal validation using 1,000 bootstrap samples yielded AUROCs of 0.85, 0.75, and 0.75 for 3-, 5-, and 10-year survival (0.86, 0.79, and 0.80 in the biopsy group), confirming the model's robustness.



Conclusions: Utilizing a large multicenter cohort, this study is the first to develop a reliable model for predicting survival in patients with AIH. The LAAB model demonstrates strong predictive performance, providing a valuable tool for risk stratification and clinical decision-making.

Keywords: Autoimmune Hepatitis, Survival, Liver Cirrhosis, Prediction

PP 2-4

Outcomes and Key Determinants in Living Donor Liver Transplants from Older Donors: A Multicenter Cohort Analysis

Eun-Ki Min, Deok-Gie Kim, Jae Geun Lee

Department of Surgery, Severance Hospital, Yonsei University, Republic of Korea

Aims: Ensuring graft survival in living donor liver transplantation (LDLT) with older donors remains challenging. The effect of living donor age on graft survival remains underexplored. We aimed to evaluate recipient and donor outcomes by donor age and identify key determinants associated with old-donor LDLT.

Methods: We included 4,035 LDLT cases from a multicenter cohort, categorizing donors as "old" or "young" based on an age cut-off of 50 years. After 1:3 propensity score matching, graft survival was compared between the groups. Risk factors for graft loss in old- versus young-donor LDLT were investigated through interaction analysis, with outcomes stratified by the number of risk factors.

Results: The old-donor group (n = 374; 9.3%) showed lower 5-year graft survival than the young-donor group (n = 3,661; 90.7%) in the matched cohort (79.6% vs. 87.7%, P=0.004). Old-donor was an independent risk factor for graft loss (adjusted hazard ratio [HR]: 1.56, 95% CI: 1.17–2.07, P=0.002). Significant interactions with old-donor LDLT included cold ischemic time ≥ 150 minutes, Model for End-stage Liver Disease score ≥ 20, and recipient body mass index ≥ 25 kg/m^2. Old-donor LDLT with two or more of these risk factors increased graft loss risk (HR 3.78, 95% CI: 1.97–7.26, *P*<0.001). Six-month donor complication rates did not differ by age (*P*=0.672).

Conclusions: Graft survival for older donors (≥50 years) is comparable to younger donors when minimal risk factors are present, but outcomes worsen with multiple risk factors. Short-term donor outcomes are unaffected by donor age.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri)

Free Paper Presentation 1

FP-1~FP-7	Hepato-Biliary and Pancreas Surgery
FP-8~FP-15	Liver Cancer, Clinical 1
FP-16~FP-22	MASLD, Clinical
FP-23~FP-30	HBV Basic and ALD
FP-31~FP-38	Acute Liver Failure and DILI
FP-39~FP-46	HBV1
FP-47~FP-54	Liver Cancer, Basic

Friday, May 30, 2025, 15:10-16:20

1. Hepato-Biliary and Pancreas Surgery

FP-1

Development and External Validation of an Online Risk Calculator for Early Mortality after Hepatic Resection in Hepatocellular Carcinoma

Ren-Jie Zhang[1], Si-Yuan Wang[2], Jia-Hao Xu[1], Han Liu[3], Yu-Ze Yang[3], Yong-Yi Zeng[4], Wei-Min Gu[5], Ya-Hao Zhou[6], Hong Wang[7], Ting-Hao Chen[8], Xian-Ming Wang[9], Ying-Jian Liang[10], Jie Li[11], Yong-Kang Diao[1], Feng Shen[1], Tian Yang[1]

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Aims: Despite improvements in surgical techniques, early mortality after hepatic resection for hepatocellular carcinoma (HCC) remains a critical concern. Current staging systems and liver function classifications lack individualized risk prediction capability to guide surgical decision-making.

Methods: A multi-institutional retrospective analysis was conducted across 11 hepatobiliary centers in China (2011-2021). The training cohort comprised patients from 9 centers, with the remaining 2 centers serving as external validation. Predictors of postoperative 90-day mortality were identified through multivariable logistic regression analysis. Model performance underwent evaluation using concordance index and calibration plots.

Results: Among 4,966 patients analyzed, the 90-day mortality rate was 4.1%. The final model incorporated six preoperative predictors: performance status, prothrombin time, albumin-bilirubin grade, aspartate aminotransferase to platelet ratio index, tumor burden score, and gross vascular invasion. The model demonstrated excellent discrimination in both training (C-index 0.816) and validation (C-index 0.801) cohorts, significantly outperforming traditional HCC staging systems (AJCC and BCLC) and liver function classifications (P<0.001). Using an optimized cutoff of 54 points, the model achieved 79.0% sensitivity and 71.8% specificity for identifying high-risk patients.

Conclusions: The validated online calculator enables accurate prediction of early mortality risk after hepatic resection for HCC. This practical tool may facilitate surgical candidate selection and support informed decision-making by providing individualized risk estimates. Further validation in international cohorts is warranted to confirm broad applicability.

Keywords: Hepatocellular Carcinoma, Hepatic Resection, Postoperative Mortality Prediction

FP-2

Role of Hepatobiliary Scintigraphy in Predicting Post-Hepatectomy Liver Failure: A Single-Center Cohort Study

Jeong-Moo Lee, Youngrok Choi, Gayoung Kim, Min Kyoung Kim, Sang Hyuk Park, Jiyoung Kim, Jae-Yoon Kim, Suk Kyun Hong, Kwang-Woong Lee, Kyung-Suk Suh

Department of Surgery, Seoul National University Hospital, Republic of Korea

Aims: Post-hepatectomy liver failure (PHLF) significantly impacts outcomes after liver resection. This study evaluates indocyanine green retention rate (ICGR15) and hepatobiliary scintigraphy (HBS) with 99mTc-mebrofenin for PHLF prediction.

Methods: This single-center retrospective cohort study included 58 patients who underwent liver resection between March 2022 and July 2024. Preoperative assessments included ICGR15, HBS, and laboratory tests. The primary outcome was PHLF, classified according to the International Study Group of Liver Surgery (ISGLS) criteria. Predictive performance was analyzed using receiver operating characteristic curves and multivariate logistic regression.

Results: PHLF occurred in 7 patients (12.1%). ICGR15 〉 15% and pre-HBS 〈13 were independently associated with PHLF, with adjusted odds ratios (aOR) of 3.4 (95% CI, 1.5-7.8) and 2.9 (95% CI, 1.3-6.5), respectively. Combined assessment of ICGR15 and HBS improved predictive accuracy (AUC: 0.82) compared to ICGR15 alone (AUC: 0.76) or HBS alone (AUC: 0.74). High negative predictive values (NPV) of ICGR15 (0.95) and HBS (0.97) highlighted their utility in identifying low-risk patients. The risk of PHLF increased significantly with the number of risk factors present, reaching 42.9% in patients with three or more risk factors (P<0.001).

Conclusions: Hepatobiliary scintigraphy with 99mTc-mebrofenin complements ICGR15 in predicting PHLF, with their combination providing superior predictive performance. High NPVs underscore the utility of these tools in identifying low-risk surgical candidates. These findings support integrating HBS into preoperative protocols for major liver resections to improve risk stratification and surgical outcomes.

Keywords: Post-Hepatectomy Failure, Hepatobiliary Scintigraphy, Liver Resection

FP-3

Preoperative Risk Stratification in Hilar Cholangiocarcinoma Using a Novel Decision Tree Model

Yuze Yang[1], Yongkang Diao[2], Zixuan Wang[1], Lu Sun[1], Han Liu[1], Mingda Wang[2], Chao Li[2], Lihui Gu[2], Han Wu[2], Guoyue Lv[1], Feng Shen[2], Ping Zhang[1], Tian Yang[2]

[1]Department of Hepatobiliary And Pancreatic Surgery, General Surgery Center, First Hospital of Jilin University, Changchun, China; [2]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Naval Medical University, Shanghai, China

Aims: Current prognostic assessment for hilar cholangiocarcinoma (hCCA) predominantly relies on postoperative pathological findings, limiting preoperative decision-making capabilities. This study aimed to develop a practical preoperative risk stratification model using readily available biomarkers to predict surgical outcomes.

Methods: A retrospective analysis was performed on 435 patients who underwent curative resection for hCCA across two high-volume hepatobiliary centers. The cohort was randomly divided into training (n=305) and validation (n=130) groups. A decision tree model was constructed using preoperative biomarkers identified through LASSO regression and multivariate Cox analysis. Model performance was assessed using Harrell's C-index and calibration plots.

Results: Three independent prognostic factors were identified: CA199 ≥39 U/L (HR=1.96, 95%CI:1.24-3.08), CA125 ≥35 U/L (HR=2.62, 95%CI:1.78-3.85), and CRP ≥5 mg/L (HR=1.79, 95%CI:1.31-2.45). The decision tree model effectively stratified patients into low- and high-risk groups. In the training cohort, low-risk patients demonstrated significantly better 3-year overall survival (56.1% vs 23.0%, P<0.0001) and recurrence-free survival (40.5% vs 21.9%, P<0.0001) compared to high-risk patients. The model maintained robust discriminative performance in the validation cohort, with consistent survival differences between risk groups.

Conclusions: This novel decision tree model, incorporating three readily available preoperative biomarkers, provides reliable risk stratification for patients with resectable hCCA. The model's simplicity and effectiveness make it a practical tool for preoperative risk assessment and surgical decision-making, potentially facilitating personalized treatment strategies.

Keywords: Hilar Cholangiocarcinoma, Decision Tree Analysis, Prognostic Stratification

FP-4

Medical Conflicts and Their Effect on Korean Liver-Related Publications: A 2019–2024 Analysis

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Department of Surgery, Samsung Medical Center, Seoul, Korea

Aims: Concerns have arisen about a potential decline in Korean liver - related research output in 2024, possibly attributable to recent medical conflicts. We investigated whether liver-related publication rates in Korea, particularly in the capital versus non - capital regions and in surgery versus hepatology, decreased in 2024 relative to global trends.

Methods: We first identified high - frequency liver disease–related keywords from PubMed searches over the past six years. Using these keywords, we retrieved publications from 2019 to 2024 (Global) and then filtered for those with at least one author affiliated with Korea (Korea). Korean - authored papers were further subdivided by capital - region (Seoul/Gyeonggi/Incheon) versus non - capital - region affiliations, and by surgical versus hepatology specialties. The annual percentage of each subgroup's publications relative to the global total (% per global) was calculated for 2019–2023 and compared to 2024 values. We used one - sample t - tests to assess whether the 2024 proportion differed significantly from the 2019–2023 mean.

Results: Between 2019 and 2023, Korea's publications comprised on average 5.21% (SD 0.28) of the global total, decreasing to 4.50% in 2024 (−13.49%, P=0.0051). The capital region's share declined from 4.09% to 3.60% (−12.13%, P=0.0129), while the non - capital region's share fell from 1.11% to 0.91% (−18.52%, P=0.0026). Surgery - affiliated papers decreased from 1.64% to 1.38% (−15.85%, P=0.028), and hepatology - affiliated papers from 2.31% to 2.04% (−11.65%, P=0.0089).

Table 1. Global and South Korean Research Output (2019-2024) and Proportional Distribution

Year	2019	2020	2021	2022	2023	2024
Global	32633	36668	40181	39212	37955	36608
Korea	1667	2012	2192	2034	1821	1649
(per global, %)	(5.11)	(5.49)	(5.46)	(5.19)	(4.80)	(4.50)
Capital region	1273	1598	1748	1599	1436	1317
(per global, %)	(3.90)	(4.36)	(4.35)	(4.08)	(3.78)	(3.60)
Non-capital region (per global, %)	394 (1.21)	414 (1.13)	444 (1.10)	435 (1.11)	385 (1.01)	332 (0.91)
Surgery (per global, %)	529 (1.62)	661 (1.80)	726 (1.81)	605 (1.54)	534 (1.41)	504 (1.38)
Hepatology (per global, %)	686 (2.10)	894 (2.44)	953 (2.37)	914 (2.33)	875 (2.31)	747 (2.04)

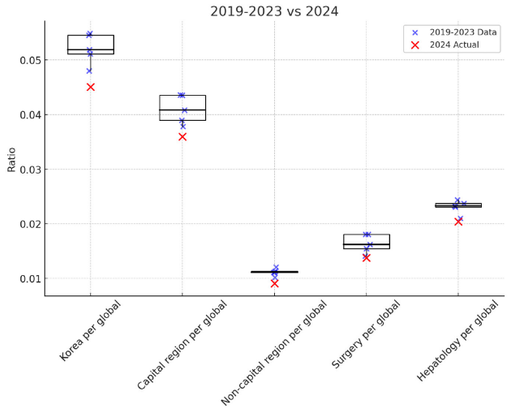
Table 2. Statistical Comparison of 2024 Research Output Against 2019-2023 Averages

	2019-2023 Avg (SD)	2024	Change from 2019-2023 Avg (%)	p-value
Korea per global (%)	5.21 (0.28)	4.5	-13.49%	0.0051
Capital region per global (%)	4.09 (0.26)	3.6	-12.13%	0.0129
Non-capital region per global (%)	1.11 (0.07)	0.91	-18.52%	0.0026
Surgery per global (%)	1.64 (0.17)	1.38	-15.85%	0.028
Hepatology per global (%)	2.31 (0.13)	2.04	-11.65%	0.0089

Conclusions: Our findings indicate a significant drop in Korea's liver disease–related publications during 2024, relative to global trends, with the decrease more pronounced in non - capital regions and in surgery. These results suggest that recent medical conflicts may have adversely affected research output

in this field, underscoring the need for policy measures and resource allocation to sustain scientific productivity.

Figure 1. Comparative Distribution of Research Output: 2019-2023 vs 2024



Keywords: Medical Conflict, Liver Diseases, Publication Trend

FP-5

The Role of Neoadjuvant Chemotherapy (nCT) in the Treatment of Patients with Resectable Pancreatic Cancer

Vervekin Ilya

Pavlov First Saint Petersburg State Medical University, Department of Abdominal Oncology, Russia

Aims: The use of nCT in the group of resectable tumors is an open question. There are isolated published data from randomized studies on its effectiveness, in the form of an increase in the frequency of R0 resection, a decrease in lymphovascular and perineural invasion, a decrease in the frequency of vascular resection, the effect on survival has not been assessed.

Methods: The presented study is a single-center, prospective clinical trial. The primary endpoint is desease-free survival (DFS). Secondary endpoints: overall survival (OS), complication rate (Clavien-Din o), histological tumor stage ypTN, tumor response to treatment (according to the College of American Pathologists (CAP) grading system), R1/R0 resection rate, resectability. The study includes patients with pancreatic adenocarcinoma that meets the resectability criteria (according to NCCN 2023). Patients (n=64) are randomized in a 1:1 ratio either to the control group (radical surgery + adjuvant chemotherapy) or to the experimental group (nCT according to the mFOLFIRINOX regimen + radical surgery + adjuvant chemotherapy).

Results: The median follow-up time was 56.7 months. The median DFS was 10.7 months (95% CI 6.9–13.7) in the control group and 14.9 months (95% CI 6.4–19.4) in the NAC group (*P*=0.035). The median OS was 16.9 months (95% CI 7.9–20.4) in the control group and 21.7 months (95% CI 12.4–24.4) in the nCT group (*P*=0.031). The surgical resection rate was 71.8% in the control group and 84.6% in the nCT group (*P*=0.017). The R0 resection rate was 57% in the control group and 81.2% in the nCT group (*P*=0.037). The frequency of vascular resection (portal vein) was 17.5% in the control group and 9% in the nCT group (*P*=0.04). The frequency of postoperative complications according to Clavien-Dindo (III-IV) was 28.5% in the control group and 18% in the nCT group (*P*=0.72).

Conclusions: The study demonstrated statistically significant superiority in the nCT group in terms of survival, resectability and the rate of R0 resections. The rate of postoperative complications did not differ statistically between the groups. Thus, nCT for resectable pancreatic cancer is a promising method that can potentially improve the treatment outcomes of patients with prostate cancer.

Keywords: Resectable Pancreatic Cancer, Folfirinox, Pancreatic Surgery

FP-6

Innovative Artificial Intelligence and Machine Learning Based Spatial Computing AR Navigation for Open, Lap, and Robotic Hepatectomy

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Aims: Precise spatial recognition is critical for successful decision-making during open and laparoscopic and robotic liver surgeries. However, real-time visualization of internal anatomy remains challenging. To overcome this, we developed a novel augmented reality (AR) navigation system that integrates spatial computing and machine learning. This system is markerless and compatible with both open, laparoscopic, and robotic hepatectomy procedures, employing a video pass-through head-mounted display (HMD) for enhanced intraoperative visualization and decision support.

Methods: Our system utilizes preoperative CT/MRI data to create detailed 3D models of the liver, tumors, arteries, veins, and bile ducts. These models are dynamically aligned with patient anatomy using an Apple Vision Pro HMD equipped with high-resolution 3D cameras, LiDAR sensors, and positional sensors. To address challenges unique to open surgeries, such as varying lighting and dynamic fields, the system incorporates specialized tracking algorithms and wide-field spatial rendering. Evaluations were conducted in simulated and cadaveric environments with experienced and novice surgeons assessing accuracy, usability, and spatial awareness.

Results: The system demonstrated spatial tracking accuracy within 0–2 mm and video latency of 0.012 seconds, meeting clinical requirements for real-time application. Surgeons reported improved spatial perception, surgical accuracy, and decision-making across open and lap-robotic settings. Its versatility allowed seamless transitions between modalities, highlighting its adaptability and potential for broader surgical applications.

Conclusions: This markerless spatial AR navigation represents a significant leap in HBP surgical support, combining cutting-edge spatial computing and machine learning to enhance precision and safety. Future optimizations and clinical trials aim to establish its use across diverse surgical specialties worldwide.

Keywords: XR VR AR MR, AI, Holoeyes

FP-7

An Evaluation of Long-Term Fasting Effects on Preoperative and Postoperative Outcomes in Liver Surgery

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Aims: Fasting is increasingly studied for its metabolic and regenerative benefits in liver surgery. Preoperative fasting reduces hepatic fat and enhances metabolic flexibility, while postoperative fasting promotes autophagy and mitigates inflammation.

Methods: This systematic review followed PRISMA guidelines (2010-2024) to evaluate the long-term effects of different fasting types—intermittent fasting, time-restricted feeding, and prolonged fasting—on liver regeneration, metabolic health, mental health, quality of life, and tumor recurrence. Long-term outcomes (6 months to 5 years) were compared across fasting types. Regression and meta-analyses were used to assess pooled effect sizes and the influence of moderating variables such as smoking habit, SES, and social capital.

Results: Intermittent fasting showed the highest liver regeneration effect size (0.48), followed by time-restricted feeding (0.45) and prolonged fasting (0.40). Improvements in metabolic health (HbA1c) were greatest with time-restricted feeding (β = -0.36), while depression scores improved most with intermittent fasting (β = -0.29). Quality of life (SF-36 Scores) improvements were notable across all fasting types, with intermittent fasting showing the largest effect (0.32). Tumor recurrence rates were lowest with intermittent fasting (10%) compared to time-restricted feeding (12%) and prolonged fasting (15%). Smoking and socioeconomic disparities significantly influenced outcomes.

Conclusions: Fasting positively impacts long-term outcomes in liver surgery, with intermittent and time-restricted fasting offering the most significant benefits. Prolonged fasting, while effective, is less sustainable and presents challenges with adherence and risk of nutritional deficits. Tailored fasting strategies addressing socioeconomic and behavioral barriers could further optimize recovery and quality of life. Future studies should explore personalized fasting protocols to refine these findings.

Keywords: Liver Surgery Outcomes, Fasting Long-Term Outcomes, Preoperative Care and Postoperative Recovery

Friday, May 30, 2025, 15:10-16:30

2. Liver Cancer, Clinical 1

FP-8

Prognostic Impact of Tumor-Associated Endothelial B7-H3 Expression in Hepatocellular Carcinoma

Yunmi Ko[1], Gwang Hyeon Choi[2], Haeryoung Kim[3], Youngeun Lee[4], Min Kyung Park[2], Yun Bin Lee[1], Eun Ju Cho,[1], Jeong-Hoon Lee[1], YoungRok Choi[5], Yoon Jun Kim[1], Jung-Hwan Yoon[1], Kyung-ho Choi[6], Su Jong Yu[1]

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Aims: B7-H3 (CD276), a newly identified member of the B7 family, is overexpressed in various solid tumors and acts as a T cell inhibitor that promotes tumor aggressiveness and proliferation. This study evaluated whether tumor or endothelial B7-H3 expression was associated with tumor behavior and prognosis in hepatocellular carcinoma (HCC) following surgical resection.

Methods: We included consecutive patients with HCC who had undergone surgical resection (n=624) or liver transplantation (n=100) at two tertiary hospitals between 2009 and 2013. Tissue microarray (TMA) was used to assess B7-H3 expression in tumor and adjacent tissues. The primary outcome was overall survival (OS), and the secondary outcome was recurrence-free survival (RFS), analyzed according to B7-H3 expression levels.

Results: Among the 624 patients in the surgical resection cohort, moderate-to-strong B7-H3 expression was observed in

20.7% (129/624) of tumors and 54.8% (342/624) of endothelial tissues. The median follow-up duration was 6.8 (interquartile range [IQR] =3.3–9.8) years. After balancing baseline characteristics using inverse probability of treatment weighting (IPTW), patients with the moderate-to-strong endothelial B7-H3 expression had significantly worse OS (adjusted hazard ratio [aHR]=1.58, 95% confidence interval [CI]=1.17–2.12, *P*=0.003) and RFS (aHR=1.33, 95% CI=1.07–1.64, *P*=0.009) compared to those with the none-to-weak expression. Similar findings were reproduced in the liver transplantation cohort, where higher endothelial B7-H3 group was indicative of unfavorable outcomes.

Conclusions: High endothelial B7-H3 expression in HCC was associated with aggressive tumor features and poor survival outcomes. Our findings suggest that B7-H3 could serve as a potential therapeutic target in HCC.

Keywords: Hepatocellular Carcinoma, B7-H3, Tissue Microarray, Prognosis

Figure 1.

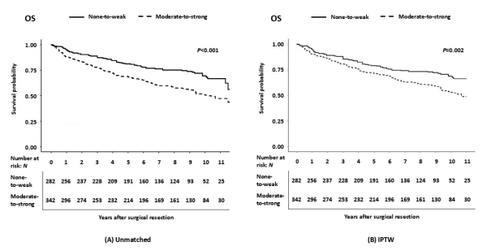
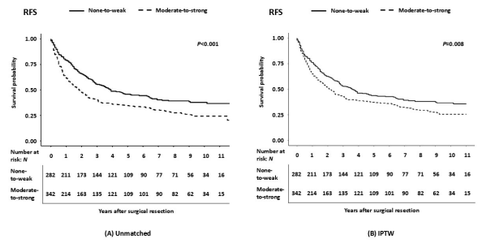


Figure 2.



FP-9

Non-Contrast Magnetic Resonance Imaging versus Ultrasonography for HCC Surveillance: A Randomized, Single-Center Trial

Hyungjin Rhee[1], Myeong-Jin Kim[1], Do Young Kim[2], Chansik An[1], Wonseok Kang[2], Kyunghwa Han[1], Yun Ho Roh[3], Kwang-Hyub Han[2], Sang Hoon Ahn[2], Jin-Young Choi[1], Jun Yong Park[2], Yong Eun Chung[1], Seung Up Kim[2], Beom Kyung Kim[2], Sunyoung Lee[1], Hye Won Lee[2], Jae Seung Lee[2]

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Aims: This study aimed to compare ultrasonography (US) and non-contrast magnetic resonance imaging (MRI) in the surveillance of hepatic malignancy.

Methods: We conducted a randomized, non-blinded, single-center trial at a single center in South Korea. Eligible individuals were aged 20–70 years with liver cirrhosis, Child–Pugh class A, and no history of liver cancer or other recent malignancy. Participants were randomized 1:1 to receive up to ten semiannual surveillance using US or non-contrast MRI with serum alpha-fetoprotein testing. The primary endpoints were the detection rates of Barcelona Clinic Liver Cancer [BCLC] stage 0 or A tumors, stage distribution at initial diagnosis, and false-positive referral rates. ClincalTrials.gov, NCT02514434.

Results: From June 2015 to November 2017, 416 patients were screened, and 414 were enrolled and assigned to the US (n=207) or MRI (n=207) group. In total, 23 participants in US group and 25 in MRI group were diagnosed with liver cancer by November 2022. The detection rates of BCLC stage 0 or A tumors were not different between the US and MRI groups (8% [95% confidence interval (CI), 5 – 13%] versus 12% [8 – 17%]). BCLC stage 0 tumors were more prevalent in the MRI group than in the US group (8% versus 3%). The MRI group had earlier BCLC stage (*P*=0.014) and lower false-positive referral rate (0.7% [95% CI, 0.4 – 1.2%] versus 3.1% [2.3 – 4.1%], *P* <0.001) compared to the US group.

Conclusions: Non-contrast MRI is a better alternative to US for the surveillance of cirrhotic patients offering earlier stage at initial diagnosis and lower false-positive referral rate.

Keywords: Cirrhosis, Hepatocellular Carcinoma, Surveillance, Magnetic Resonance Imaging

FP-10

Outcomes by Transarterial Chemoembolization (TACE) Modality from Participants (pts) with Embolizationeligible Hepatocellular Carcinoma (HCC) Treated with Durvalumab (D) + Bevacizumab (B) + TACE and Placebos (PBO) + TACE: EMERALD-1 Subgroup Analysis

Jeong Heo[1], Takuji Okusaka[2], Jung-Hwan Yoon[3], Bruno Sangro[4], Stephen L. Chan[5], Joseph P. Erinjeri[6], Marco Matos[7], Thomas Decaens[8], Eric X. Chen[9], Muhammad S. Beg[10], Ana M. Matilla[11], Le Thi Tuyet Phuong[12], Rebecca Griffin[13], Stephanie I. Udoye[14], Sandra Indiviglio[15], Masatoshi Kudo[16]

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Aims: EMERALD-1 (NCT03778957) met its primary endpoint, showing improved progression-free survival (PFS) in pts with locoregional HCC treated with D + B + TACE versus PBO + TACE (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.61–0.98). This analysis assessed the impact of TACE modality (conventional TACE [cTACE] or drug-eluting bead [DEB]-TACE) on efficacy and safety outcomes.

Methods: Pts in this analysis received D (1500 mg) or PBO for D (Q4W) plus cTACE or DEBTACE (investigator choice; TACE modality was a stratification factor). After completing the last TACE, pts received D (1120 mg) + B (15 mg/kg) or PBO for D + B (Q3W). PFS, time to progression (TTP), and overall response rate (ORR; BICR per RECIST v1.1) with D + B + TACE and PBO + TACE (intent-to-treat population) are reported by TACE modality. Safety was assessed in the safety analysis set (pts received ≥1 dose of study treatment [tx], regardless of randomization).

Results: Overall, 59.3% of pts received cTACE and 40.7% received DEB-TACE in the D + B + TACE arm; similarly, 58.5% of pts received cTACE and 41.5% received DEB-TACE in the PBO + TACE arm. Most pts received 1 or 2 TACE procedures in both cTACE (60% in D + B + TACE arm; 67.2% in PBO + TACE arm) and DEB-TACE groups (55.6% in D + B + TACE arm; 53.6% in PBO + TACE arm). Baseline characteristics in the cTACE and DEB-TACE groups were similar, with some differences in the relative distribution of BCLC, HAP, and tumor burden (BCLC Score A; 29.0% vs 17.9%: HAP Score A; 36.5% vs 25.0%: tumor burden within up-to-7 criteria; 56.4% vs 37.5%, respectively). Baseline characteristics were generally well balanced across tx arms within the cTACE and DEB-TACE groups. PFS, TTP, and ORR improved with D + B + TACE versus PBO + TACE, regardless of TACE modality (Table). In the D + B + TACE and PBO + TACE arms, max Grade 3–4 adverse events possibly related to study tx were reported by 25/100 (25.0%) and 3/116 (2.6%) pts in the cTACE group, and 16/54 (29.6%) and 9/84 (10.7%) pts in the DEB-TACE group, respectively.

Conclusions: Overall, pts receiving D + B + TACE had improved PFS, TTP, and ORR versus PBO + TACE regardless of TACE modality. Safety was manageable with both cTACE and DEB-TACE.

Clinical Trial Identification: NCT03778957

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Keywords: Hepatocellular Carcinoma, Transarterial Chemoembolization, Durvalumab, Bevacizumab

Table

	D + B and cTACE (n=121)	PBO and cTACE (n=120)	D + B and DEB-TACE (n=83)	PBO and DEB-TACE (n=85)
Median (95% CI) PFS, months	19.4 (12.4–22.3)	11.1 (7.2–14.0)	11.1 (7.2–14.2)	6.7 (5.0–7.3)
PFS HR (95% CI)	0.80 (0.59–1.10)		0.74 (0.51–1.06)	
Median (95% CI) TTP, months	22.3 (19.4–27.7)	13.6 (9.2–16.6)	15.0 (11.1–22.4)	6.9 (5.1–11.1)
TTP HR (95% CI)	0.70 (0.49–0.98)		0.55 (0.36–0.83)	
Pts with measurable disease at baseline, n	119	119	83	84
ORR, n (%) pts with response*	62 (52.1)	43 (36.1)	26 (31.3)	17 (20.2)
ORR, odds ratio (95% CI)	1.93 (1.15–3.27)		1.80 (0.89–3.69)	

*Includes confirmed complete or partial response.

FP-11

Clinical Utility of Circulating Tumor DNA in Early-Stage Biliary Tract Cancer Following Curative Resection

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Aims: To assess (1) the prognostic value of ctDNA, (2) its comparison with CA19-9, and (3) its ability to detect recurrence versus standard surveillance in early-stage biliary tract cancer (BTC) following curative resection.

Methods: A retrospective analysis was performed on patients with stage I-III BTC who underwent curative resection between September 2019 and April 2023. ctDNA analysis was conducted using a personalized, tumor-informed 16-plex mPCR-NGS

assay. Plasma samples (n=195) were collected during the MRD window (within 2 to 12 weeks after surgery and before adjuvant therapy) and longitudinally until death or last follow-up (surveillance window). The prognostic value of ctDNA was compared to CA19-9.

Results: A total of 56 patients were included, with a median follow-up of 12.8 months. ctDNA detection during the MRD window (median RFS: 6.6 months vs. not reached; hazard ratio [HR]: 26 [95% CI, 2.6–265]; *P*<.0001) and during the surveillance window (median RFS: 19.3 months vs. not reached; HR: 20 [95% CI, 2.6–153]; *P*<.0001) were associated with poorer RFS. Sixteen patients recurred. ctDNA detection preceded the first positive imaging finding in 68.8% (11/16) of the patients by an average of 3.5 (range: 0.2–8.4) months. ctDNA identified recurrence before or on the confirmed relapse date in 93.8% (15/16) of the patients with an average lead time to confirmed relapse of 3.7 (range: 0.5–10.1) months, resulting in a sensitivity of 93.8%. CA 19-9 did not show a correlation with RFS (HR: 1.17 [95% CI, 0.24–5.71]; *P*=.844), in contrast to ctDNA.

Conclusions: The analyses from our real-world cohort study show that (1) ctDNA positivity was associated with poor RFS, (2) ctDNA was a superior surveillance tool compared to CA19-9, and (3) ctDNA demonstrated the potential for earlier detection of recurrence compared to standard surveillance in resected BTC.

Keywords: CTDNA, MRD, Biliary Tract Cancer, Prognostic Factor

FP-12

Early Changes in Neutrophil-to-Lymphocyte Ratio as a Prognostic Marker for Tumor Response to Atezolizumab and Bevacizumab in Hepatocellular Carcinoma: A Multicenter Retrospective Study

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Aims: Atezolizumab and bevacizumab has been used in the treatment of advanced hepatocellular carcinoma (HCC). However, reliable predictive biomarkers for evaluating tumor response to this therapy remain limited. This study aimed to investigate the predictive value of early changes in the neutrophil to lymphocyte ratio (NLR) in patient with HCC undergoing treatment with atezolizumab and bevacizumab.

Methods: This multicenter retrospective study included 677 patients with HCC who received atezolizumab and bevacizumab. Factors associated with tumor response were analyzed.

Results: At the time of the first tumor response assessment, the rates of complete remission (CR), partial response (PR), stable disease (SD), and progressive disease (PD) were 0.3 %, 16.7 %, 52.7 % and 30.3 %, respectively. The objective response rate and disease control rate were 17.0 % and 69.7 %, respectively. Progression free survival and overall survival were significantly associated with first tumor response (*P*<0.001). Multivariate analysis identified virus infection [hazard ratio (HR) = 1.881, 95% confidence interval (CI) = 1.237 – 2.858, *P*=0.003], BCLC stage (HR = 4.207, 95% CI =1.653 – 10.707, *P*=0.003), and NLR change at 3 weeks (HR = 0.387, 95% CI = 0.251 – 0.595, P <0.001) as independent predictive factors for objective tumor response. The first tumor response rates according to NLR change at 3 weeks were 67.8 % vs. 32.2% for CR/PR, 49.0% vs. 51.0 for SD, and 38.5% vs. 61.5% for PD, respectively (*P*<0.001). The mean NLR at 3 weeks in patients who achieved CR/PR, SD and PD were 2.7, 3.6, and 4.8, respectively (*P*<0.001).

Conclusions: NLR change observed at 3 weeks is correlated with the first tumor response, which is subsequently associated with survival outcomes. Early changes in NLR may serve as an early predictor of a lack of response to atezolizumab and bevacizumab treatment. Therefore, NLR is a readily measurable biomarker with the potential to aid in the timely identification of HCC patients who could benefit from atezolizumab and bevacizumab treatment.

Keywords: Hepatocellular Carcinoma, Atezolizumab and Bevacizumab, Tumor Response, Neutrophil to Lymphocyte Ratio

FP-13

Comparative Efficacy of Lenvatinib versus Sorafenib as Sequential Therapies Following Atezolizumab and Bevacizumab Treatment in Advanced Hepatocellular Carcinoma: A Multicenter Retrospective Study

Jun Sik Yoon[1], Yeo Wool Kang[2], Jung Eun Song[3], Joonho Jeong[4], Yu Rim Lee[5], Jae Hyun Yoon[6], Young Mi Hong[7], Sang Youn Hwang[8], Hyun Young Woo[9], Soo Young Park[5], Yanghyun Baek[2], Jeong Heo[9], Sung Jae Park[1], Won Young Tak[5], Youn Jae Lee[1], Sung-Bum Cho[10]

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Aims: Atezolizumab plus bevacizumab (AtezoBev) therapy is recommended as the first-line systemic treatment for advanced hepatocellular carcinoma (HCC) in most guidelines. However, sequential treatment for patients who have experienced disease progression after AtezoBev therapy remains unclear. We aimed to compare the efficacy of lenvatinib and sorafenib as sequential therapies following AtezoBev failure.

Methods: This multicenter retrospective study included patients with advanced HCC who received lenvatinib or sorafenib as sequential treatment after AtezoBev failure from 7 referral centers in Korea. To adjust for baseline characteristics between the two groups, we performed propensity score (PS) matching analysis.

Results: We included 221 patients (median age: 65 years; male: 86.4%) who received second-line systemic therapy with lenvatinib (n=92) or sorafenib (n=129). The lenvatinib group had superior progression-free survival (PFS) compared to the sorafenib group (adjusted hazard ratio [aHR], 0.39; 95% confidence interval [CI], 0.25–0.63; *P*<0.001), but not overall survival (OS) (aHR, 0.76; 95% CI, 0.49–1.17; *P*=0.21) (Figure 1). The results were reproducible after PS matching analysis (Figure 2).

Conclusions: Lenvatinib demonstrated superior PFS and comparable OS compared to sorafenib as a sequential treatment after AtezoBev failure. These findings were consistent with previous results, and further studies are warranted to identify the optimal patient subgroup that may derive survival benefits from lenvatinib.

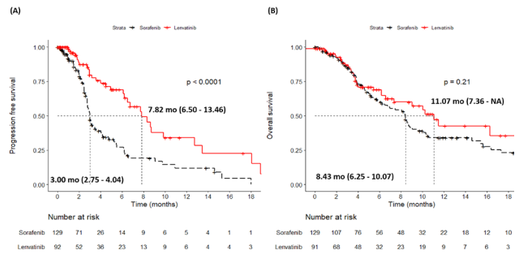

Figure 1.

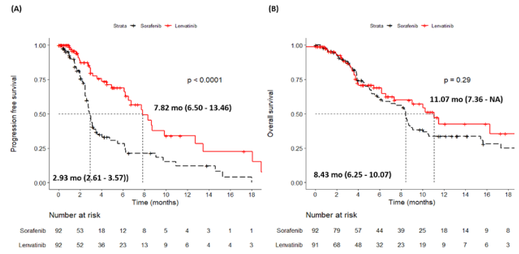

Figure 2.

Keywords: Hepatocellular Carcinoma, Lenvatinib, Sorafenib, Sequential Therapy

FP-14

Risk of Variceal Bleeding in Patients Receiving Atezolizumab–Bevacizumab Treatment for Hepatocellular Carcinoma

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Aims: Real-world data on the actual risk of variceal bleeding (VB) in patients receiving atezolizumab–bevacizumab (Atezo–Bev) treatment remain limited. This study aimed to assess the risk of VB and identify risk factors in patients with advanced hepatocellular carcinoma (HCC) receiving Atezo–Bev treatment.

Methods: This retrospective study included 640 patients with HCC who underwent endoscopy before Atezo–Bev treatment at two hospitals in Korea. The primary outcome was the occurrence of VB. With non-VB event considered as competing events.

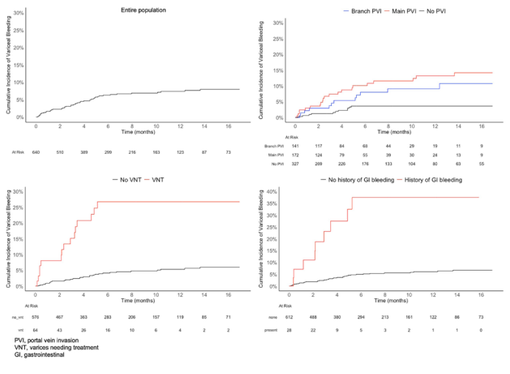
Results: Of the 640 patients, the mean age was 61.3 years and 528 (82.5%) patients were male. Main etiology of HCC was chronic hepatitis B virus (69.5%) and BCLC stage C was in 563 (88.0%). Portal vein invasion was present in 313 (48.9%).

During a median follow-up of 5.6 months, 45 patients (7.0%) developed VB. The cumulative incidence of VB was 6.3% at 6 months and 7.4% at 12 months. No patient died from VB. In multivariable analysis, factors associated with an increased risk of VB included main PVI (subdistribution hazard ratio [SHR]:3.49, 95% confidence interval [CI]:1.63–7.44), low platelet count (SHR:0.994, 95% CI:0.99–1.00), a history of gastrointestinal bleeding (SHR:3.70, 95% CI:1.49–9.16), and varices needing treatment (VNT; SHR:2.67, 95% CI:1.26–5.64).

Conclusions: A low platelet count, main PVI, history of gastrointestinal bleeding, and VNT were significant risk factors for VB

in patients receiving Atezo–Bev treatment for HCC. Identifying these factors can guide clinicians in assessing and managing the risk of VB in real-world settings.

Keywords: Hepatocellular Carcinoma, Bevacizumab, Variceal Bleeding



FP-15

Indeterminate Nodule-Like Arterial Phase Hyperenhancement in the Liver on CT: Differentiation of HCCs from Vascular Pseudolesions Using a CT Radiomics Approach

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Aims: To investigate the diagnostic value of CT radiomics for distinguishing hepatocellular carcinomas (HCCs) from vascular pseudolesions in indeterminate nodule-like arterial phase hyperenhancement (NAPH) observations detected in HCC high-risk patients.

Methods: In this retrospective study, 259 CT-detected NAPHs (<20 mm, eventually diagnosed as HCCs [n=51] or vascular pseudolesions [n=208] on subsequent liver MRI) from 181 patients were collected and divided into training set (204 NAPHs with 35 HCCs) and validation set (55 NAPHs with 16 HCCs) according to the CT exam date. In the training set, a CT radiomics model to distinguish HCCs from vascular pseudolesions using multivariable logistic regression was developed by selecting 2D CT radiomics features of NAPHs on arterial phase imaging, where the best subset was chosen using the maximum R^2 method after decorrelation with classic minimum redundancy maximum relevance. The CT radiomics model and a combined model incorporating CT radiomics features and significant conventional imaging features, was evaluated for performance using receiver operating characteristic (ROC) curve analysis in the training and validation sets.

Results: Out of 1,226 extracted radiomics features of NAPHs, four second order features were chosen for building the CT radiomics model to distinguish HCCs from vascular pseudolesions. The developed radiomics model resulted in areas under the ROC curve (AUCs) were 0.794 (95% confidence interval [CI]: 0.731-0.847) in the training set; and 0.688 (95% CI: 0.548-0.806) in the validation set, which were higher than the AUCs of lesion size (mm) [IJ1] (0.547 [95% CI: 0.476-0.617], P<0.001; 0.502 [95% CI: 0.364-0.640], P=0.126). The combined model which incoporated lesion location (subcapsular vs non-subcapsular) and the radiomics features showed AUCs of 0.821 (95% CI: 0.762-0.871) and 0.722 (95% CI: 0.585-0.834) in the training and validation sets, respectively.

Conclusions: For indeterminate NAPHs on CT, CT radiomics analysis on arterial phase imaging may help differentiate HCC from vascular pseudolesions, which can impact the subsequent diagnostic work-up or management strategy.

Keywords: Hepatocellular Carcinoma, Nodule-Like Arterial Phase Hyperenhancement, Ct Radiomics, Differential Diagnosis

Friday, May 30, 2025, 15:10-16:20

3. MASLD, Clinical

FP-16

Metabolic Dysfunction-Associated Fibrosis 5 (Maf-5) Score and the Risk of Liver-Related Events in the General Population

Byeong Geun Song[1], GoEun Park[2], Myung Ji Goh[1], Wonseok Kang[1], Geum-Youn Gwak[1], Yong-Han Paik[1], Moon Seok Choi[1], Joon Hyeok Lee[1], Dong Hyun Sinn[1]

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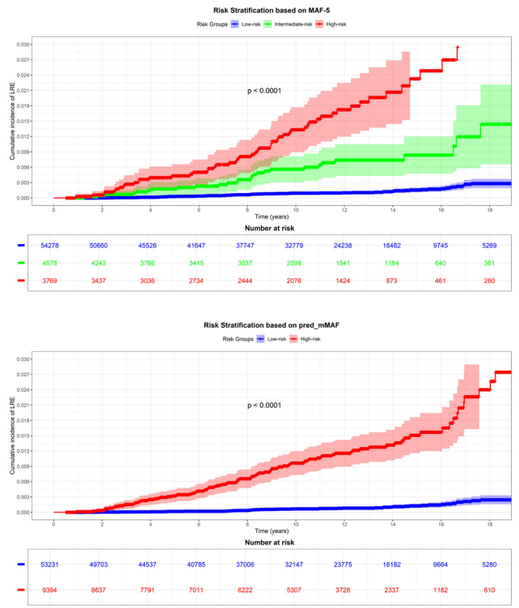
Aims: Recently, a metabolic dysfunction-associated fibrosis (MAF-5) was proposed as a referral tool to identify individuals at high risk of liver fibrosis. However, its ability in identifying individuals at risk of liver-related events (LREs), which is hard clinical endpoint of screening, is unknown.

Methods: A retrospective cohort of 62,625 adult participants without history of cancer, organ transplantation, chronic viral hepatitis, or heavy alcohol intake was followed up for the development of LREs. LREs were defined as development of hepatocellular carcinoma and/or complication of liver cirrhosis. The MAF-5 score was calculated and tested for its predictability of LREs, compared to other non-invasive biomarkers of liver fibrosis. We also assessed whether modification of MAF-5 score can enhance performance of LREs prediction.

Results: During a median of 11.2 years of follow-up, 147 cases of LREs were identified. The MAF-5 score could stratify participants at different risks of LREs. Age was an independent risk factor for LRE, and when age was used as covariate (aMAF-5 score), it showed better C-index (0.870 vs. 0.818) and better integrated AUC (0.858 vs. 0.784) compared to MAF-5 score. When participants were further classified according to aMAF-5 score, the LREs risk differed by aMAF-5 score within same MAF-5 score category. When aMAF-5 score was used with MAF-5 score, using either criterion (either positive) could improve sensitivity with a tradeoff in specificity, while using both criterion (both positive) could improve specificity, with a tradeoff in sensitivity. Subgroup analysis showed good performance of MAF-5 and aMAF-5 score regardless of age group (>60 vs. ≤60 years), gender, and presence of metabolic syndrome.

Conclusions: The MAF-5 score was able to classify LREs risk. In addition, modification of MAF-5 score using age (aMAF-5) could further enhance its performance in stratifying risk of LREs. These scores can be used to identify individuals at risk of LREs.



Keywords: Non-Alcoholic Fatty Liver Disease, Fibrosis, Liver Cirrhosis, Liver Neoplasms

FP-17

Cost-Effectiveness Analysis of Masld Screening Using FIB-4 Based Two-Step Algorithm in the Medical Check-up

Hye-Lin Kim[1], Hyo Young Lee[2], Eileen Laurel Yoon[2], Jihyun An[3], Ha Il Kim[3], Joo Hyun Sohn[3], Jae Eun Ryu[4], In Young Kang[4], Ramsey Cheung[5], Donghee Kim[5], Dae Won Jun[2]

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Aims: Screening for metabolic dysfunction-associated steatotic liver disease (MASLD) across the entire general population is not currently a recommended strategy. However, it is not uncommon to receive a medical check-up or health check-up for a various of reasons. We tried to investigate whether advanced fibrosis screening in MASLD patients is cost-effective for adults aged 40-49 years during medical or health check-up.

Methods: The target group for analysis was adults who received medical check-ups for various reasons in the United States. We constructed a hybrid model of the decision tree model and Markov model to compare expected costs and quality-adjusted life-years (QALYs) between 'screening' and 'no screening' groups from healthcare system perspectives. Patients diagnosed MASLD with advanced fibrosis by FIB4 and VCTE were given intensive lifestyle intervention (ILI). The incremental cost-effectiveness ratio (ICER) was calculated for a 30-year horizon.

Results: Assuming effect of ILI is limited to regression of liver fibrosis, ICER of the FIB-4-based two steps algorithm was $103,405 per QALY in adults aged 40-49 years, which was slightly above the threshold value ($100,000/QALY). And in those in adults aged 50-59 and 60-69 years, the ICER was $137,593 and $197,901 per QALY, respectively. If we assume the effect of ILI can improve liver fibrosis as well as cardiovascular disease events, ICERs of screening in aged 40-49 and 50-59 years were $74,596, and $95,974 per QALY, respectively. In an analysis that included additional positive effect on extrahepatic cancer by ILI, estimated ICERs were below the threshold in those in aged 40-49 and 50-59 years.

Conclusions: Advanced fibrosis screening in MASLD patients using the FIB-4-based two-step algorithm and ILI was cost-effective for adults aged 40-49 years, taking into account both liver fibrosis and cardiovascular disease.

Keywords: MASLD, FIB-4, ICER

FP-18

The Prognostic Impact of Statin Exposure in Metabolic Dysfunction-Associated Steatotic Liver Disease

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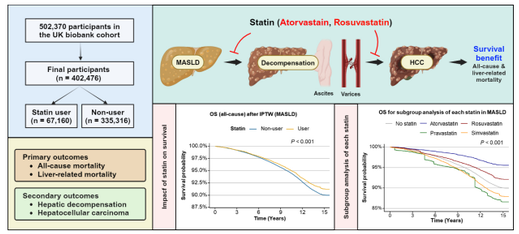
Aims: MASLD is an increasing global health concern associated with metabolic syndromes such as obesity and type 2 diabetes. While statins are widely used to manage hypercholesterolemia, their potential protective effects against liver-related outcomes in MASLD have not been thoroughly explored.

Methods: This study investigates the impact of statin use on outcomes in patients with metabolic dysfunction-associated steatotic liver disease (MASLD). A population-based study cohort was analyzed using data from the UK Biobank, which included 402,476 participants after exclusions. Inverse probability of treatment weighting (IPTW) was utilized to balance baseline characteristics. The primary outcomes included all-cause mortality and liver-related mortality, with secondary outcomes covering the incidence of hepatocellular carcinoma (HCC) and hepatic decompensation. Subgroup analyses were conducted to assess the effects of specific statin types and gender differences.

Results: Statin use correlated with a 19% reduction in all-cause mortality and a 37% reduction in liver-related mortality in the MASLD cohort. Notably, atorvastatin was significantly effective in reducing all-cause mortality, liver-related mortality, hepatic decompensation, and HCC risk. Gender-specific analyses demonstrated that female statin users experienced the most significant reductions in mortality and HCC incidence. Statin use significantly improved survival and decreased liver-related outcomes in MASLD patients, with gender-specific analyses showing enhanced effects for female users.



Conclusions: The findings suggest the importance of statin selection and highlight that gender-specific strategies may enhance treatment efficacy in the MASLD cohort.

Keywords: MASLD, Statin, Hepatic Decompensation, Hepatocellular Carcinoma

FP-19

Influence of Skeletal Muscle Loss on CKD Development in Metabolic Dysfunction-Associated Steatotic Liver Disease Patients

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is associated with an elevated risk of chronic kidney disease (CKD), a major global health concern. The role of sarcopenia, another emerging issue, in this association remains unclear. This study aimed to investigate whether sarcopenia increases the risk of CKD incidence in MASLD patients and whether progressive muscle mass loss further exacerbates this risk.

Methods: This study included 19,867 adults without CKD who underwent at least two health examinations between 2003 and 2021. MASLD was diagnosed by ultrasonography. Appendicular skeletal muscle mass was measured by bioelectrical impedance analysis, and sarcopenia was assessed using the skeletal muscle mass index (SMI). Changes in skeletal muscle mass were calculated as the difference in SMI between follow-up and baseline. MASLD severity was determined using the fibrosis-4 score. CKD was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m^2.

Results: Over a follow-up of 124,236 person-years (median duration, 6.1 years), 993 participants developed CKD. The adjusted hazard ratio (aHR) for incident CKD in participants with sarcopenia compared to those without was 1.41 (95% CI: 1.12–1.77) in MASLD. Furthermore, gradual muscle loss was associated with a higher CKD risk, demonstrating a dose-dependent relationship. Participants with progressive muscle loss had an aHR of 1.13 (95% CI: 1.00–1.29) for CKD development, compared to those with preserved or increased muscle mass. The risk of CKD increased in proportion to MASLD severity.

Conclusions: In conclusion, sarcopenia was independently associated with the development of incident CKD in MASLD, with the risk increasing as muscle mass decreased over time. This relationship was particularly evident in individuals with advanced fibrosis. Evaluating sarcopenia and preventing muscle loss could be beneficial in identifying those at elevated risk for CKD development and potentially delaying its onset in MASLD.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Sarcopenia, Skeletal Muscle Loss, Chronic Kidney Disease

FP-20

Risk of Liver-Related Events in Metabolic Dysfunction-Associated Steatotic Liver Disease: Impact of Cardiometabolic Risk Factor Count and Its Longitudinal Changes

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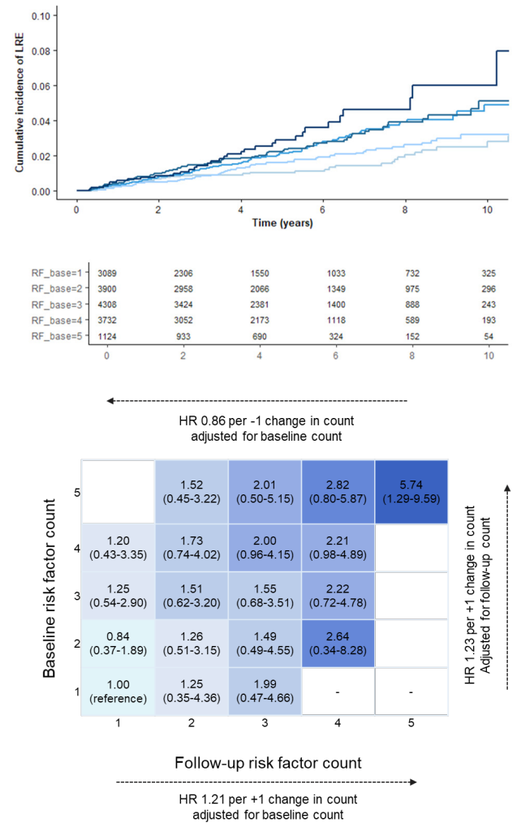
Aims: Liver-related events (LREs) can occur in patients with metabolic dysfunction–associated steatotic liver disease (MASLD). We investigated the risk of LREs in patients with MASLD based on the cardiometabolic risk factor (CMRF) count and its changes over time.

Methods: Data from patients with MASLD who underwent vibration-controlled transient elastography (VCTE) at 16 tertiary referral centers between February 2004 and January 2023 were analyzed (VCTE prognosis study cohort). Patients were stratified according to the CMRF count. Patients who underwent follow-up examinations at 2 years were categorized based on changes in their CMRF count from baseline. LRE risk was evaluated using a multivariable-adjusted Cox proportional hazards model.

Results: Among 16,603 patients (mean [SD] age, 52.5 [13.7] years; 9600 [57.8%] were male), 316 (1.9%) patients developed LREs during a median follow-up of 51.7 months (IQR, 25.2-85.2). The risk of LREs increased gradually with a higher baseline CMRF count (1: reference; 2: HR=1.25 [95% CI: 0.78–1.98]; 3: HR=1.79 [95% CI: 1.17–2.76]; 4: HR=1.85 [95% CI: 1.19–2.86]; 5: HR=2.69 [95% CI: 1.59–4.54]; per 1-higher: HR=1.29 [95% CI: 1.15–2.90]). Among those with follow-up data, an increase in CMRF count was associated with a higher risk of LREs (per +1 change; HR=1.21 [95% CI: 1.18–1.27]), with a greater risk observed in those who consistently had high CMRF counts compared to those who newly developed high CMRF counts (per +1 baseline count; HR=1.23 [95% CI: 1.21–1.35]). Conversely, a reduction in CMRF count was associated with a lower risk of LREs (per -1 change; HR=0.86 [95% CI: 0.82–0.89]).

Conclusions: Both baseline CMRF count and its longitudinal changes were significantly associated with LRE risks in patients with MASLD. Accurate identification of these markers may facilitate personalized management of MASLD-related LRE risk.



Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Cardiometabolic, Risk Factor Count, Liver-Related Event

FP-21

Impact of Steatotic Liver Disease and Metabolic Risk Factors on Post-Surgical Outcomes in HBV-Related Hepatocellular Carcinoma

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Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Aims: The impact of steatotic liver disease and metabolic risk

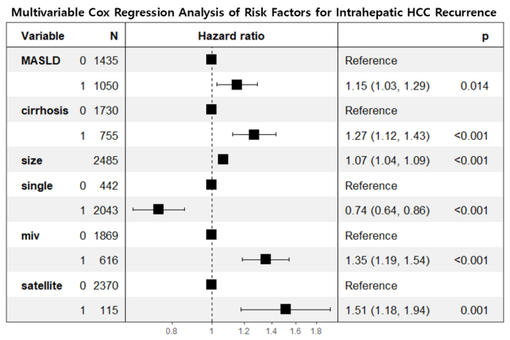
factors on post-operative outcomes in patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) remains unclear. This study aims to evaluate the impact of MASLD and metabolic risk factors on HCC recurrence and overall survival following curative resection.

Methods: A retrospective cohort study was conducted on 2,485 patients with very early or early-stage HBV-related HCC who underwent curative surgical resection between 2010 and 2018 at Asan Medical Center, Korea. Baseline data, including the presence of histologic steatosis and metabolic risk factors—obesity, hypertension, dyslipidemia, and diabetes—were collected. Using this baseline data, patients were stratified according to the diagnostic criteria of MASLD, based on metabolic risk factors and hepatic steatosis. The risks of HCC recurrence and overall mortality were analyzed according to MASLD status and metabolic risk profiles.

Results: Among the 2,485 patients, 1,050 (42.3%) were diagnosed with MASLD. Compared to non-MASLD patients, those with MASLD had a higher prevalence of metabolic comorbidities and cirrhosis, lower alpha-fetoprotein levels, and less microvascular invasion. Over a median follow-up period of 4.9 years, 1,087 (43.7%) cases of recurrence and 475 (19.1%) deaths were documented. Patients with MASLD had a significantly elevated risk of intrahepatic HCC recurrence compared to those without MASLD (adjusted hazard ratio [aHR], 1.15; 95% confidence interval [CI], 1.03–1.29). Notably, the risk of recurrence demonstrated a clear increasing trend in proportion to the number of metabolic risk factors, with a 7% elevation in patients with a single factor and a 25% elevation in those with three or more factors. However, MASLD was not significantly associated with overall mortality (aHR: 1.06; 95% CI: 0.88–1.28). Subgroup analysis demonstrated that the impact of MASLD on recurrence risk was more prominent in non-obese patients (aHR, 1.35; 95% CI, 1.03–1.78) than in obese patients (aHR, 1.15; 95% CI, 1.01–1.32), suggesting that obesity status may modify the effect of MASLD on post-surgical HCC recurrence.

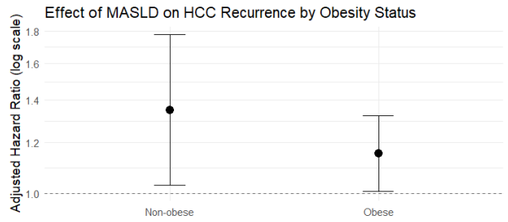
Multivariable Cox Regression Analysis of Risk Factors for Intrahepatic HCC Recurrence

Variable		N	Hazard ratio	p
MASLD	0	1435	Reference	
	1	1050	1.15 (1.03, 1.29)	0.014
cirrhosis	0	1730	Reference	
	1	755	1.27 (1.12, 1.43)	<0.001
size		2485	1.07 (1.04, 1.09)	<0.001
single	0	442	Reference	
	1	2043	0.74 (0.64, 0.86)	<0.001
miv	0	1869	Reference	
	1	616	1.35 (1.19, 1.54)	<0.001
satellite	0	2370	Reference	
	1	115	1.51 (1.18, 1.94)	0.001



Association Between Increasing Metabolic Risk Burden and Intrahepatic HCC Recurrence

Variable		N	Hazard ratio	p
MRG	Ref. group	1435	Reference	
	MR level 1	360	1.07 (0.90, 1.27)	0.424
	MR level 2	314	1.19 (1.00, 1.41)	0.049
	MR level 3	376	1.25 (1.07, 1.47)	0.005
size		2485	1.06 (1.03, 1.09)	<0.001
single	0	442	Reference	
	1	2043	0.74 (0.64, 0.85)	<0.001
miv	0	1869	Reference	
	1	616	1.36 (1.20, 1.55)	<0.001
satellite	0	2370	Reference	
	1	115	1.59 (1.24, 2.04)	<0.001



Conclusions: Steatotic liver disease is associated with an increased risk of intrahepatic HCC recurrence after curative resection for HBV-related HCC, particularly in non-obese patients and those with multiple metabolic risk factors. These findings highlight the importance of personalized post-operative surveillance and management strategies based on obesity status and metabolic risk profiles.

Keywords: MASLD, Recurrence, Obesity

FP-22

Allyl Nonanoate: A Bile Metabolite and Potential Biomarker for Hepatic Fibrosis in MASLD

Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], In Young Kang[1], Jin Kim[1], Hye Young Kim[1], Seung Min Lee[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: Metabolic dysfunction-associated steatosis (MASLD) is a prevalent chronic liver disease with limited treatment options due to unclear pathophysiology. Bile acids play a critical role in MASLD progression; however, we hypothesized that serum or fecal bile acids may not directly reflect hepatic bile acid signaling due to their multi-step metabolic processing. To address this, we conducted metabolomic analysis to investigate distinguishing bile metabolites obtained from gallbladder samples of biopsy-proven MASLD patients compared to healthy controls.

Methods: Primary bile samples and liver biopsies were collected from 68 patients undergoing cholecystectomy, including 19 healthy controls and 49 MASLD patients with varying degrees of hepatic fibrosis. Metabolomic profiling of bile acids was conducted using mass spectrometry to identify metabolites associated with hepatic fibrosis. RNA sequencing was performed on HT29 cells treated with the identified metabolite, and its fibrotic effects were further investigated using the human hepatic stellate cell line LX-2.

Results: Among the metabolites increased in patients with fibrosis (139 in mild fibrosis and 173 in significant fibrosis) compared to controls, eight bile metabolites showed a positive dose-dependent correlation with fibrosis severity. Allyl nonanoate was ultimately identified as an elevated metabolite in fibrosis patients. Gene set enrichment analysis revealed downregulation of pathways related to cell cycle progression, including the G2/M checkpoint. In vitro, allyl nonanoate demonstrated a dose-dependent reduction in the mRNA expression of fibrosis markers FN1 and Col1A1.

Conclusions: This study identified allyl nonanoate as a bile metabolite associated with hepatic fibrosis in MASLD patients. These findings highlight the potential of primary bile samples as a valuable resource for identifying novel biomarkers and therapeutic targets.

Keywords: Allyl Nonanoate, Hepatic Fibrosis, Bile, MASLD

Friday, May 30, 2025, 15:10-16:30

4. HBV Basic and ALD

FP-23

Misclassification of Alcohol Use Disorder in MASLD and MetALD: Prevalence, Clinical Characteristics, and Outcomes

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Aims: Within metabolic and alcohol-associated liver disease (MetALD), there exists a continuum where the condition can conceptually shift between being metabolic dysfunction associated steatosis disease (MASLD) or alcoholic liver disease (ALD). However, alcohol use disorder (AUD) can be included in these diagnoses. This study aimed to investigate the prevalence and clinical characteristics of misclassified AUD among patients with MASLD and MetALD.

Methods: The study included a total of 3,362,552 participants from the 2011–2012 National Health Screening Program. Steatotic liver disease was defined as a Hepatic Steatosis Index score of 36 or higher. Significant alcohol intake was calculated based on a self-reported questionnaire. AUD was defined as having received medical care for an alcohol-related condition at least once during the study period. The average follow-up period for participants was 9.8 years. The misclassified AUD as MASLD and MetALD groups demonstrated significantly higher cumulative incidence rates for both HCC and liver related complications compared to the pure MASLD and MetALD (MASLD without AUD and MetALD without AUD) groups (both P values for log-rank tests <.0001).

Results: MASLD and MetALD prevalence were 23.8% and 1.9%, respectively. AUD was identified in 1.1% (8,481 individuals) of MASLD and 4.7% (2,989 individuals) of MetALD cases. Misclassified AUD was associated with significantly higher all-cause and liver-related mortality. Adjusted hazard ratios for liver-related mortality were 6.53 for AUD misclassified as MASLD and 6.98 for AUD misclassified as MetALD. Extrahepatic cancer mortality risk was also elevated (adjusted hazard ratio: 1.33 in MASLD; 1.44 in MetALD).

Conclusions: A significant number of AUD cases were misclassified as MASLD and MetALD in crosssectional assessment of alcohol consumption. The AUD misclassified as MASLD or MetALD had higher liver-related mortality than the pure MASLD and MetALD groups.

Keywords: MASLD, METALD, AUD

FP-24

Circulating Fungal Mycobiome and Lipid Dysregulation Induces Mitochondrial Dysfunction Mediated Shock in Severe Alcoholic Hepatitis

Gaurav Tripathi[2], Vasundhra Bindal[2], Neha Sharma[2], Sushmita Pandey[2], Vipul Sharma[2], Manisha Yadav[2], Nupur Sharma[2], Babu Mathew[2], Sanju Yadav[2], Meenu Bajpai[4], Rakhi Maiwall[1], Shiv Kumar Sarin[1], Jaswinder Singh Maras[2]

[1]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi; [2]Departments of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi

Aims: Severe alcoholic hepatitis (SAH) has a high mortality, with sepsis as a leading cause of death. Fungal overgrowth and lipid dysregulation contribute to disease progression, yet their contribution to the induction of shock remains unclear. This study identifies lipid and fungal peptide signatures predicting septic shock and early mortality in SAH patients.

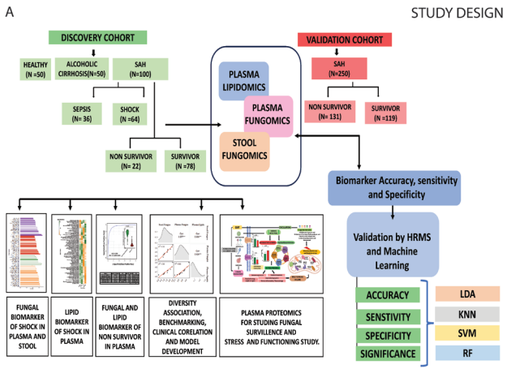
Methods: Stool and plasma samples from a cohort (n=50

healthy controls, n=50 alcohol-associated ic cirrhosis, n=100 SAH patients with sepsis (n=36), and septic shock(n=64) were subjected to circulating fungal peptide and lipidome analysis using high-resolution mass spectrometry (HRMS). Shock and non-survival specific changes in the fungal peptides and lipidome were identified, correlated, and benchmarked against clinical parameters and severity indices (MELD, SOFA, CTP, mDF). The top 5 lipid species and fungal peptides were used to create probability of detection (POD) models for septic shock and early mortality and were validated in a separate cohort of 300 ACLF patients using HRMS and machine learning.

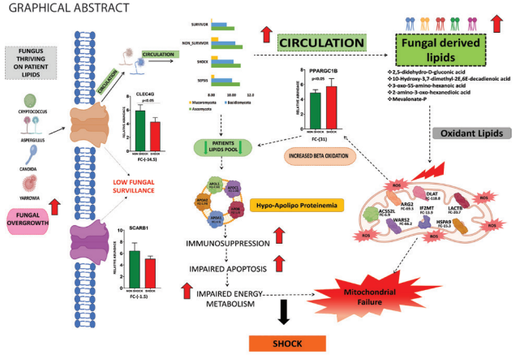
Results: Plasma and stool lipidome analysis identified more than 3388 lipid species spanning 94 classes and 570 subclasses (FDR<0.01). SAH Patients with septic shock showed 453 lipid species in stool and 326 in plasma upregulated and linked to fatty esters, fatty amides, fatty acyl alcohols, phenolic lipids, and bile acids (P<0.05). Lipid alpha diversity was the lowest in septic shock patients as compared to other groups (P<0.05) with a significant decrease in free fatty acids and others. Fungal peptide-based community analysis identified 106 fungal species in plasma and stool (FDR>0.01). Fungal diversity was significantly lower in SAH patients with shock and non-survivors (P<0.05). Notably, patients with shock and early mortality showed a significant increase in more than 40 fungal species, including Paracoccidioides (FC >3000) and Bipolaris maydis (FC >172, P<0.05). Increased levels of Aspergillus species (A. clavatus FC>8, A. fischeri FC>10, A. niger FC>15) and Candida species (C. parapsilosis FC >25, C. albicans FC >3, C. dublinliensis FC >8) were also found in septic shock and non-survivor. *Aspergillus flavus* (Log FC >1.9 in plasma; Log FC >9 in stool; P<0.05), *Aspergillus niger* (Log FC >41 in plasma; Log FC >40 in stool; P<0.05), *Candida albicans* (Log FC >10 in plasma; Log FC >14 in stool; P<0.05), *Cryptococcus neoformans* (Log FC >71 in plasma; Log FC >19 in stool; P<0.05), and *Yarrowia lipolytica* (Log FC >7 in plasma; Log FC >228 in stool; P<0.05) IIn septic shock and non-survivor, increased fungal growth of Aspergillus and Candida led to decreased host fatty acids (P<0.05). POD models for shock and early mortality correlated with lactate, noradrenaline, FiO2, AKI, TLC, neutrophil counts, and severity scores (MELD, CTP, AARC; R^2>0.7, P<0.05), showing AUC>0.99 and HR=10 (P<0.05). Increased fungal species -specific 10-Hydroxy-3,7-dimethyl-2E,6E-decadienoic acid (FC>25), and 2,5-didehydro-D-gluconic acid (FC >157) demonstrated > 91% diagnostic accuracy and >90% sensitivity/specificity for predicting shock and early mortality.

Conclusions: Conclusion: Our study identifies lipid mediators derived from fungal infections, associated with mitochondrial failure, as independent predictors of shock and early mortality in septic patients with severe alcohol-associated hepatitis.

Keywords: Diagnosi, Septic Shock, Lipidomics, Fungomics



GRAPHICAL ABSTRACT



FP-25

Impact of Gastrectomy on the Risk of Alcohol-Related Liver Disease: A Nationwide Population-Based Cohort Study in Korea

Sang Yi Moon[1], Dongwoo Kang[2], Jungkuk Lee[2], Yeo Wool Kang[1], Junho Park[3], Samuel S. Lee[3], Yang Hyun Baek[1]

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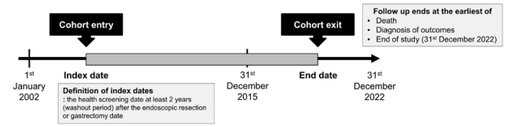
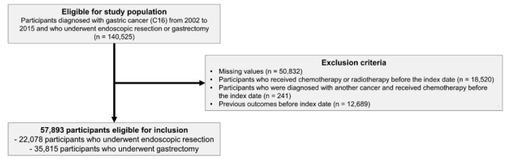
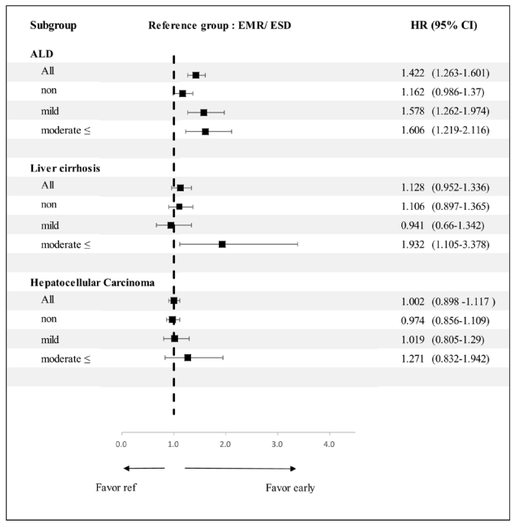
Aims: After a gastrectomy, the same amount of alcohol may have effects similar to binge drinking. This study aims to evaluate the relationship between gastrectomy, alcohol consumption, and the diagnosis of liver-related diseases by comparing individuals with and without gastrectomy based on their alcohol intake.

Methods: From 2002 to 2015, a total of 140,525 patients diagnosed with gastric cancer who underwent either endoscopic resection or gastrectomy were identified through the National Health Insurance Service. Gastric cancer was defined using the ICD-10 code (C16) and classified into two groups based on the procedure code: the endoscopic resection group and the gastrectomy group. The index date was set as the date of the health screening conducted at least two years (washout period) after the procedure or surgery. Alcohol consumption was categorized based on self-reported intake on the index date (no, mild, above moderate). The primary outcome was the incidence of newly diagnosed alcohol-related liver disease (ALD), liver cirrhosis (LC), and hepatocellular carcinoma (HCC) during the follow-up period.







Results: The analysis included 22,078 patients who underwent endoscopic resection and 35,815 who underwent gastrectomy, with a median follow-up of 6.9 years. Using the endoscopic resection group as the reference, the adjusted hazard ratio (aHR) for ALD in the gastrectomy group increased with higher alcohol consumption (no: 1.162 [95% CI 0.986–1.37], mild: 1.578 [95% CI 1.262–1.974], above moderate: 1.606 [95% CI 1.219–2.116]). Similarly, the aHR for LC in the gastrectomy group increased with alcohol intake, showing a significant risk at moderate or higher levels (above moderate: 1.932 [95% CI 1.105–3.378]). However, the incidence of HCC did not differ significantly between the two groups based on alcohol consumption.

Conclusions: Patients who have undergone gastrectomy may be at increased risk of developing liver-related diseases as a result of alcohol consumption.

Keywords: Alcohol Consumption, Alcoholic Liver Disease, Cirrhosis, Gastrectomy

FP-26

Intrahepatic IgA Accumulation Activates Macrophages and Exacerbates Hepatic Inflammation in Alcoholic Liver Disease

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Aims: Immunoglobulin A (IgA) plays a key role in immune defense by neutralizing pathogens at mucosal surfaces. However, emerging evidence suggests that IgA may also contribute to hepatic inflammation. In the context of alcoholic liver disease (ALD), whether intrahepatic IgA accumulates and directly interacts with macrophages in liver remains unclear. In this study, we aim to investigate these IgA–macrophage interactions and elucidate how these interactions contribute to the progression of alcoholic liver disease.

Methods: This study included 100 patients with ALD, and liver function-related parameters, including serum IgA levels, Total/direct bilirubin, and AST/ALT were measured. The NIAAA model was conducted over a two-week period to establish a mouse model of alcoholic liver disease. Mouse blood samples were collected to measure AST/ALT. Intrahepatic IgA-macrophages interactions were analyzed by performing single-cell RNA sequencing analysis and flow cytometry (FACS) after dissociating the liver tissue. Paraffin-embedded liver sections were then subjected to immunohistochemistry to determine the expression of IgA, as well as the expression of macrophage-related markers, including CD68, F4/80 within the liver.

Results: In the alcohol-exposed group, AST, direct bilirubin, and serum IgA levels were significantly higher than in the control group, indicating liver injury. Single-cell RNA sequencing (scRNA-seq) and flow cytometry (FACS) revealed increased interactions between intrahepatic IgA and macrophages in a mouse model of alcoholic liver disease. Flow cytometry analysis further demonstrated heightened binding between

IgA and F4/80^{+}CD11b^{+} macrophages. Additionally, scRNA-seq confirmed an increased number of macrophages, identified by the expression of Timd4 and Clec4f. Upregulated levels of F4/80 (Adgre1), CD68, IL-1β (Il1b) suggested enhanced macrophage activation and proliferation. Immunohistochemistry of paraffin-embedded liver sections showed increased IgA expression alongside macrophage-related markers, including CD68 and F4/80. Notably, IgA binding to hepatic macrophages was elevated, further supporting the concept of intrahepatic IgA accumulation and its potential role in liver pathology.

Conclusions: These findings suggest that intrahepatic IgA accumulation plays a crucial role in the progression of alcoholic liver disease (ALD) by interacting with macrophages, highlighting its involvement in intrahepatic immune responses. Overall, our study underscores the pathological role of IgA in ALD and indicates that targeting IgA–macrophage interactions may offer a novel therapeutic strategy.

Keywords: IGA, Macrophage, Alcoholic Liver Disease

FP-27

Circulating HBcrAg Levels Reflect Transcriptionally Active cccDNA and Predict Advanced Fibrosis in HBeAg-Negative Inactive Carriers

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[1]Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, [2]The Catholic University Liver Research Center, [3]Department of Biomedicine & Health Sciences, Graduate School, The Catholic University of Korea, Seoul, [4]Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Aims: Establishing effective antiviral strategies for HBeAg-negative patients, especially those with normal ALT levels and low HBV DNA, is challenging. This study aims to identify circulating biomarkers that reflect intrahepatic cccDNA transcriptional activity and fibrosis progression, thereby guiding antiviral therapy for these patients.

Methods: This study included 160 HBeAg-negative CHB patients; stratified by HBV DNA and ALT levels. Serum HBV DNA, HBsAg, and HBcrAg levels were measured by commercial assays and intrahepatic markers (cccDNA, total HBV DNA, 3.5kb RNAs, and total HBV RNA) were quantified by qPCR. HBV integration was analyzed by NGS-based HBV capture assay. Liver fibrosis was assessed using the METAVIR scoring system.

Results: Serum HBcrAg level was highest in patients with higher ALT and HBV DNA levels and it significantly correlated with intrahepatic cccDNA and its transcriptional activity (all r>0.4, P<0.001). Furthermore, HBcrAg was significantly associated with ALT levels and inflammatory grade (P<0.01). Interestingly, HBcrAg well correlated with cccDNA transcriptional activity and better predicted advanced fibrosis (AUROC=0.704, P<0.05) compared to APRI and FIB4 in patients with low HBV DNA levels and normal ALT. Higher HBcrAg levels correlated with increased HBV integration breakpoints (P<0.01). Among 82 patients with >1 year follow-up, 6.8% (3/44) in the high HBcrAg group developed HCC, while none in the low HBcrAg group did. The estimated 5-year incidence of HCC among patients with higher HBcrAg levels was 9.2%.

Conclusions: Circulating HBcrAg levels correlate with intrahepatic cccDNA transcriptional activity and inflammation in HBeAg-negative CHB, with a reliable indicator of advanced fibrosis in inactive carriers. These findings highlight HBcrAg as a biomarker for assessing cccDNA activity, liver fibrosis, and HCC risk, aiding antiviral decision-making in HBeAg-negative patients.

Keywords: Hepatitis B Core-Related Antigen, Fibrosis, CCCDNA, Inactive Carrier

FP-28

HBV Core Antigen and Impaired Placental Immunity: A Key Driver of HBV Entry Receptor Expression

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[1]All India Institute of Medical Sciences Bhopal, India; [2]SAM Global University Bhopal; [3]Amrita Research Center, Delhi NCR, Amrita Vishwa Vidyapeetham, Faridabad

Aims: Pregnant women infected with Hepatitis B Virus (HBV) present a significant risk of transmitting the virus to their newborns, potentially leading to chronic HBV infection and subsequent liver diseases. Despite the identification of the placenta as a reservoir for HBV, the mechanisms facilitating vertical transmission remain poorly understood. Our study sought to illuminate the connection between impaired placental innate immunity, hepatitis B core antigen (HBcAg) expression, and HBV entry receptors.

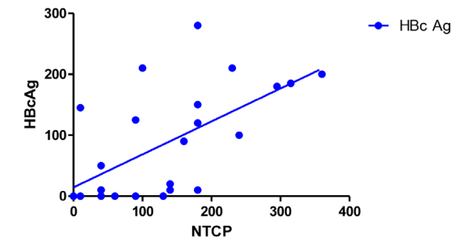
Methods: Utilizing serological and virological analyses, immunohistochemistry, and real-time PCR, we enrolled HBsAg-positive pregnant females undergoing antenatal check-ups at a central Indian tertiary care hospital from 2019 to 2020. Among these subjects, totaling 24, those negative for hepatitis A, C, and E, as well as human immunodeficiency virus (HIV), were included for analysis and healthy pregnant women were included as a control.

Results: In our investigation, we observed a downregulation of crucial immune mediators such as interferon gamma, STING, and IRF3 in the placenta of HBV-positive pregnant women compared to healthy controls. Additionally, we explored the correlation between HBcAg expression in the placenta and the levels of HBV entry receptors, specifically sodium taurocholate co-transporting polypeptide (NTCP) and hepatitis B e antigen (HBeAg). Our findings indicated a significant direct correlation between HBcAg expression and NTCP levels, suggesting a potential association between HBV replication and placental infection. However, no correlation was observed with HBeAg levels.

Conclusions: Our study underscores the significance of targeting viral load and HBc expression within the placenta to mitigate the risk of vertical HBV transmission. Further research elucidating the mechanisms of placental HBV infection could offer novel therapeutic strategies to reduce the burden of chronic HBV infection globally.

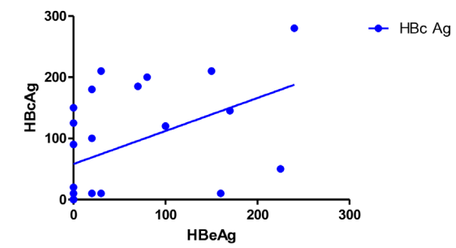
Keywords: Hepatitis B Vertical Transmission, Hepatitis B Chronic Infection, Placental Immunity and HBV, Liver Diseases

Significant correlation between HBcAg expression and NTCP



P=0.0015

Significant correlation between HBcAg expression and HBeAg



P=0.02,

y = 0.9047x

R^2 = -0.072

FP-29

Chronic Hepatitis B Genotype C Mouse Model with Persistent Covalently Closed Circular DNA

Deok Hwa Seo[1], Wonhee Hur[2], Juhee Won[3], Ji-Won Han[4], Seung-Kew Yoon[4], Songmee Bae[2], Kyun-Hwan Kim[3], Pil Soo Sung[1,4]

[1]Department of Medical Sciences, Graduate School of The Catholic University of Korea; [2]Division of Chronic Viral Diseases, Center for Emerging Virus Research, National Institute of Health (NIH), Cheongju Republic of Korea; [3]Department of Precision Medicine, School of Medicine, Sungkyunkwan University, Suwon, Republic of Korea; [4]Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea

Aims: The persistence of viral covalently closed circular DNA (cccDNA) poses a major obstacle for antiviral therapy against Hepatitis B virus (HBV). The lack of appropriate animal models supporting HBV cccDNA formation has significantly limited both basic and translational research. The aim of this study is to establish a novel mouse model harboring cccDNA, providing new insights for HBV-related research.

Methods: In this study, we aimed to establish a mouse model that produces the formation and maintenance of HBV cccDNA. We infected C57BL/6 mice with HBV, collected liver samples at different time points to assess cccDNA levels, viral replication, and host immune responses.

Results: Our findings demonstrate successful establishment of a novel mouse model harboring HBV cccDNA. We observed sustained viral replication and the presence of cccDNA in mouse hepatocytes. Furthermore, we detected HBsAg,HBeAg and HBcAg associated with HBV infection. This model provides an important tool for studying HBV and evaluating potential therapeutic interventions aimed at eradicating HBV infection by targeting cccDNA. It also offers an opportunity to provide new insights into the mechanisms of HBV persistence and the effectiveness of antiviral treatments in a controlled *in vivo* system.

Conclusions: The establishment of this novel mouse model harboring HBV cccDNA opens up new avenues for research on HBV persistence and antiviral therapy. This model can facilitate the evaluation of novel therapeutic agents targeting cccDNA and provide insights into mechanisms underlying viral clearance. Ultimately, this research may contribute to the development of more effective treatments for chronic HBV infection.

Keywords: Recombiant AAV, CCCDNA, Mouse Model

FP-30

Thiazole-Coumarin-Azomethine Derivatives as Dual TLR7/STING Agonists for Innate Immune Activation in Chronic Hepatitis B: Computational Design and Pharmacokinetic Profiling

Rizki Rachmad Saputra[1], Muhammad Priyadi[2], Reny Rosalina[1],

Dwi Hermayantiningsih[1], Luluil Maknun[3]

[1]Department of Chemistry, Universitas Palangka Raya, Indonesia; 2Department of Pharmacy, Universitas Palangka Raya, Indonesia; [3]Applied Chemistry Laboratory, Nugen Bioscience Indonesia, Indonesia

Aims: Chronic hepatitis B (CHB) affects 296 million individuals globally, and current antiviral therapies ineffective to achieve a functional cure. Nucleos(t)ide analogs (NAs) suppress viral replication but do not eliminate covalently closed circular DNA (cccDNA), the persistent HBV reservoir. Toll-like receptor 7 (TLR7) and stimulator of interferon genes (STING) are key mediators of antiviral immunity, triggering interferon responses essential for HBV clearance. TLR7 activation enhances type I interferon production, while STING stimulates IRFs and NF-κB, promoting immune reactivation. However, existing agonists have systemic toxicity and poor liver selectivity. This study aims to develop novel, liver-targeted TLR7/STING dual agonists with improved efficacy, pharmacokinetics, and safety, optimizing their potential as HBV immunotherapeutics.

Methods: Five ternary thiazole-coumarin-azomethine derivatives were screened through molecular docking using AutoDock Vina against TLR7 (PDB: 5GMG) and STING (PDB: 6DXL). ADMET predictions (pkCSM) assessed absorption, metabolism, clearance, and toxicity. β-Cyclodextrin complexation was modeled to enhance bioavailability.

Results: Compound 6i had superior binding affinities for TLR7 (-10.7 kcal/mol) and STING (-9.4 kcal/mol), outperforming loxoribine (-8.1 kcal/mol) and amidobenzimidazole (-9.6 kcal/mol) as references. Compounds 6j and 6k also had significant interactions (-10.4 to -9.8 kcal/mol). The dual agonistic activity depicted that it has the ability to restore antiviral immunity by boosting interferon production and cccDNA suppression, hence facilitating HBV clearance. ADMET study projected 100% intestinal absorption, low CYP inhibition, minor BBB permeability (-1.08 to -1.25 log BB), and moderate lipophilicity (Log P: 6.05-6.81), resulting in optimal distribution. Compound 6j exhibited the best metabolic stability (clearance: 0.066 log ml/min/kg), whereas 6k had the lowest toxicity (LD50: 3.214 mol/kg). β-Cyclodextrin complexation predicted bioavailability enhancement due to good binding affinity and H-bonding interactions.

Conclusions: The screened TLR7/STING dual agonists, ternary thiazole-coumarin-azomethine derivatives, exhibited potent receptor binding, favorable pharmacokinetics, and liver-targeted delivery. These findings support their potential as next-generation immunotherapies for CHB, warranting further optimization and experimental validation.

Keywords: Chronic Hepatitis B, Innate Immunity, TLR7/Sting Agonists, Computational Studies

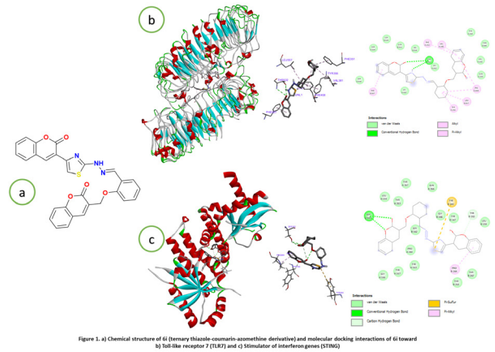


Figure 1. a) Chemical structure of 6i (ternary thiazole-coumarin-azomethine derivative) and molecular docking interactions of 6i toward TLR7 - STING

Table 1. ADMET Profile of 6i, 6j, and 6k (ternary thiazole-coumarin-azomethine derivatives)

GENERAL PROFILES			
Molecules/Pubchem ID	**6i**	**6j**	**6k**
MW	521.554	551.58	600.45
Binding Affinity			
TLR7 (kcal/mol)	-10.7	-10.4	-9.8
STING (kcal/mol)	-9.4	-9.5	-9.8
LIPOPHILICITY			
Consensus Log P	6.0479	6.0565	6.8104
WATER SOLUBILITY			
Log solubility (log mol/L)	-3.336	-3.442	-3.466
PHARMACOKINETICS			
BBB Permeability (log BB)	-1.078	-1.256	-1.225
CYP1A2 inhibitor	No	No	No
Intestinal Absorption (Human) (% Absorbed)	100	100	100
Total Clearance (log ml/min/kg)	0.03	0.066	-0.122
DRUGLIKENESS			
Lipinski #violations	1	1	1
Bioavailability Score	0.55	0.55	0.55
MEDICINAL CHEMISTRY			
Leadlikeness #violations	2	2	2
Synthetic Accessibility	4.2	4.37	4.19
TOXICITY			
Oral Rat Acute Toxicity (LD50) (mol/kg)	3.205	3.376	3.214

Friday, May 30, 2025, 15:10-16:30

5. Acute Liver Failure and DILI

FP-31

TRAIP Alleviates DDC-Induced Cholestatic Liver Injury through Modulating PI3K/Akt/mTOR Signaling

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[1]Division of Hepatobiliary Surgery, the First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi China; [2]Key Laboratory of Early Prevention and Treatment for Regional High Frequency Tumor (Guangxi Medical University), Ministry of Education, Nanning, Guangxi, China; [3]Guangxi Key Laboratory of Immunology and Metabolism for Liver Diseases (Guangxi Medical University), Nanning, Guangxi, China

Aims: Cholestasis represents a pathological state characterized by impairments in bile synthesis, secretion, and/or excretion due to intrahepatic or extrahepatic etiologies. TRAIP (TRAF-interacting protein) has recently been shown to play key roles in various cellular processes, including NF-κB activation, DNA damage response, mitosis, and tumorigenesis etc. Here, we aim to explore the role and mechanism of TRAIP in 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC)-induced CLI, which has never been reported.

Methods: Mice with liver-specific overexpression (HTG) and knockout (LKO) of TRAIP and their wildtype (WT) littermates were subject to and DDC-induced CLI model. Serum and liver tissues were harvested at different time as indicated to detect the changes in liver injury, inflammation, proliferation, and fibrosis between $TRAIP^{HTG}$ or $TRAIP^{LKO}$ mice and their WT littermates. High-throughput RNA sequencing (RNA-seq) of the liver tissues from $TRAIP^{LKO}$ mice and their WT littermates at day 7 after DDC treatment was used to investigate the mechanism of TRAIP in CLI. RNA-seq data were further validated by western blotting and quantitative real time polymerase chain reaction using liver tissues from mouse CLI model and immortalized hepatic cells treated with different bile acids.

Results: The expression levels of TRAIP were significantly up-regulated in liver tissues from DDC-induced CLI mouse model when compared to their controls. In DDC induced mouse CLI model, $TRAIP^{HTG}$ alleviated the liver damage, inflammation, immune cells infiltration, and cholestatic liver fibrosis when compared to the WT littermates, while $TRAIP^{LKO}$ played the opposite effect, which promoted liver damage, inflammation, immune cells infiltration, and liver fibrosis in these CLI mouse models, indicating that TRAIP play a protective role in DDC-induced CLI. RNA-seq data showed that TRAIP mediated cell apoptosis, autophagy and regulated PI3K/Akt/mTOR signaling pathway in DDC-induced CLI. We further validated these findings in liver tissues from DDC-induced CLI mouse model and cell lysates treated with different bile acids. Taken together, TRAIP may promote cell survival and homeostasis by promoting the initiation of autophagic signaling after cholestasis, which induced the expression of TRAIP, resulting in alleviating hepatic inflammatory infiltration and fibrosis.

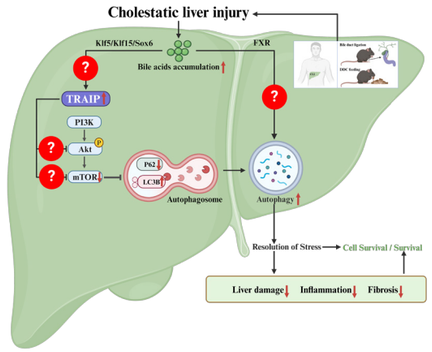

Figure 1. Scientific Hypothesis Diagram.

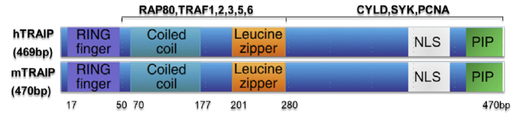

Figure 2. Structural Organization of the TRAIP Gene.

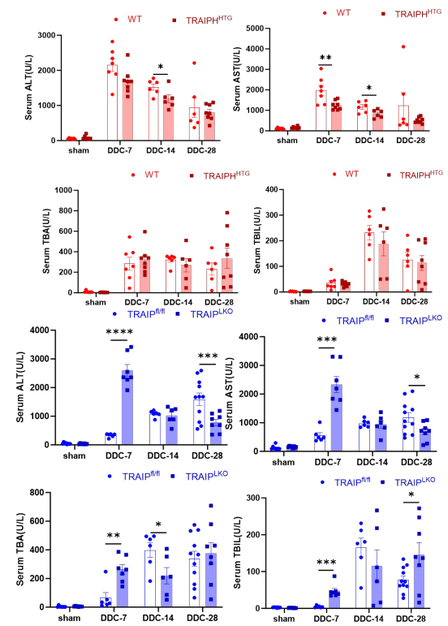

Figure 3. The Effect of TRAIP on Liver Damage in DDC-Induced Cholestatic Models.png

Conclusions: TRAIP alleviates DDC-induced CLI through promoting hepatic cell autophagy under cholestatic stress by regulating PI3K/Akt/mTOR signaling. Targeting TRAIP or autophagic signaling may be a promising treatment for CLI.

Keywords: Cholestatic Liver Injury, Traip, Inflammation, Autophagy

FP-32

NOX2 Is a Promising Target against Acute Liver Injury by Reversing Oxidative Stress, Mitochondrial Dysfunction and cGAS-STING Pathway-Dictated Inflammatory Response

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Aims: It is crucial to further characterize acute liver injury (ALI) in hopes of identifying novel therapeutic target. Recently, NOX2 which belongs to the sole family as enzymatic source of ROS has been linked to versatile pathologies, while its implication and regulation in ALI remains elusive.

Methods: We performed *in vivo* experiments using carbon tetrachloride (CCl_4)-induced ALI on wild-type (WT) and NOX2 knock out ($NOX2^{KO}$) mice. Transcriptomic analysis, immunoblotting, various assays related to mitochondrial dysfunction, inflammatory response and autophagic process were conducted.

Results: NOX2 was significantly increased in liver tissues of ALI-WT mice challenged by CCl_4. However, genetic ablation of NOX2 dramatically ameliorated ALI-associated hepatic dysfunction and pathology in mice. Oxidative stress indicative of Nrf2 alteration and relevant measures were ameliorated in ALI-$NOX2^{KO}$ mice. Several DNA repair/damage response, mitochondria and inflammatory pathways were identified according to RNA-sequencing. Moreover, NOX2 ablation reversed various aspects concerning mitochondrial dysfunction, that is, ultrastructural appearance, ATP synthesis, mtDNA release alongside mitophagy. On contrary, process in relation to mitochondrial dynamics was not impacted upon NOX2 modulation. Mechanistically, deletion to overexpressed NOX2 in the context of CCl_4-induced ALI may suppress toxicant-triggered inflammation and damages attributable to mitochondrial damage-dictated cGAS-STING pathway, NLRP3 activation as well as impaired mitophagy.

Conclusions: Collectively, genetic inhibition of NOX2 alleviates ALI by maintaining mitochondrial homeostasis and suppressing resultant mtDNA leakage-mediated inflammation and cell deaths.

Keywords: NOX2, Acute Liver Injury, CGAS-Sting Pathway, Oxidative Stress, Mitochondria

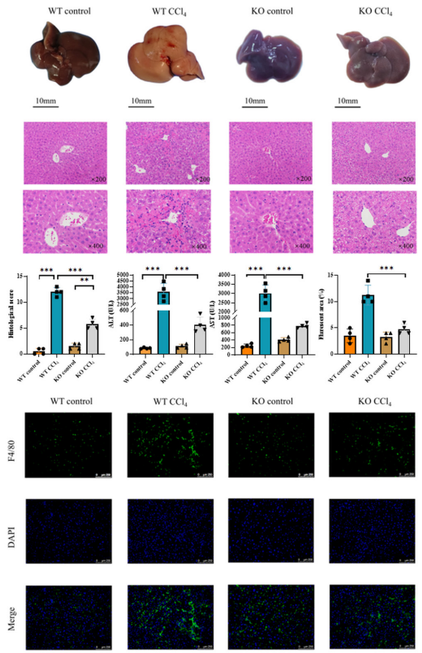

Figure 1.

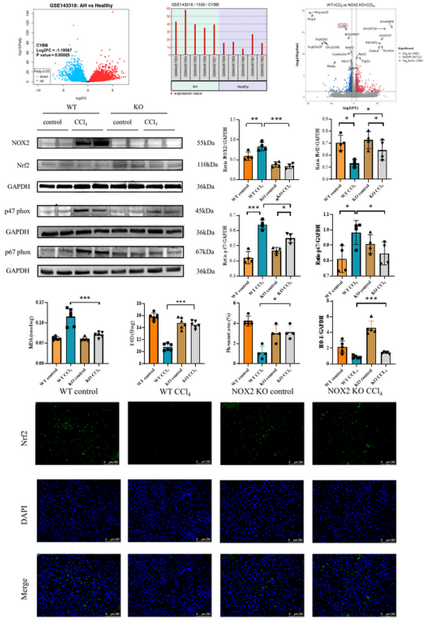

Figure 2.

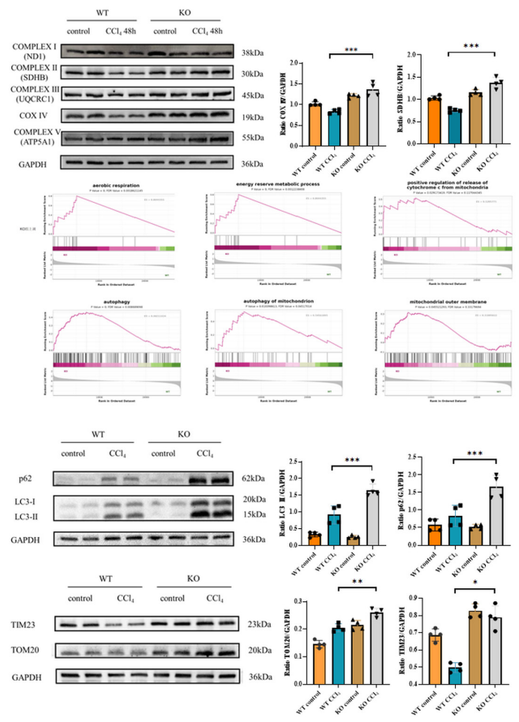

Figure 3.

FP-33

Plasma Derived Exosomes Multi-Omics Analysis Classifies Bacterial Peptide and Metabolomic Cargo as Predictor of Early Mortality in Acute Liver Failure

Neha Sharma[1], Sushmita Pandey[1], Rimsha Saif[1], Gaurav Tripathi[1], Manisha Yadav[1], Nupur Sharma[1], Babu Mathew[1], Abhishak Gupta[3], Vasundhra Bindal[1], Sanju Yadav[1], Rakhi Maiwall[2], Shvetank Sharma[1], Shiv Kumar Sarin[2], Jaswinder Singh Maras[1]

[1]Departments of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi; [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi; [3]Artemis Hospital Gurgaon

Aims: Acute liver failure (ALF) is a deadly condition linked to blood microbial and metabolic imbalance. Plasma exosomes may offer a non-invasive biomarker for early mortality risk.

Methods: Plasma samples from 320 individuals (270 ALF patients, 50 healthy controls) were used for extracellular vesicle (EV) isolation via PRoSPR and characterized using Transmission Electron Microscopy (TEM), Dynamic Light Scattering (DLS), Nanoparticle Tracking Analysis (NTA), and proteomics. Meta-proteomics and metabolomics were conducted on exosomes from 50 ALF patients and 20 controls. EV data were correlated with clinical features and ALF complications. A diagnostic metabolite panel was identified and validated in an independent cohort (220 ALF patients: 153 non-survivors, 67 survivors) using high-resolution mass spectrometry (HRMS) and machine learning.

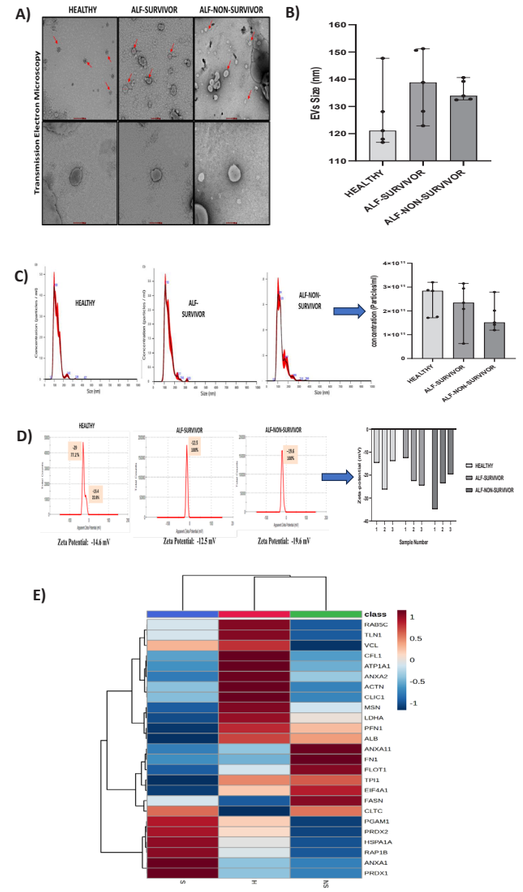

Figure 1.

Results: Exosomes (50–200 nm) had a concentration of 3.25 × 10^9 ± 0.55 particles/mL, a zeta potential of -23.67 ± 3.6 mV, and >40 EV-specific proteins. Exosomal metabolomics identified over 1000 metabolites and bacterial peptides from >15 phyla and >25 genera. More than 800 metabolites were differentially expressed in ALF, especially in non-survivors (fold change >1.5, P<0.05), with enriched linoleic acid metabolism and pyruvaldehyde degradation linked to inflammation and glycation (P<0.01). Increased bacterial diversity and Proteobacteria/Firmicutes abundance were observed in non-survivors,

correlating with metabolic dysfunction (P<0.05). Significant correlations (r^2>0.7, P<0.05) were found between exosomal metaproteomics, metabolomics, and clinical severity. Elevated EV levels of Streptomyces coelicolor and Enterobacteriaceae in non-survivors strongly correlated with mortality-associated metabolites (r^2>0.8). A six-metabolite panel achieved >85% diagnostic accuracy (AUC=0.88), distinguishing high-risk patients, with validation showing >90% sensitivity, specificity, and accuracy.

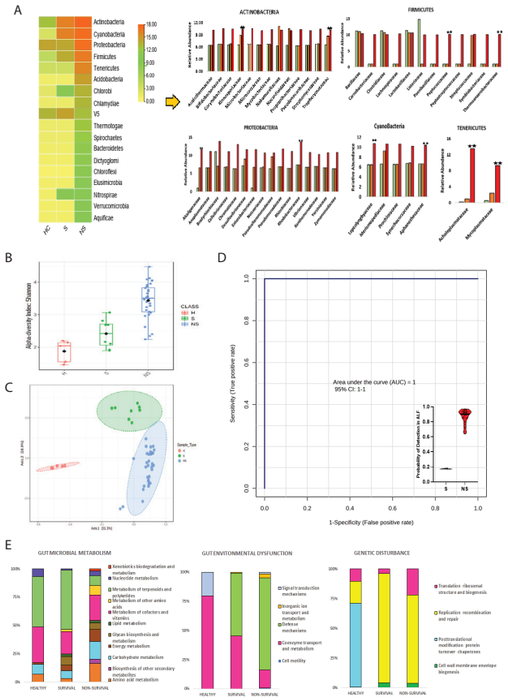

Figure 2.

Conclusions: Plasma-derived exosome metabolite profiling reveals hyper-inflammation and glycation in non-survivors, offering a promising tool to predict early mortality in ALF patients.

Keywords: Liver Failure, Metabolome, Metaproteome, Exosomes

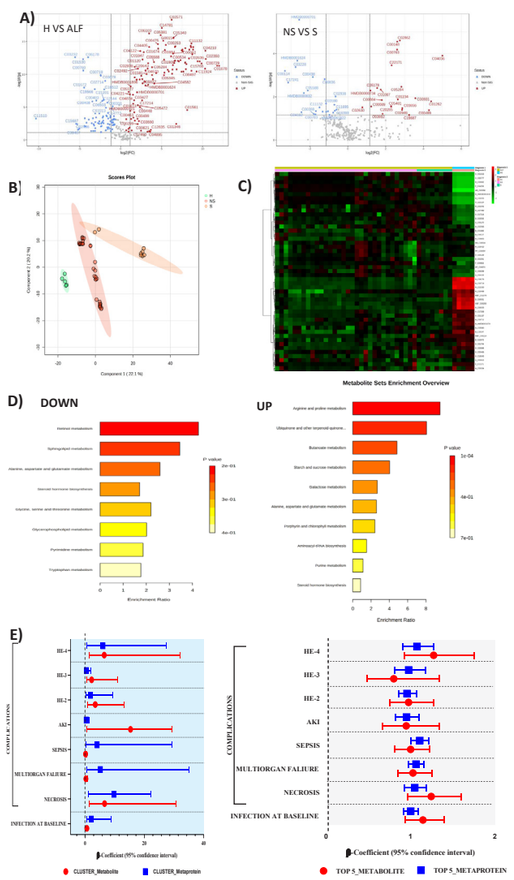

Figure 3.

FP-34

Genetic Polymorphism Analysis That Associated with Metabolism and Idiopathic Pathway of Antituberculosis Drug Induced Liver Injury

Putrya Hawa

Department of Pharmacology, Indonesia Defense University

Aims: This study evaluated the relationship between genetic risk factors and both the metabolism and idiopathic mechanisms interaction of ATLI (Antituberculosis Drug induced liver injury) through molecular simulation and network interaction.

Methods: We identified of gene that associated with drug metabolism and liver injury pathways by using KEGG, Genecard and PharmKGB. Gene variant of selected enzyme was chosen based on protein-protein interaction analysis by using Cytoscape. Genetic variants were analyzed by using SIFT and Polyphen-2 to predict their impact on protein structures and functions. The SNPs sequence was investigated using BLAST to predict any difference. The possible active sites of the protein were predicted and visualize the interacting residues of the ligand-receptor complex.

Results: In this study, we found that NAT2, CYP2E1, UGT1A1, HLA-B, and GSTT1 associated with ATLI (Antituberculosis drug induced liver injury). Protein-protein interaction analysis by using Cytoscape revealed that NAT2 and CYP2E1 related to drug metabolism and HLA-B associated with immune-mediated liver injury. Genetic variant analysis using SIFT and PolyPhen-2 revealed that rs1799930, rs1799931 were slow acetylator variants increased ATLI risk. rs2031920 and rs3813867 associated with elevated expression of CYP2E1 that may lead reactive oxygen species (ROS) production. variants of rs9271378, rs3129055 (HLA-B) associated with elevated idiosyncratic reactions to antituberculosis drug. Molecular docking and active site predictions showed differential binding affinities of antituberculosis drug with variant proteins, potentially impacting their renoprotective effects.

Conclusions: rs1799930, rs1799931, rs2031920, rs3813867, rs9271378, rs3129055 predicted hepatotoxic effect of antituberculosis drug. Personalized genetic screening before antituberculosis therapy may minimize side effects and optimize treatment outcomes. Future clinical studies and functional validation are necessary to integrate these findings into clinical practice.

Keywords: Genetic, Polymorphism, Antituberculosis, Liver Injury

FP-35

N-Acetylcysteine Reduces Mortality and Length of Stay in Adult with Non-Acetaminophen-Induced Acute Liver Failure: Evidence from a Meta-Analysis

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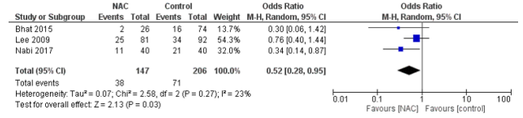
[1]General Practitioner Department, Muhammadiyah Lamongan Hospital; [2]General Practitioner Department, Gresik Ibnu Sina Regional Hospital

Aims: N-acetylcysteine is widely recognized for its efficacy in managing acetaminophen-induced acute liver failure. However, its therapeutic role in non-acetaminophen-induced acute liver failure remains uncertain. This meta-analysis aims to evaluate the effects of N-acetylcysteine on acute liver failure caused by non-acetaminophen-related factors.

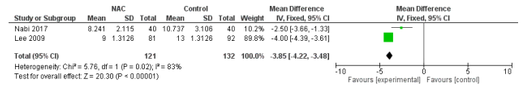
Methods: A systematic literature search was conducted using the PubMed database up to March 2025. The association between N-acetylcysteine treatment and clinical outcomes was assessed by calculating odds ratios (ORs) and 95% confidence intervals (CIs) using RevMan 5.4.

Results: A total of three studies involving 353 participants were included in the meta-analysis. The findings indicate that N-acetylcysteine administration in cases of non-acetaminophen-induced acute liver failure was associated with a reduction in mortality compared to the standard of care (OR: 0.53; 95% CI: 0.28−0.95; P=0.03). Additionally, it significantly shortened the average hospital stay (MD: -3.85; 95% CI: −4.22 to −3.48; P<0.00001).

Conclusions: These results suggest that N-acetylcysteine may reduce mortality and hospital length of stay in patients with non-acetaminophen-induced acute liver failure when compared to standard treatment. Further research is warranted to confirm these findings and establish clinical guidelines for its use in this population.



Forest plot mortality



Forest plot length of stay

Keywords: N-Acetylcysteine, Non-Acetaminophen-Induced Acute Liver Failure, Mortality, Length of Stay

FP-36

Elevated Plasma Chenodeoxycholic Acid as a Prognostic Marker and Therapeutic Target in Acute Liver Failure: Role of Bacteroides Intestinalis AM1 Intervention in Bile Acid Modulation and Mitigation of Liver Injury

Sushmita Pandey[1,2], Shiv Kumar Sarin[1], Jaswinder Singh Maras[1]

[1]Molecular and cellular medicine, Institute of Liver and Biliary Sciences New DelhiInstitute of Liver and Biliary Sciences New Delhi; [2]Dr. B R Ambedkar Center for Biomedical Research, University of Delhi

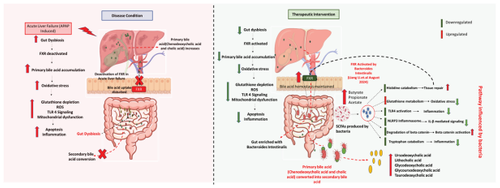
Aims: Acute liver failure (ALF) is a life-threatening condition with altered metabolic and microbial profiles contributing to liver disease severity. We studied circulating metabolites, bile acids and microbial signatures to differentiate ALF non-survivors and explored the potential of Bacteroides intestinalis AM1 in bile acid modulation and mitigation of liver injury.

Methods: Plasma metabolomics and meta-proteomics were conducted in 40 ALF patients and 5 healthy controls (training cohort), with validation in 160 ALF patients (test cohort) using High resolution mass spectrometry (HRMS) and machine

learning (ML). A non-survival indicator panel identified chenodeoxycholic acid (CDCA) as a key inflammatory driver (logFC > 10; P<0.05; AUC > 0.95), particularly in non-survivors. Increase in CDCA levels prompted us to explore Bacteroides intestinalis AM1 (109 CFU/ml), which successfully reduces CDCA (PMID: 19243441). A therapeutic dose was administered to an APAP-induced mouse model (250 & 500 mg/kg, i.p.), and liver injury and hepatocyte death were analyzed through histological, proteomic, and metabolomic changes in the liver.

Results: ALF non-survivors had distinct metabolomic profile showing increase in CDCA, tryptophan, tyrosine, pathways related to inflammation, cell death and stress response (P<0.01, FDR<0.01, FC>1.5). Plasma of non-survivors showed higher alpha/beta diversity (P<0.05) with increase in Proteobacteria, Firmicutes, Actinobacteria (P<0.05), functionally associated to energy, amino acid and xenobiotic metabolism (P<0.05). In the non-survivors, the increase in bacterial-taxa and functionality correlated with specific increases in CDCA (cell death and inflammation), 4-(2-Amino phenyl)-2,4-dioxobutanoate, L-Tyrosine, other metabolites, clinical parameters and outcome (R2>0.85, P<0.05). Probability of detection (POD) of non- survival based on these metabolites was >99% with adiagnostic accuracy of 98% (AUC=0.98(0.92-1.0). Elevated levels of CDCA (logFC>10) correlated with disease severity and mortality in ALF patients and mice model. Using an ALF mouse model, we colonized the mice with Bacteroides intestinalis AM1 to examine its therapeutic effects on CDCA breakdown. B. intestinalis AM1 colonies reduced CDCA levels, suppressed inflammation, and prevented acute liver injury by reversing necroapoptosis and modulating glutathione (oxidative repair), tryptophan (inflammation), histidine (tissue repair) metabolism.

Graphical Abstract



Conclusions: The plasma microbiome and metabolome of ALF non-survivors exhibits distinct characteristics. Elevated baseline CDCA levels are linked to a higher risk of early mortality. Intervention with "B intestinalis AM1" shows promise in lowering CDCA levels, reducing necrosis, and mitigating inflammation in ALF. A clinical trial is needed to validate these findings.

Keywords: Acute Liver Failure, Chenodeoxycholic ACID, Bacteriodes Intestinalis-AM1, Therapeutic

FP-37

Gallic Acid-Loaded Gold Nanoparticles Prevent High Fat Diet-Induced Non-Alcoholic Fatty Liver Disease via Modulating Endoplasmic Reticulum, ATF6/AMPK/PPARα/p-eIF2α Levels, and the NF-κB/SMAD-4 Protein Expression

Deepika Singh

Pharmaceutical Sceinces, SIHAS, SHUATS

Aims: Non-alcoholic fatty liver disease (NAFLD) is a prevalent metabolic disorder characterized by excessive lipid accumulation in the liver, leading to inflammation and fibrosis. Emerging therapeutic strategies focus on targeting molecular pathways involved in lipid metabolism, oxidative stress, and inflammatory responses. In this study, we investigated the protective effects of gallic acid-loaded gold nanoparticles (GA-AuNPs) against NAFLD and their underlying mechanisms of action.

Methods: GA-AuNPs were fabricated by the green synthesis method and were characterized. We observed the effects of gallic acid-loaded gold nanoparticles (GA-AuNPs) against NAFLD and endoplasmic reticulum stress modulation using in vitro and in vivo experimental models in rodents. GA-AuNPs were administered to HFD-induced NAFLD rats at a dose level of 10, 20, and 30 mg/kg B.W. to observe its potent effects and underlying mechanism. We measure the Serum glutamate pyruvic transaminase (SGPT), SGOT, ALP, alpha fetoprotein, Insulin resistance, activating transcription factor 6 (ATF6), homeostatic model assessment of insulin resistance (HOMA-IR), phosphorylated eukaryotic initiation factor 2α (p-eIF2α), gamma-glutamyl transpeptidase (γ-GT), lipid profile (TG, TC, HDL, etc). Tissue was used to study the histopathology.

Results: FESEM study showed spherical formation of NPs with excellent zeta potential. It reduced the levels of p-eIF2α levels with activation of AMPK and PPARα, SGPT modulates ER stress and reduces γ-GT levels with increased liver function and insulin sensitivity and improves HOMA-IR. It mitigates ALT, ALT, SGOT, hepatic TG, VLDL, HDL and TC and supports lipid metabolism and inflammatory cytokines like TNF-α, IL-1β, Il-6, IL-10, IL-18, and IL33; inflammatory parameters like COX-2, iNOS, VEGF, PGE2, NFκB, respectively. It significantly suppressed the NF-κB and SMAD-4 protein expression. Histology analysis supports reduced hepatic steatosis, inflammation, and fibrosis with significant improvement in liver architecture.

Conclusions: These results suggest that GA-AuNPs hold potential as a novel therapeutic approach for NAFLD by targeting key molecular pathways associated with lipid metabolism and inflammatory signaling.

Keywords: Gallic Acid, Gold Nanoparticles, NAFLD, AMPK/PPAR A/P-EIF2 A, NF-K B, SMAD-4, Endoplasmic Reticulum Stress

FP-38

Quantum Chemical Features Meet Clinical Data for DILI Prediction: Integrating Electronic Density Distribution of Antibiotics with Patient EMR Data

Seongbin Kim[1], Seungjun Yu[1], Gyueun Park[1], Hyo Jung Cho[2], Soon Sun Kim[2], Ji Eun Han[2], Jae Youn Cheong[2], Charmgil Hong[1]

[1]School of Computer Science and Electrical Engineering, Handong Global University, Pohang, Korea; [2]Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Aims: Drug-induced liver injury (DILI) results from adverse drug exposure and can cause hepatic impairment or fatal outcomes. Previous prediction methods have relied on single-modality approaches using EMR or biological markers, or models considering only 2D drug structures. However, research incorporating quantum chemical properties of drugs is still in its early stages. This study enhances DILI prediction by integrating Electron Localization Function (ELF) maps with EMR data.

Methods: ELF maps were generated for 59 antibiotics prescribed to 6,028 patients from 2016 to 2020 and integrated with their EMR data. Patients who developed suspected DILI symptoms according to the Council for International Organizations of Medical Sciences (CIOMS) criteria after antibiotic administration were labeled as positive cases. To extract meaningful spatial electron distribution features, the ELF maps were processed using pre-trained 2D CNN models (ResNet50 and EfficientNetV2-M). Concurrently, EMR data was processed using a Feature Tokenizer Transformer (FT-Transformer). These representations were fused through a cross-attention mechanism to predict DILI risk. The model was optimized using 5-fold cross-validation with Optuna for hyperparameter tuning.

Results: Our multimodal approach significantly outperformed baseline methods. The ResNet50-based model achieved AUROC and AUPRC scores of 0.8186 $\pm$ 0.0851 and 0.388 $\pm$ 0.1561, while the EfficientNet-based model reached 0.7363 $\pm$ 0.1913 and 0.3201 $\pm$ 0.2008. Both exceeded the single-modality EMR-based model (FT-Transformer), which achieved the following scores of 0.6475 $\pm$ 0.0117 and 0.1790 $\pm$ 0.0128. Importantly, regardless of the underlying CNN architecture used (ResNet50 or EfficientNetV2-M), the addition of ELF maps consistently yielded substantially significant improvements in prediction performance compared to using EMR data alone.

Conclusions: Our work demonstrates the effectiveness of a novel integration of ELF maps with patient EMR data, which significantly improved DILI risk prediction accuracy. This multimodal approach enhances drug safety assessment and supports clinical decision-making.

This work was supported (1) by the MSIT(Ministry of Science, ICT), Korea, under the Global Research Support Program in the Digital Field program (RS-2024-00431394) supervised by the IITP (Institute for Information & Communications Technology Planning & Evaluation) and (2) by the National IT Industry Promotion Agency (NIPA) grant funded by the MSIT, Korea, under the Development of AI Precision Medical Solution (Doctor Answer 2.0, S0252-21-1001).

"This research was supported by the MSIT(Ministry of Science and ICT), Korea, under the National Program for Excellence in SW) supervised by the IITP(Institute of Information & Communications Technology Planning & Evaluation) in 2024"(2023-0-00055).

Keywords: DILI, Machine Learning, Quantum Chemistry, Electron Localization Function

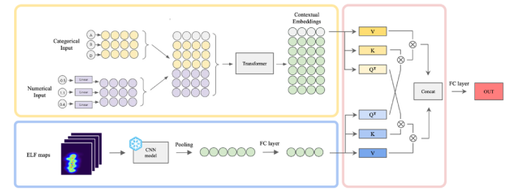


Figure: Our proposed framework that integrates structured EMR data (top yellow box) with ELF (3D electron density) maps of drug molecules (bottom blue box). The EMR features are processed through a transformer-based encoder, while the ELF maps are embedded through a CNN model. The learned representations are then combined through a cross-attention mechanism (right red box) to make the final prediction.

Model	Test AUROC	Test AUPRC
EMR-Only (FT-Transformer)	0.66729	0.21309
EMR + ELF (FT-Transformer + ResNet50)	0.81857	0.38803
EMR + ELF (FT-Transformer + EfficientNetV2-M)	0.73628	0.32006

Table: Performance comparison. Baseline: EMR-Only, Proposed approach: EMR + ELF.

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6. HBV 1

FP-39

Inverted U-Shaped Association between Hepatitis B Core-Related Antigen and HCC Incidence in Patients with Chronic Hepatitis B

Min Ji Son[1], Ji Eun Han[1], Yoon Je Cho[1], Hyelynn Jeon[2], Hye Young Chang[3], Hyo Jung Cho[1], Jae Youn Cheong[1], Hyun Woong Lee[4], Soon Sun Kim[1]

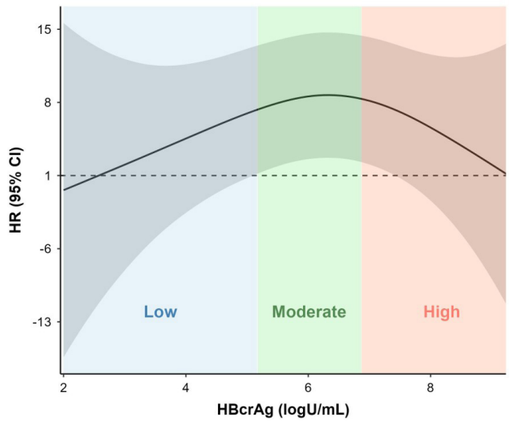
[1]Department of Gastroenterology, Ajou University School of Medicine, Suwon, South Korea; [2]Office of Biostatistics, Medical Research Collaborating Center, Ajou Research Institute for Innovative Medicine, Ajou University Medical Center, Suwon, South Korea; [3]Gangnam Severance Medical Research Center, Younsei unicersity College of Medicine, Seoul, South Korea; [4]Department of Internal Medicine, Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, South Korea

Aims: Despite advancements in antiviral therapy, chronic hepatitis B (CHB) remains a major global cause of hepatocellular carcinoma (HCC). Persistent high viral load drives disease progression, highlighting the need for a sensitive biomarker to as-

sess viral activity. While antiviral therapy suppresses HBV DNA replication, it does not eliminate intrahepatic cccDNA, which allows residual transcriptional activity to persist. Hepatitis B core-related antigen (HBcrAg) reflects cccDNA transcription and may serve as a biomarker. This study investigated whether baseline HBcrAg levels can predict HCC development.

Methods: This retrospective study included 204 patients with chronic hepatitis B who initiated antiviral therapy between September 2015 and February 2023. Patients were followed for HCC development until October 2023, with a median follow-up duration of 5.5 years. Kaplan-Meier and Cox regression analyses were performed. HBcrAg levels were measured using a chemiluminescence immunoassay on the LUMIPULSE G12000 automated analyzer (Fujirebio, Tokyo, Japan). Baseline HBcrAg levels were categorized into tertiles: low (<5.17 log U/mL), moderate (5.17–6.87 log U/mL), and high (≥6.87 log U/mL).

Results: HCC was diagnosed in 24 out of 204 patients. Kaplan-Meier analysis and the log-rank test revealed that patients in the moderate HBcrAg group (5.17–6.87 log U/mL) had the highest cumulative incidence of HCC during follow-up. The 5-year cumulative incidence of HCC was 8.4% (95% CI: 1.0–15.2) in the low HBcrAg group, 20.2% (8.6–30.3) in the moderate group, and 3.2% (0.0–7.5) in the high group (log-rank *P*=0.001). The multivariable Cox regression analysis included the following covariates: sex, age, liver cirrhosis (LC), platelet count, total bilirubin, albumin, creatinine, FIB-4, HBeAg positivity, HBsAg, and HBcrAg. Higher total bilirubin (HR 1.90; 95% CI, 1.06–3.43, *P*=0.031) and moderate HBcrAg levels (HR 5.29; 95% CI, 1.60–17.58, *P*=0.006) were associated with an increased risk of HCC development. In contrast, a higher HBsAg level (HR 0.03; 95% CI, 0.00–0.53, *P*=0.016) was associated with a lower risk of HCC development.



Conclusions: These findings indicate that patients with pre-treatment moderate HBcrAg levels exhibited the highest incidence of HCC during the follow-up period despite receiving antiviral treatment. Based on this trend, pre-treatment HBcrAg levels may serve as a potential biomarker for predicting the long-term risk of HCC.

Keywords: Hepatitis B, Chronic, Hepatitis B Core-Related Antigen, Carcinoma, Hepatocellular, Antiviral Agents

FP-40

Tenofovir Alafenamide vs. Tenofovir Disoproxil Fumarate in Lowering the Risk of HCC Development in Patients with Chronic Hepatitis B: A Propensity Scores Matching Analysis

Seong Hee Kang, Hyung Joon Yim, Sun Young Yim, Young-Sun Lee, Young Kul Jung, Yeon Seok Seo, Ji Hoon Kim, Jong Eun Yeon, Kwan Soo Byun

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Aims: Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are both recommended as first-line treatments for antiviral-naïve patients with chronic hepatitis B (CHB). However, it remains controversial which drug is more effective in preventing hepatocellular carcinoma (HCC). We aimed to compare the effects of TAF and TDF on HCC risk.

Methods: We included 1,628 treatment-naïve CHB patients who underwent antiviral therapy with either a TAF-based regimen (TAF group: n = 335) or TDF only (TDF group: n = 1,293) between 2007 and 2021. The TAF group consisted of patients who received TAF as a first-line treatment and those who switched from TDF to TAF. Propensity score (PS) matching was used to reduce the effects of confounding factors.

Results: After PS matching, we analyzed data from 334 patients in the TAF group (mean age: 48.0 ± 11.7 years; 192 men [57.5%]) and 573 patients in the TDF group (mean age: 47.4 ± 11.6 years; 326 men [56.9%]). During a 60-month follow-up, 8 patients in the TAF group (2.4%) and 46 patients in the TDF group (8.0%) developed HCC. TAF treatment was associated with a significantly lower risk of HCC compared to TDF (hazard ratio [HR], 0.34; 95% confidence interval [CI], 0.16-0.72; *P*<0.001). In multivariate analysis, factors independently associated with HCC development included age (adjusted HR [aHR], 1.07; *P*<0.001), liver cirrhosis (aHR, 2.02; *P*=0.045), diabetes (aHR, 4.78; *P*<0.001), alcohol use (aHR, 3.07; *P*=0.002), and TAF treatment (aHR, 0.22; *P*<0.001).

Conclusions: TAF treatment was associated with a 66% lower risk of HCC compared to TDF treatment. Further studies with larger sample sizes and longer follow-up periods are needed to confirm these findings.

Keywords: Chronic Hepatitis B, Hepatocellular Carcinoma, Treatment

FP-41

HCC Risk in Treatment-Naïve Chronic Hepatitis B Patients Treated with Tenofovir Alafenamide or Tenofovir Disoproxil Fumarate: A Korean Nationwide Study

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Aims: In phase 3 trials, tenofovir alafenamide (TAF) showed antiviral efficacy comparable to that of tenofovir disoproxil fumarate (TDF) for chronic hepatitis B (CHB), with an improved safety profile. This study aimed to compare the clinical efficacy of TAF and TDF in terms of the risk of hepatocellular carcinoma (HCC).

Methods: We conducted a nationwide historical population cohort study on treatment-naïve adult patients with CHB receiving TAF (n=29,309) or TDF (n=58,046) as first-line therapy from 2017 to 2022 using data from the Korean National Health Insurance Service database. Cumulative HCC incidence and associated risk factors were estimated using competing risk factors. Propensity score (PS)-matched analysis was used to minimize the confounding effects.

Results: A total of 20,994 patients were included in the TAF group, and 33,191 in the TDF group. The annual incidence of HCC was significantly lower in the TAF group (7.5/1,000 patient-years [PYs]) than in the TDF group (10.3/1,000 PYs; SHR, 0.74; *P*<0.001). After PS matching, TAF continued to exhibit a protective effect against HCC (7.5/1,000 PYs vs. 9.9/1,000 PYs; *P*<0.001). Multivariable analysis with Fine–Gray proportional subdistribution hazards model identified TAF as significantly associated with a reduced HCC incidence (SHR: 0.76; *P*<0.001). Subgroup analysis confirmed the hepatoprotective effect of TAF against HCC even in patients with cirrhosis (SHR: 0.78; *P*=0.003).

Conclusions: This study showed that TAF had a hepatoprotective effect against HCC in patients with CHB, providing valuable guidance for clinicians in selecting the appropriate initial treatment for these patients.

Keywords: Chronic Hepatitis B, Hepatocellular Carcinoma, Tenofovir Alafenamide Fumarate, Tenofovir Disoproxil Fumarate

FP-42

Superior Efficacy of Besifovir in Reducing HCC Risk Compared to Tenofovir in CHB Patients: A Nationwide Cohort Study

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Aims: Besifovir dipivoxil maleate (BSV) offers a novel therapeutic option for chronic hepatitis B (CHB). However, its long-term efficacy in preventing hepatocellular carcinoma (HCC) remains unclear.

Methods: We conducted a retrospective cohort study using the Korean Health Insurance Review and Assessment Service database from 2018 to 2022. The study included 32,383 CHB patients (BSV: n = 2,358; Tenofovir dipivoxil fumarate [TDF]: n = 30,025). The primary outcome was HCC incidence, with cirrhosis development as a secondary endpoint.

Results: In the entire population, the BSV group (2,358 individuals, 5,918 person-years) reported 57 cases of HCC, while the TDF group (30,025 individuals, 83,587 person-years) reported 1,268 cases of HCC. After propensity score matching, the BSV group demonstrated a significantly lower HCC incidence (9.63 per 1,000 person-years; 95% CI: 7.43–12.49) compared to the TDF group (15.36 per 1,000 person-years; 95% CI: 13.72–17.18), with an incidence rate ratio (IRR) of 1.59 (*P*=0.001). This protective effect was consistent across both cirrhotic (hazard ratio [HR]: 1.609, *P*=0.028) and non-cirrhotic subgroups (HR: 1.831, *P*=0.002). Cox regression analysis revealed a lower risk of cirrhosis in the BSV group (HR: 0.670, 95% CI: 0.597–0.753, *P*<0.001).

Conclusions: BSV demonstrates superior efficacy in reducing HCC risk compared to TDF, regardless of baseline cirrhosis status.

Keywords: Besifovir Dipivoxil Maleate (BSV), Tenofovir Disoproxil Fumarate (TDF), Hepatocellular Carcinoma (HCC)

Figure 1. Study population flowchart

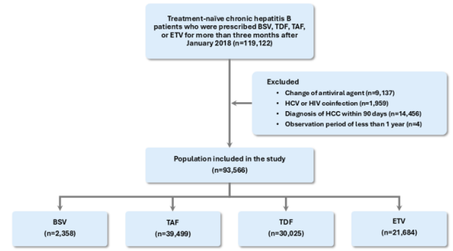


Figure 2. Kaplan-Meier plots for hepatocellular carcinoma (HCC) incidence by antiviral agents in all patients

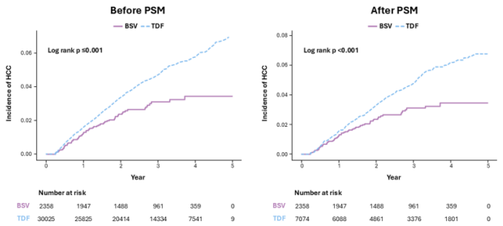
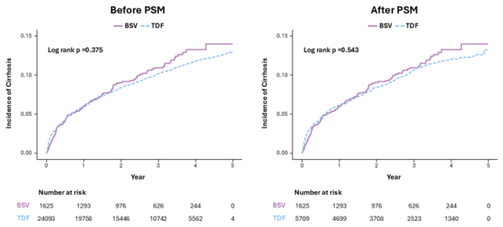


Figure 4. Kaplan-Meier plots for cirrhosis incidence by antiviral agents in non-cirrhotic patients



FP-43

E-Cigarette Use and Hepatocellular Carcinoma Risk in Patients with Chronic Hepatitis B

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Aims: Smoking is a risk factor for hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB) infection. E-cigarettes may offer a new avenue for behavior change in current smoker, but the prognostic implications of changes in smoking habits (continuing with combustible cigarettes, switching to e-cigarettes, or quitting) on the risk of HCC remains unclear.

Methods: We enrolled 127,196 HBV patients who were identified as smokers during their initial health screening examination from 2014 to 2023 and had undergone a subsequent health screening within four years. Using a smoking questionnaire between the initial and the second health screenings, participants were categorized into three groups: those who continued using combustible cigarettes, those who successfully quit, and those who switched to e-cigarettes. The primary outcome was the incidence of HCC. Sensitivity analysis was performed using a target study emulation framework.

Results: Of the total study population, 86,338 patients (67.9%) continued to use combustible cigarettes, 20,493 (16.1%) switched to e-cigarette use, and 19,521 (15.3%) successfully quit smoking. Over a 5-years follow-up period, the cumulative incidence of HCC was lower among those who switched to e-cigarettes (2.1%) and quitters (3.5%), compared to those who continued smoking combustible cigarettes (4.2%). Multivariable-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for the incidence of HCC were 0.787 (0.711–0.873) for e-cigarette switchers and 0.785 (0.710–0.867) for successful quitters, compared to continued combustible cigarette users. The matched set, based on target study emulation, included 48,397 continued smokers and 20,991 e-cigarette users, showing no significant differences in baseline characteristics. The emulation approach consistently demonstrated that switching to e-cigarettes was associated with a lower incidence of HCC (HR = 0.888; 95% CI = 0.841-0.937) compared to continued smoking.

Conclusions: Among smokers with CHB, switching to E-cigarette use or quitting smoking was associated with reduced risk of HCC than with continued combustible cigarette use.

Keywords: Chronic Hepatitis B, Hepatocellular Carcinoma, Smoking, E-Cigarette

FP-44

Prediction of Long-Term HBsAg Seroclearance in HBeAg-Negative Chronic Hepatitis B Patients

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Aims: Predicting the long-term HBsAg seroclearance, an ideal endpoint, is relevant for decision-making regarding antiviral therapy for chronic hepatitis B (CHB) patients. This study aimed to identify predictors and develop a prediction model for HBsAg seroclearance in hepatitis B envelop antigen (HBeAg)-negative CHB patients.

Methods: A total of 2,032 untreated HBeAg-negative patients who underwent a 2-year baseline observation period were enrolled. Prediction models were developed using independent predictors of seroclearance, and their performance was evaluated through internal and external validation using an independent cohort of 753 patients, along with sensitivity analyses.

Results: The estimated annual incidence of HBsAg seroclearance was 2.22% (15,508 person-years). Hepatitis B virus DNA Level (Low-to-intermittently high-level viremia), Old age, male Sex, and hepatitis B Surface antigen level <250 IU/mL independently predicted seroclearance. Subsequently, two prediction models were developed: HepBLOSS-1 and a simplified version, HepBLOSS-2. These models demonstrated excellent performance in predicting seroclearance at 5, 10, and 15 years, with C-indices and time-dependent area under the receiver operating characteristics curve (AUROC) values of 0.81–0.89. The 10-year cumulative incidence rate in patients with scores >=13 in HepBLOSS-1 and those with scores of 8 in HepBLOSS-2 was over 50%. Both models underwent rigorous internal and external validation, demonstrating outstanding predictability with time-dependent AUROCs exceeding 0.80. The predicted seroclearance rate closely aligned with the observed rate in both models.

Conclusions: The HepBLOSS models for HBsAg seroclearance exhibited an outstanding ability to stratify the probability of seroclearance over a 15-year period. These models hold promising potential to guide treatment decisions, aiming to achieve a functional cure in patients with CHB.

Keywords: Hepatitis B, Hepatitis B Surface Antigen, Seroclearance, Prediction

FP-45

Kinetics of Hepatitis B Surface Antigen Loss Following 8 Years of Tenofovir-Based Treatment with Chronic Hepatitis B

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Aims: Sustained hepatitis B surface antigen (HBsAg) loss is a marker of hepatitis B virus (HBV) functional cure and remains the goal of antiviral treatment for patients with chronic HBV infection (CHB). We sought to characterize patients with CHB achieving HBsAg loss after long-term antiviral treatment in 2 large, Phase 3 studies of tenofovir alafenamide (TAF).

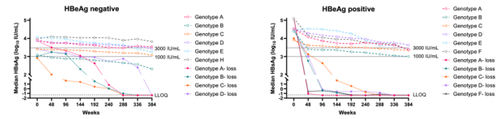
Methods: In 2 studies (GS-US-320-0108/0110), hepatitis B e antigen (HBeAg)-negative (Study 108; n=425) and -positive (Study 110; n=873) patients with CHB were treated with TAF or tenofovir disoproxil fumarate followed by TAF for up to 8 years. HBsAg levels were measured using the Abbott Architect assay (quantification limit ≤0.05 IU/mL);. The rapid-phase kinetics of HBsAg loss were calculated as the time required for a negative HBsAg result, starting from a constant rate of decline of at least 0.12 log_{10}IU/mL/month.

Results: Median (IQR) BL HBsAg levels were 3.51 (3.14, 3.85) and 4.22 log_{10} IU/mL (3.68, 4.64) for Studies 108 and 110, respectively. At year 8, the median (IQR) decline in HBsAg level was 0.60 (−1.16, −0.19) log_{10} IU/mL from BL, with 2%–3% of patients experiencing HBsAg loss. Both HBeAg-negative (10/425; 2%) and -positive patients (29/873; 3%) had similar HBsAg loss rates, with longer median duration in HBeAg-negative patients than HBeAg-positive patients (300 vs 126 weeks, respectively; *P*=.02; Figure). HBV genotype (GT) affected HBsAg loss rates, with the highest in GT F (2/5; 40%), followed by GT A (9/85; 11%; Figure). Despite GT C being the most common (48%), its HBsAg loss rate was 2% (11/618).

Conclusions: Long-term tenofovir-based treatment resulted in low rates of HBsAg loss, consistent with prior long-term studies. Although proportions of HBsAg loss were similar for HBeAg-negative/-positive patients, HBeAg-positive patients required less time to achieve HBsAg loss. GTs A and F had higher rates of HBsAg loss.

Keywords: Tenofovir Alafenamide, Tenofovir, HBSAG Kinetics, Chronic Hepatitis B

Figure. HBsAg Decline in Relation to HBeAg Status and Viral Genotype



FP-46

Incidence and Risk of Controlled Attenuated Parameter-Based Non-Alcoholic Hepatosteatosis Development in Korean Patients with Chronic Hepatitis B

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Aims: Chronic hepatitis B (CHB) and non-alcoholic hepatosteatosis are common chronic liver diseases. Previous studies have debated their comorbid epidemiology, relying on ultrasonography for detecting hepatosteatosis, which is less reliable. This study aimed to assess the incidence rate and risk factors for hepatosteatosis development using transient elastography in Korean patients with CHB.

Methods: We retrospectively reviewed patients with CHB who started medical follow-up at a tertiary medical center in South Korea between 2012 and 2023. Hepatosteatosis development was defined as controlled attenuation parameter (CAP) greater than 238 dB/m. Patients with significant alcohol intake and baseline hepatosteatosis assessed by ultrasonography or CAP were excluded. Hazard ratio (HR) and 95% confidence intervals (CIs) were analyzed by Cox regression analysis.

Results: Among 3,200 patients with chronic hepatitis B (49.3% male, median age: 50.6 years), hepatosteatosis was developed in 817 patients during the median follow-up of 50.2 months, who were male-dominant (60.3% vs. 45.6%) and who had higher body mass index (BMI) (median 23.5 vs. 21.7 kg/m2), higher proportion of diabetes mellitus (8.4% vs. 6.3%), lower platelet counts (median 178 vs. 199 $\times 10^9$/L), higher levels of aspartate aminotransferase (median 26 vs. 25 IU/L), alanine aminotransferase (median 26 vs. 22 IU/L), fasting glucose (median 95 vs. 94 mg/dL), liver stiffness (LS) (median 6.3 vs. 5.6 kPa), and CAP (217 vs. 206 dB/m) (all P<0.05). Incidence of 2-, 3-, 5-, 8-, and 10-year steatosis development was 7.4%, 14.4%, 26.7%, 38.9%, and 49.4%, respectively, resulting in an overall incidence rate of 5.837 per 100 person-years – higher than the previously reported 4.06 per 100 person-years from ultrasonography-based Korean study. Multivariate Cox regression analyses revealed that the male sex (HR=1.398, 95% CI 1.174–1.664), higher BMI (HR=1.010, 95% CI 1.007–1.013), cirrhosis (HR=1.331, 95% CI 1.061–1.670), higher baseline LS (HR=1.010, 95% CI 1.000–1.020) and CAP (HR=1.019, 95% CI 1.015–1.023) were significantly associated with hepatosteatosis development in patients with CHB.

Conclusions: The incidence rate of transient elastography-based hepatosteatosis was higher than that reported from ultrasonography in South Korea. Male patients with higher BMI and liver fibrosis are at increased risk for developing hepatosteatosis.

Keywords: Hepatitis B, Chronic, Fatty Liver, Epidemiology, Transient Elastography

Friday, May 30, 2025, 15:10-16:30

7. Liver Cancer, Basic

FP-47

Aggressiveness-Promoting, Fibroblast Activation Protein-STAT3 Positive Feedback Loop is Activated by IL-6 in Cancer Associated Fibroblasts of Hepatocellular Carcinoma

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Aims: Cancer-associated fibroblasts (CAFs) play a pivotal role in the tumor microenvironment by influencing various processes such as cell migration, proliferation, and immune suppression. IL-6, a key inflammatory cytokine, activates the JAK/STAT3 signaling pathway, which is known to regulate various cellular functions. Fibroblast Activation Protein (FAP) has been identified as a crucial player in this context, with its expression being regulated by IL-6. However, the functional role and potential mechanisms of soluble FAP (sFAP) induced by IL-6 in CAFs remain unclear. This study aims to elucidate the role of sFAP and its impact on the regulation of the tumor microenvironment.

Methods: Single-cell RNA-sequencing (scRNA-seq) analysis was performed using tissue from 3 patients with HCC. Single-cell suspensions were converted to barcoded scRNA-seq libraries using a Chromium Next GEM Single-Cell 3p RNA Library v3.1 Kit (10× Genomics) to estimate 10,000 cells per library, following the manufacturer's instructions. CAFs were isolated from tumor tissues obtained from hepatocellular carcinoma (HCC) patients. CAFs were treated with IL-6 to investigate the activation of the JAK/STAT3 pathway and the subsequent upregulation of FAP. The concentrations of sFAP and IL-6 in the culture supernatant were measured by ELISA, following the kit instructions.

Hep3B cells were cultured in conditioned media derived from CAFs. Vimentin expression was reduced in cells cultured with conditioned media from siFAP-treated CAFs compared to those cultured with media from siControl-treated CAFs.

Results: To isolate and characterize CAF subpopulations, we analyzed single-cell data and identified surface proteins that were uniquely expressed in each CAF subpopulation. For mCAFs, we identified FAP as a surface marker and observed high expression of JAK1, JAK2, and STAT3. IL-6 treatment led to a significant increase in P-STAT3 expression and FAP upregulation in CAFs. Inhibition of FAP resulted in a marked reduction in P-STAT3 levels and JAK/STAT3 pathway activation. Additionally, both membrane-bound FAP and sFAP levels were increased upon IL-6 treatment. IL-6 treatment led to a significant increase in P-STAT3 expression and FAP upregulation in CAFs. Inhibition of FAP resulted in a marked reduction in P-STAT3 levels and JAK/STAT3 pathway activation. Additionally, both membrane-bound FAP and sFAP levels were increased upon IL-6 treatment. When FAP expression was reduced, an increase in NK cell activity was observed. Furthermore, Hep3B cells cultured in conditioned media derived from siFAP-treated CAFs exhibited lower vimentin expression, an EMT marker, compared to those cultured with media from siControl-treated CAFs.

Conclusions: In conclusion, this study demonstrates that IL-6-induced FAP upregulation is closely linked to JAK/STAT3 pathway activation in CAFs. Inhibiting FAP reduces JAK/STAT3 signaling and P-STAT3 levels while also affecting NK cell activity and EMT marker expression. These findings highlight the critical role of FAP in tumor microenvironment modulation and suggest its potential as a therapeutic target in cancer treatment.

Keywords: Cancer-Associated Fibroblasts, JAK/STAT3, FAP

FP-48

Significance of Shelterin Component TPP1 Upregulation and Telomerase Activation in the Clinico-pathological Features of Hepatocellular Carcinoma

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Aims: Telomere dysfunction and its associated shelterin complex are implicated in cancer, yet the roles of telomerase and shelterin genes in hepatocellular carcinoma (HCC) remain poorly understood. This study aims to investigate the clinico-biological functions of telomerase and shelterin components in HCC development and progression.

Methods: We analyzed tumor and matched nontumor tissues from 272 HCC patients who underwent surgery. mRNA expression and telomere length were assessed via RNA-seq and qRT-PCR, while telomerase activity was measured using the TRAP assay. TERT, TPP1, and other shelterin genes were correlated with clinico-pathological features. Findings were validated using The Cancer Genome Atlas (TCGA) HCC data.

Results: In both TCGA and surgical cohorts, TERT and TPP1 expression were elevated in tumor versus non-tumor tissues, with increased telomerase activity and shortened telomere length in tumors. In our in-house cohort, higher TERT and TPP1 expression correlated with advanced-stage and poorly differentiated HCC (all P<0.05), and AFP levels were elevated in patients with high TPP1 expression (P<0.05). RNA-seq analysis revealed a positive correlation between TPP1 expression and proliferation (MKI67, PCNA, E2F1, MYC) and EMT markers (MMP-9, Snail 1/2, ITGAV, CXCR4), which were also corroborated by TCGA HCC datasets. TPP1 expression was positively correlated with telomerase activity, particularly in non-HBV-infected HCC (P<0.05), where telomerase activation varied by TPP1 levels. High TPP1 expression was significantly associated with recurrence and poor prognosis post-surgery in HCC.

Conclusions: Upregulation of TPP1, alongside increased telomerase activity, is linked to advanced HCC and poor outcomes. TPP1 may serve as a valuable prognostic marker for HCC.

Keywords: Telomere, Shelterin, Prognostication, HCC

FP-49

AK7 Drives HCC Progression by Enhancing Stemness, EMT, and Hypoxia Adaptation

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Aims: Hepatocellular carcinoma (HCC) is one of leading cause of cancer-related mortality worldwide, with limited treatment options and poor prognosis. Although AK7 has been implicated as a potential tumor suppressor in ovarian cancer, its role in HCC remains largely unexplored. This study aimed to elucidate the function of AK7 in HCC progression and metastasis.

Methods: AK7 expression was analyzed in publicly available HCC datasets (GSE77314, GSE124535), Mendeley data and single-cell transcriptomic analysis (GSE149614). AK7 expression was further validated in HCC tissue samples using qRT-PCR. Functional studies were performed HCC cell lines using wound healing, migration, and invasion assays, following AK7 knockdown. Additionally, *in vivo* studies were conducted using an orthotopic liver cancer model.

Results: Our analysis revealed that AK7 expression was significantly elevated in HCC tissues and strongly associated with poor prognosis in TCGA LIHC. Single-cell transcriptomic analysis revealed that AK7 expression was predominantly enriched in endothelial cells and hepatocytes, with a marked upregulation in tumor clusters compared to benign cell populations. *In vitro*, AK7 knockdown suppressed epithelial–mesenchymal transition (EMT) markers, angiogenic factors, and stemness-related genes. Consistently, animal model showed that silencing AK7 impaired metastatic dissemination *in vivo*.

Conclusions: Our findings establish AK7 as a key driver of HCC progression, influencing invasion, metastasis, angiogenesis, and stemness. Additionally, high AK7 expression correlates with hypoxia- and angiogenesis-related signaling, suggesting a potential link between tumor -stromal interactions and metastatic expansion. Targeting AK7 may provide a novel therapeutic strategy for HCC treatment.

Keywords: HCC, AK7, Stemness, HYPOXIA

FP-50

NADPH Oxidase 2 Regulates Epithelial-Mesenchymal Transition Signaling via Sterol Regulatory Element-Binding Protein 2 and Promotes Hepatocellular Carcinoma Survival

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Aims: Nicotinamide adenine dinucleotide phosphate oxidase (NOX) family enzymes play a crucial role in the generation of reactive oxygen species (ROS), which significantly contribute to the development of various cancers, including hepatocellular carcinoma (HCC). NOX2 has been reported to be important in various types of cancer, but the role of NOX2 in HCC has yet to be explored.

Methods: The HCC cell lines used were HepG2, Huh-7, SNU-398, SNU-449, and Hepa1-6, while the normal hepatocyte used was AML-12. NOX2 activity was induced by palmitate. The mouse HCC model was induced using transposon technology to promote HCC development. RNA sequencing was performed on mouse tumor tissue. Tissues from HCC patients were analyzed by Western blot to assess the protein levels between tumor (N=149) and paired tissues (N=149). HCC tissue was obtained from patients who underwent surgery at Chungnam National University Hospital.

Results: Palmitate-induced activation of NOX2 stimulates SREBP2 and ROS production in HCC cells, with NOX2 activity being triggered at the plasma membrane. Additionally, cell debris activates both NOX2 and SREBP2, suggesting that lipid components play a key role in this process. Moreover, NOX2 overexpression enhances migration, whereas its inhibition promotes FAO and reduces migration. Inhibition of SREBP2, on the other hand, decreases EMT signaling and migration. Finally, NOX2 inhibition or ROS reduction induces apoptosis, highlighting the crucial role of NOX2 in HCC survival. In animal models, NOX2 depletion in the liver significantly decreased the size and number of HCCs, alongside reduced SREBP2 activity and EMT signaling. RNA-seq analysis of NOX2-deficient mouse tumor tissues showed a decrease in genes related to lipid synthesis, cell adhesion and migration. Furthermore, a correlation between the expression of NOX2 or N-cadherin and SREBP2 activity was observed in patient tissue samples. In TCGA, NOX2 expression showed a correlation with SREBP2, Slug, and N-cadherin. If NOX2-SREBP2 expression is high, the patient's overall survival was lower.

Conclusions: In HCC, NOX2 activity induces migration through SREBP2-mediated EMT signaling, exacerbating the progression of HCC.

Keywords: NOX2, SREBP2, EMT Signaling, HCC

FP-51

Diagnostic and Prognostic Impact of Circulating Exosome microRNA for the Early Stage of HBV Induced HCC

HyoJu Kim[1], Tom Ryu[1], Young Chang[1], Sung Hwan Yoo[2], Jeong-Ju Yoo[3], HyoJu Kim1, Young Chang1, Sang Gyune Kim[3], Do Seon Song[4], Young Sun Lee[5], Su Jong Yu[6], Sae Hwan Lee[7], Hyuk Soo Eun[8], Won Kim[9], Jae Young Jang[1], Young Seok Kim[3], Hong Soo Kim[7], So Young Jin[10], Seongho Ryu[11]0, Hyun Woong Lee[2], Soung Won Jeong[1]

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Aims: Despite advances in the diagnosis of early-stage hepatocellular carcinoma(HCC) through radiologic findings and tumor markers, early detection remains challenging. Among the well-known biomarkers in liquid biopsy methods, exosome microRNAs(exomiRs) have emerged as promising biomarkers due to their stability in body fluids and their role in intercellular communication. We investigated the diagnostic and prognostic markers of exomiRs in early HBV induced HCC.

Methods: This multicenter prospective study enrolled 24 patients diagnosed with early-stage hepatitis B virus (HBV)-induced hepatocellular carcinoma (HCC) (tumor size ≤ 3 cm), with 24 paired pre- and post- operative samples and 8 cirrhosis samples available for comprehensive analysis. To investigate the potential of exomiRs as biomarkers for early HCC detection, peripheral blood samples were collected from the enrolled patients, and exosomes were isolated using standard ultracentrifugation techniques by Gene2Us. ExomiRs sequencing data was processed using the SCHMC in-house pipeline, based on miRDeep2 and edgeR, with miRBase version 22.1. Expression counts were normalized to RPM values and scaled using Python and R.

Results: Among 50 differentially expressed exomiR candidates, 23 exomiRs were the most highly expressed exosome microRNAs in pre-operative plasma of early HBV-HCC derived cancer patients. Notably, one exomiR(hsa-miR-Diagxx1) was detected at the most highly differentially expressed level in the exosome miRNA obtained from pre-operative plasma compared to post-operative plasma(Log2 FC>2, p value<0.05). Additionally, four of the 24 patients relapsed, and the median follow-up period was 35 months. Patients with high expression of three exomiRs(hsa-miR-Prxx1, hsa-miR-Prxx2, hsa-miR-Prxx3) in pre-operative exosome miRNAs had significantly worse recurrence-free survival of HCC (p value<0.05).

Conclusions: For early-stage HBV-HCC, liquid biopsy of exomiRs could be an effective method for easier and quicker diagnosis and prognosis prediction. The one diagnostic and three prognostic exomiRs could serve as efficient targets for early HBV induced HCC.

Keywords: Hepatitis B Virus, Hepatocellular Carcinoma, Exosome, Circulating Microrna

Figure 1

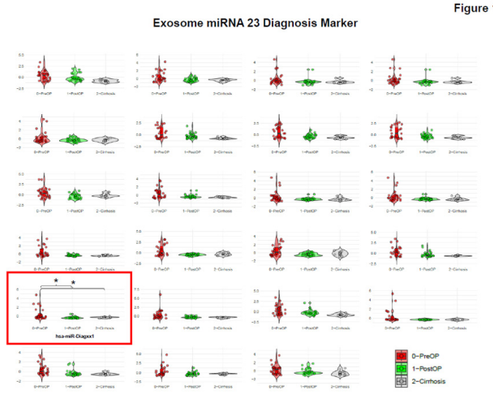
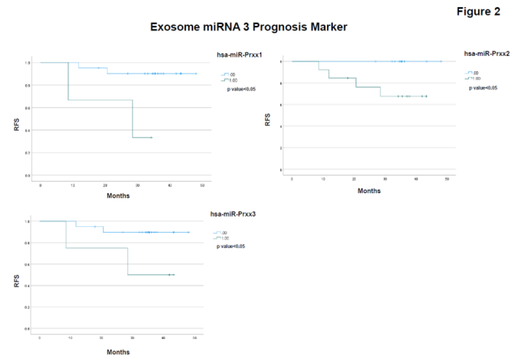


Figure 2



FP-52

Investigation for Prognostic Value of Circulating Tumor DNA by Serum KMT2B Gene and Fragmentation Analysis for the Hbv-Derived HCC after Curative Resection

Sung Hwan Yoo[1], Tom Ryu[2], HyoJu Kim[2], Young Chang[2], Jeong-Ju Yoo[3], Sang Gyune Kim[3], Do Seon Song[4], Young-Sun Lee[5], Su Jong Yu[6], Sae Hwan Lee[7], Hyuk Soo Eun[8], Won Kim[9], Jae Young Jang[2], Young Seok Kim[3], Hong Soo Kim[7], So-Young Jin[10], Hyun Woong Lee[1], Soung Won Jeong[2]

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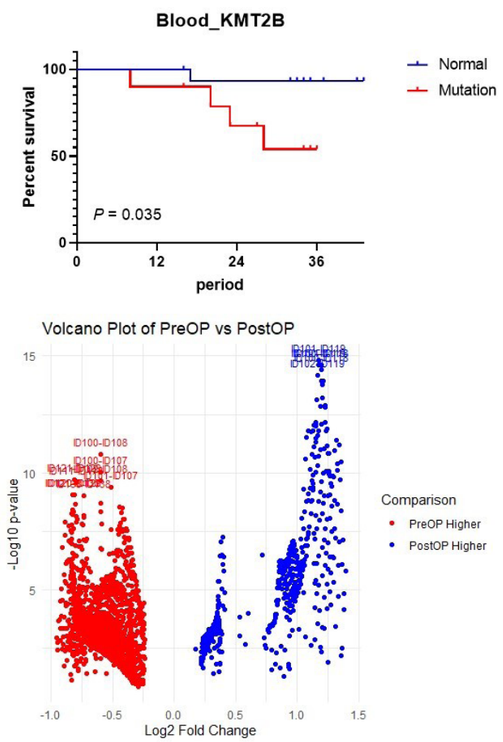
Aims: In recent years, the concept of circulating tumor DNA (ctDNA) using liquid biopsy has gained significant attention as a novel diagnostic approach. Here, we report that profiling fragmentation and target genes enrichment of peripheral blood would be one of the effective predictive tools for detecting the early recurrence of hepatitis B virus (HBV) derived hepatocellular carcinoma (HCC) after resection.

Methods: The multicenter prospective study enrolled 41 patients with HBV induced HCC (tumor size ≤ 3cm) after curative resection. For variants analysis, we designed 19 targeted genes, and which were selected based on previous studies. Peripheral blood was obtained and ctDNA was extracted before

and after operation from the plasma. Also, genomic DNA was isolated from formalin-fixed paraffin-embedded tissue blocks. Isolated DNA were handled for capture probes utilizing target enrichment kit and target panel Next Generation Sequencing analysis was used for further analysis.

Results: Nine of the 41 patients relapsed, and the median follow-up period was 35 months. Median value of alpha-fetoprotein and protein induced by vitamin K absence or antagonist-II was 17.1 ng/mL and 30.85 mAU/mL, respectively. Among the 19 targeted genes, the most frequently mutated genes in per-operative blood and cancer tissue were *APOB, ARID1A, KMT2B, and CTNNB1*. Among these four mutated genes, the gene that showed statistical correlation with cancer recur after surgery was *KMT2B* in pre-operative blood (*P*=0.035). In ctDNA fragmentation analysis, fragment length frequency showed significant high frequency of ctDNA in pre-operative blood samples compared to post-operative blood samples, especially 100-108 fragment lengths.

Conclusions: For predicting of recurrence of earlier stage of HBV-HCC after curative resection, using ctDNA combined with *KMT2B* gene mutation in pre-operative blood and fragmentation analysis could be one of the leading valuable diagnostic methods.



Keywords: Circulating Tumor DNA, KMT2B, Fragmentation Analysis

FP-53

Identification of Novel Links between Cirrhosis and Hepatocellular Carcinoma through Mechanisms of Immune Microenvironment

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Kyungpook National University

Aims: Hepatocellular carcinoma (HCC), a major type of primary liver cancer, represents the leading cause of cancer-related mortality in the worldwide. HCC commonly arises in patients with underlying chronic liver disease, such as cirrhosis. However, only 1-3% of patients with hepatic cirrhosis undergo into HCC. Even though only a few proportions of cirrhosis could develop to HCC, no one raised any doubt whether HCC could be developed by cirrhosis-independent manner. Here we investigate a new link between cirrhosis and HCC using the first genetic mouse model of liver cirrhosis.

Methods: In this study, we will generate the first genetic mouse model of liver cirrhosis recapitulating clinical features of the disease, by the specific elimination of microspherule protein 1 (MCRS1) in hepatocytes. Using this unprecedented and unique genetic tool with other model systems, combined with state-of-the-art technologies, we will propose a new crosstalk between liver cells and immune cells to understand better in liver diseases.

Results: Here we investigate a new link between cirrhosis and HCC using the first genetic mouse model of liver cirrhosis. This unique genetic tool help to better understand the mechanisms of liver cirrhosis and to understand its role and function in HCC development. Moreover, we report on the specific interaction between hepatic stellate cells (HSC), one of liver cell types, and hepatic immune cells using different genetically modified mouse models. The aim of this study is that HSC could be a major regulator of liver antitumor immunosurveillance to prevent HCC.

Conclusions: Primary liver cancer (most commonly HCC) in Asia, over 10,000 cases are diagnosed every year of liver cancer. More than half of all people diagnosed with primary liver cancer have cirrhosis, leading to the assumption that liver cirrhosis is a risk factor for HCC but only 1-3% of patients with cirrhotic liver undergo into HCC development. Moreover, therapeutic options remain very limited if not inexistent for cirrhosis and HCC. Thus, limited and inefficient therapeutic options render the curative treatment of the disease almost impossible. We propose an ambitious and new challenging concept offering an innovative demarcation line from the existing literature: cirrhosis is a protective mechanism against HCC rather than a risk factor! This project will integrate an inter- and multi-disciplinary research using complex mouse models, human data, immunology, and state-of-the art approaches providing a disruptive and provocative novel concept to set a major advance toward personalized medicine. Thus, our study is socially relevant and will have an important socio-economic impact for HCC patients.

Keywords: BILE ACID Transporter, Liver Cirrhosis, Mouse Model

FP-54

Association between Gut Microbial Dynamics and Clinical Outcomes in Patients with Hepatocellular Carcinoma Receiving Chemoembolization: A Prospective Study

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Aims: Transarterial chemoembolization (TACE) may cause intestinal dysbiosis by elevating portal vein pressure. We aimed to evaluate the association between gut microbiota and clinical outcomes in patients with hepatocellular carcinoma (HCC) undergoing TACE.

Methods: This single-center, prospective cohort study included 96 adult HCC patients treated with TACE from April 2021 to November 2023. Fecal samples were collected before TACE (P0), one day (P1), and one month (P2) after TACE. Fecal 16S rRNA taxonomy was analyzed to evaluate microbial diversity, composition, and dynamic changes at each time point. The primary outcome was the association between the initial response to TACE and microbial composition and changes in the stool.

Results: Out of the total participants, 63 (65.6%) were responders and 33 (34.4%) were non-responders. The stool of responders had higher alpha-diversity than that of non-responders at baseline, and a higher abundance of short-chain fatty acid-producing bacteria at all time points. Alpha-diversity significantly decreased one day after TACE (*P*<0.05 for P1 vs. P0) and tended to recover one month later in the responders, albeit without statistical significance for P2 vs. P0. Regarding beta-diversity, there were some changes in both responders and non-responders during the post-TACE period, albeit with different patterns. A low abundance of *Roseburia cecicola* (hazard ratio [HR], 3.44; 95% confidence interval [CI], 1.10–10.8; *P*=0.03) and *Dialister_uc* (HR, 3.90; 95% CI, 1.32–11.57; *P*=0.01) at baseline was associated with worse overall survival.

Conclusions: Microbial diversity and specific microbial components showed dynamic associations with clinical outcomes in TACE-treated HCC patients, who may benefit from alleviating dysbiosis.

Keywords: Gut Microbiome, Biomarker, Hepatocellular Carcinoma, Transarterial Chemoembolization

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DAY 3: May 31 (Sat)

Free Paper Presentation 2

FP-55~FP-62	Liver Cancer, Clinical 2
FP-63~FP-70	HBV 2
FP-71~FP-78	HCV
FP-79~FP-86	MASLD, LC and Others, Basic
FP-87~FP-94	Liver Transplantation 1
FP-95~FP-102	Liver Transplantation 2

Saturday, May 31, 2025, 13:10-14:30

8. Liver Cancer, Clinical 2

FP-55

A Machine Learning Model to Predict the Treatment Response of Atezolizumab plus Bevacizumab in Patients with Hepatocellular Carcinoma Incorporating Computed Tomogram-Derived Imaging Biomarkers

Moon Haeng Hur[1], Bo Hyun Kim[2], Byeong Geun Song[3], Dong Hyun Sinn[3], Youngsu Park[2], Yuri Cho[2], Jeayeon Park[1], Yunmi Ko[1], Hyunjae Shin[1], Yun Bin Lee[1], Eun Ju Cho[1], Su Jong Yu[1], Yoon Jun Kim[1], Jung-Hwan Yoon[1], Jeong-Hoon Lee[1,4]

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Aims: Despite the growing number of patients receiving atezolizumab plus bevacizumab (Atezo/Bev) for hepatocellular carcinoma (HCC), reliable models to predict treatment response in advance remain lacking. We aimed to develop machine learning models that can predict objective response (complete or partial response) after Atezo/Bev therapy incorporating clinical data and imaging biomarkers derived from abdominal computed tomography (CT).

Methods: A total of 500 consecutive patients with HCC who received Atezo/Bev as a first-line systemic therapy between 2020 and 2023 were included from 3 referral centers in Korea. Blood test results, including alpha-fetoprotein (AFP) and protein induced by vitamin K absence-II (PIVKA-II), were collected right before initiating Atezo/Bev and at the first imaging follow-up visit, 6–9 weeks after the first therapy. In patients with available imaging biomarkers derived from baseline CT (n=389), seven additional biomarkers were obtained using a deep learning-based CT auto-segmentation software: volume of abdominal visceral fat, muscle, liver, and spleen; total fat-to-trunk volume ratio; liver and muscle Hounsfield unit (HU). Patients were randomized 1:1 to either the training or test cohorts and gradient boosting machine algorithm was employed to develop the models.

Results: During a median follow-up of 9.6 (interquartile range [IQR]=5.7–14.2) months, 129 patients (25.8%) achieved objective response. Model 1 was developed using eight clinical variables: MoRAL score ($2x\sqrt{\text{AFP}} + 11x\sqrt{\text{PIVKA-II}}$), ALBI score, neutrophil-to-lymphocyte ratio (NLR), and eosinophil count at the first imaging follow-up and change in these variables from baseline. This model demonstrated an area under the receiver operating characteristic curve (AUROC) of 0.748 (95% confidence interval [CI]=0.764–0.812) in the training cohort and 0.747 (95% CI=0.679–0.809) in the test cohort. Model 2, which incorporated seven imaging biomarkers in addition to clinical variables, showed improved predictive accuracy in both the training (0.789, 95% CI=0.717–0.862) and test cohorts (0.769, 95% CI=0.691–0.839).

Conclusions: Using the clinical data and CT-derived imaging biomarkers, these machine learning-based models can predict response and help determine future treatment plans in advance for HCC patients receiving Atezo/Bev therapy.

Keywords: Liver Cancer, Immunotherapy, Artificial Intelligence, Response Prediction

FP-56

Association of Survival with Discordance between Preoperative Radiology and Postoperative Pathology in Patients with Hepatocellular Carcinoma

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Aims: There are no studies about the discordance between preoperative radiologic and postoperative pathological findings in patients with hepatocellular carcinoma (HCC) who have undergone resection. Thus, we investigated the impact of these discrepancies on the prognosis in patients with HCC who underwent resection.

Methods: This study included patients who were diagnosed with HCC on MRI and underwent resection within 1 month of diagnosis. Overall 1,790 patients from the Korean Primary Liver Cancer Registry from 2008 to 2016 and 185 patients from Chungnam national university hospital from 2008 to 2019 were included in the nationwide and hospital cohorts, respectively. For five factors, such as maximum tumor diameter, tumor number, vascular invasion, bile duct invasion, lymph node (LN) metastasis, the prognosis according to the discrepancies between MRI and pathologic findings were analyzed using the Kaplan-Meier method and Cox regression analysis.

Results: In the nationwide cohort, when all five factors were concordant, the 1-year, 3-year, and 5-year survival rates were 96.5%, 87.3%, and 80.8%, respectively. The survival rate was lower when all five factors did not match than when all were concordant (P<0.001). A similar trend was observed in the hospital cohort without reaching significance (P=0.260). Multivariate analysis showed that radiologic-pathologic discrepancies in >2 factors (hazard ratio, [HR] 3.251), vascular invasion (HR 2.044 and HR 2.596) and LN metastasis (HR 8.157 and HR 7.209) on pathology or both imaging and pathology, respectively, were independent survival predictors (all P<0.001). Similarly, LN metastasis on imaging emerged as an independent predictor (HR 3.386, P=0.009). Age, an alpha-fetoprotein ≥200 ng/mL, and modified Union for International Cancer Control stage were additional independent predictors.

Conclusions: This is the first study to demonstrate that radiologic-pathologic discordances in HCC patients who underwent resection are significantly associated with worse survival. More accurate preoperative evaluation is essential for optimizing treatment and improving prognosis.

Keywords: Discordance, Hepatocellular Carcinoma, Lymph Nodes, Survival Rates

Figure 1.

Figure 2.

FP-57

Differential Therapeutic Effectiveness of Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma Based on Chronic Hepatitis B Viral Activity and Etiology: A Multicenter Cohort Study

Yunmi Ko[1], Hyunjae Shin[1,2], Byeong Geun Song[3], Moon Haeng Hur[1], Youngsu Park[1,2], Jeayeon Park[1], Yuri Cho[2], Yun Bin Lee[1], Eun Ju Cho[1], Bo Hyun Kim[2], Su Jong Yu[1], Dong Hyun Sinn[3], Yoon Jun Kim[1], Jung-Hwan Yoon[1], Jeong-Hoon Lee[1]

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Aims: Atezolizumab plus bevacizumab (Atezo/Bev) has been used as the first-line therapy for unresectable hepatocellular carcinoma (HCC). Previous studies reported potential differences in treatment responses to immune checkpoint inhibitors (ICIs) between viral and non-viral HCC, possibly due to variations in tumor microenvironments. This study aimed to investigate the impact of hepatitis B virus (HBV) DNA detectability, which may be associated with hepatic inflammatory status

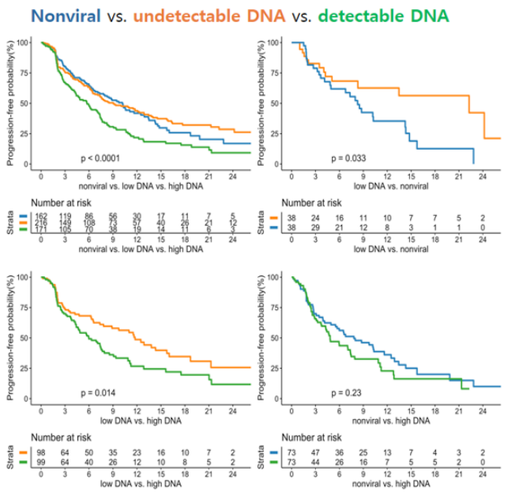
among HBV-related HCC patients, on treatment outcomes of Atezo/Bev.

Methods: This retrospective study included intermediate to advanced HCC patients, initially treated with Atezo/Bev between January 2016 and December 2022 at three tertiary hospitals in Korea. Patients were classified into either the non-viral group or the chronic hepatitis B (CHB) group, with the latter being further divided based on HBV DNA detectability. The primary outcome was progression-free survival (PFS) and the secondary outcome was overall survival (OS).

Results: A total of 549 patients were eligible for this analysis. The CHB/detectable HBV DNA, CHB/undetectable HBV DNA, and non-viral groups included 216, 171, and 162 patients, respectively. After performing propensity score matching (PSM), baseline characteristics were well balanced across the groups (all standardized mean differences < 0.1). The CHB/detectable-DNA group had significantly shorter PFS (hazard ratio [HR]=1.59, 95% confidence interval [CI]=1.09–2.33, *P*=0.02) and OS (HR=1.37, 95% CI=1.06–1.96, *P*=0.01) than CHB/undetectable-DNA group. However, the CHB/detectable-DNA group showed comparable PFS (HR=1.28, 95% CI=0.86–1.91, *P*=0.23) and OS (HR=1.06, 95% CI=0.83–1.85, *P*=0.35) to the non-viral group.

Conclusions: Detectable HBV DNA was associated with shorter PFS and OS than undetectable HBV DNA in CHB patients with unresectable HCC receiving first-line Atezo/Bev. These findings suggest that HBV DNA detectability may indicate intrahepatic inflammation, potentially influencing ICI response. As antiviral treatment can mitigate this effect, it may help enhance the effectiveness of Atezo/Bev.

Keywords: Chronic Hepatitis B, Intrahepatic Inflammation, Hepatocellular Carcinoma, Immunotherapy



FP-58

Identification of Plasma Protein Biomarkers for Predicting Response to Atezolizumab-Bevacizumab in Unresectable Hepatocellular Carcinoma

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Aims: Despite the clinical benefits of atezolizumab-bevacizumab (atezo-bev) in unresectable hepatocellular carcinoma (HCC), reliable and actionable predictive biomarkers remain to be elucidated.

Methods: We collected plasma samples from 44 patients with unresectable HCC before and after atezo-bev treatment. Matched, quality-controlled samples (n = 35; pre-treatment and after three cycles) were analyzed for 174 proteins using the Olink panel. Biomarker selection was performed using mixed linear regression, followed by Lasso logistic regression and five-fold cross-validation. A clinical model incorporating key features was developed using recursive feature elimination with logistic regression, and its predictive performance was evaluated using ROC-AUC analysis.

Results: Plasma levels of sPD-L1 and VEGF significantly changed after atezo-bev treatment but did not differ between responders and non-responders. Mixed linear regression identified time-dependent differences in GDF-15, SHPS-1, CAIX, VEGFR-2, TRAIL, and IGFBP-2 between responders and non-responders. Baseline CCL16 and MCP-4 levels were significantly higher in responders, whereas TNFSF13B was elevated in non-responders. A LASSO-based model incorporating pre-treatment MCP-4, TNFSF13B, CCL16, SHPS-1, VEGFR-2, and Δ values of GDF-15 and VEGFR-2 achieved an accuracy of 0.71 and an AUROC of 0.95, outperforming a clinical model using AFP changes (AUROC = 0.77).

Conclusions: Plasma protein profiling and its dynamic changes identified potential biomarkers for predicting atezo-bev response in HCC, supporting its role as a liquid biopsy tool for therapeutic guidance

Keywords: Biomarker, Liquid Biopsy, Machine Learning, Atezolizumab Plus Bevaciuzmab

FP-59

Efficacy and Safety of Sorafenib as a Later-Line Treatment in Advanced Hepatocellular Carcinoma: A Phase 2 Study

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Aims: Sorafenib has long been used as a first-line therapy for advanced hepatocellular carcinoma (HCC). However, with immune checkpoint inhibitor (ICI)–based combination therapy now established as the first-line standard for advanced HCC, prospective data on its efficacy and safety of sorafenib in the second- or later-line setting remain limited. This study aimed to evaluate the clinical outcomes and safety profile of sorafenib in patients with previously treated advanced HCC following ICI-based therapy.

Methods: This study is a single-center, single-arm, prospective phase 2 trial. Patients with advanced HCC who had previously received systemic therapy were enrolled between March 10, 2022, and April 17, 2024, with data cutoff on March 7, 2025. The primary endpoints were progression-free survival (PFS) and safety, while secondary endpoints included overall survival (OS) and disease control rate.

Results: Among the 50 enrolled patients, 49 were included in the final analysis after excluding one due to protocol violation. The median age was 66.1 years (interquartile range [IQR]=58.2–71.6), and 45 (91.8%) were male. The median follow-up duration was 9.7 months (IQR=5.2–17.8). The median PFS was 1.9 months (95% confidence interval [CI]=1.7–3.5), and the median OS was 10.0 months (95% CI=7.6–17.6). No patients achieved a complete response or partial response, and 16 patients (32.7%) attained disease control. Subgroup analysis revealed no significant differences between the second-line (n=35) and third-line (n=14) treatment groups, with a median PFS of 1.8 months (95% CI=1.7–3.6) versus 3.5 months (95% CI=1.2–3.7; *P*=0.80) and a median OS of 9.7 months (95% CI=7.1–17.6) versus 12.4 months (95% CI=6.2–not estimable; *P*=0.15). Adverse events (AEs) occurred in 47 patients (96.0%), with grade ≥3 AEs reported in 24 patients (49.0%). The most common grade≥3 AEs included hand-foot skin reaction (20.4%), skin rash (12.2%), hypertension (8.2%), and proteinuria (4.1%). Five patients discontinued sorafenib due to AEs.

Conclusions: Sorafenib demonstrated modest efficacy, as a later-line treatment in advanced HCC patients previously treated with systemic therapy. Its consistent safety profile supports its continued role in subsequent-line therapy.

Keywords: Hepatocellular Carcinoma, Sorafenib, Phase 2 Trial, Progression-Free Survival

Table 1. Baseline characteristics

Variables	Sorafenib (n=49)	Variables	Sorafenib (n=49)
Age, years	66.1 (58.2-71.6)	Line of sorafenib therapy, no.(%)	
Sex, no.(%)		2nd-line	35 (71.4%)
M	45 (91.8%)	3rd-line	14 (28.6%)
F	4 (8.2%)	Number of Intrahepatic Tumor nodules, no.(%)	
Cause of HCC, no.(%)		0	7 (14.3%)
HBV	33 (67.3%)	1	4 (8.2%)
HCV	4 (8.2%)	2	1 (2.0%)
Others	12 (24.5%)	3	6 (12.2%)
ECOG performance status, no.(%)		4	31 (63.3%)
0	40 (81.6%)	Largest Tumor size, cm	2.4 (1.7–3.3)
1	9 (18.4%)	Beyond up-to-seven criteria, n(%)	30 (61.2%)
Diabetes melitus, no.(%)	15 (30.6%)	Liver occupation > 50%, no.(%)	3 (6.1%)
Hypertension, no.(%)	24 (49.0%)	Portal vein Invasion, no.(%)	10 (20.4%)
Hyperlipidemia, no.(%)	1 (2.0%)	Vp2	3 (6.1%)
Surgical History, no.(%)	19 (38.8%)	Vp3	4 (8.2%)
Liver transplantation History, no.(%)	7 (14.3%)	Vp4	3 (6.1%)
Prior loco-regional therapy, no.(%)	31 (63.3%)	Hepatic vein invasaion, no.(%)	4 (8.2%)
TACE	26 (53.1%)	Extrahepatic Spread, no.(%)	36 (73.5%)
TARE	3 (6.1%)	AJCC stage, 8th, no.(%)	
RFA	1 (2.0%)	II	9 (18.4%)
Prior Radiotherapy, no.(%)	29 (59.2%)	IIIa	1 (2.0%)
Child-Pugh score, no.(%)		IIIb	1 (2.0%)
5	33 (67.3%)	IVa	1 (2.0%)
6	8 (16.3%)	IVb	37 (75.5%)
7	7 (14.3%)	Modified UICC stage, no.(%)	
8	1 (2.0%)	II	2 (4.1%)
Child-Pugh class, no.(%)		III	9 (18.4%)
A	41 (83.7%)	IVa	2 (4.1%)
B	8 (16.3%)	IVb	36 (73.5%)
ALBI grade, no.(%)		BCLC, no.(%)	
2	45 (91.8%)	A	1 (2.0%)
3	4 (8.2%)	B	9 (18.4%)
Albumin, g/dL	3.8 (3.6–4.2)	C	39 (79.6%)
Bilirubin, mg/dL	0.7 (0.6–1.1)		
AST, U/L	38 (28–60)		
ALT, U/L	28 (18–38)		
PT, INR	1.06 (0.99–1.14)		
Platelet count, x10³/μL	161 (112–201)		
AFP, ng/mL	74.5 (10.9–1150.8)		
PIVKA-II, mAU/mL	847 (273–3308)		

Figure 1. Progression free survival

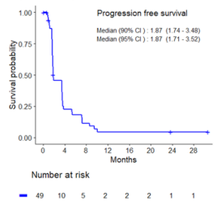


Figure 2. Overall survival

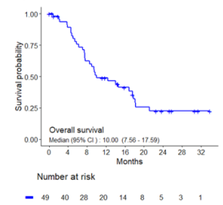


Figure 3. Progression free survival of subgroup analysis

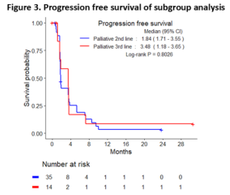
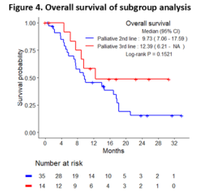


Figure 4. Overall survival of subgroup analysis



FP-60

Can an Ai Predictive Model Be Integrated into Clinical Decision-Making for Predicting Open Conversion in Minimally Invasive Liver Resection?

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Aims: Minimally invasive liver resection (MILR) offers significant benefits, but unplanned open conversion (OC) poses challenges, increasing complications and compromising oncologic outcomes. Identifying patients at high risk for OC based solely on preoperative factors could allow for better surgical planning, including selecting planned open surgery for high-risk patients. This study aims to develop and evaluate an AI predictive model using preoperative data to guide clinical decision-making for MILR.

Methods: A retrospective cohort of 1,280 patients who underwent MILR between 2004 and 2022 was analyzed. Among these, 120 patients (9.4%) experienced unplanned OC. Preoperative variables and radiological findings were used to develop an AI model. Model performance was assessed using the area under the receiver operating characteristic (AUROC), sensitivity, specificity, and accuracy. Clinical feasibility was evaluated by analyzing the model's potential impact on preoperative decision-making.

Results: The AI model achieved an AUROC of 0.89 (95% CI: 0.85–0.93) in predicting OC, with sensitivity and specificity of 83% and 81%, respectively. Tumor size (>5 cm), proximity to major vascular structures (within 1cm), and hypoalbuminemia (3.5g/dl) were identified as key predictors. Integrating AI tools into preoperative planning simulations has been shown to reduce unplanned OC rates by 17.6% through more informed surgical strategy selection, including recommendations for planned open surgery in high-risk cases.

Conclusions: This study highlights the potential of an AI predictive model to guide clinical decision-making in MILR. By identifying patients at high risk for OC, the tool supports strategic planning, potentially improving patient outcomes and resource allocation.

FP-61

Comparison of Treatment Efficacy and Safety Profile of Atezolizumab plus Bevacizumab in BCLC B and C Patients with Hepatocellular Carcinoma

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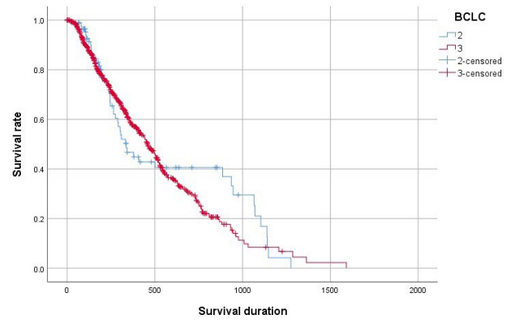
Aims: Hepatocellular carcinoma (HCC) remains a significant global health burden, with limited treatment options for advanced stages. The combination of atezolizumab and bevacizumab has emerged as a standard first-line therapy, demonstrating improved survival outcomes. However, its efficacy and safety may differ between patients with Barcelona Clinic Liver Cancer (BCLC) stage B and C. This study aims to compare the therapeutic outcomes and adverse events of atezolizumab plus bevacizumab (ATE/BEV) between these two stages, providing insights into its optimal use. Understanding these differences may aid in refining treatment strategies and improving prognosis for patients with locally advanced HCC.

Methods: A retrospective analysis was conducted on 819 HCC patients treated with ATE/BEV across nine academic tertiary hospitals. Finally, 103 patients with BCLC stage B and 704 patients with BCLC stage C were included in the analysis

Results: Baseline demographics, including mean age (67.68 vs. 66.03, *P*=0.123), gender distribution (86.9% vs. 86.9%, *P*=0.896), and maximum tumor diameter (6.76 vs. 6.85, *P*=0.863), were comparable between BCLC B and C groups. However, the BCLC B group exhibited a significantly higher mean tumor count (2.98 vs. 2.17, *P*<0.001). While disease control rates were similar (75.9% vs. 68.7%, *P*=0.180), the objective response rate was significantly higher in the BCLC C group (15.7% vs. 25.6%, *P*=0.049). Kaplan-Meier analysis revealed no significant difference in overall survival between the groups.

Conclusions: ATE/BEV showed comparable efficacy in BCLC B and C hepatocellular carcinoma. Further subgroup analysis and large cohort studies are needed to identify patients with better prognostic outcomes from this treatment.

Keywords: Hepatocellular Carcinoma, Ateolizumab Plus Bevacizumab, BCLC Stage, Prognosis



FP-62

Radiofrequency Ablation versus Minimally Invasive Liver Resection for Small Solitary Hepatocellular Carcinoma (3cm) with MRI Features for Predicting Microvascular Invasion

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Aims: Percutaneous radiofrequency ablation(pRFA) and minimally invasive liver resection(MILR) are treatments for small solitary hepatocellular carcinoma(HCC). However, comparative studies on their outcomes are limited. This study aimed to identify preoperative predictors of microscopic vascular invasion(MVI), a key prognostic factor, and evaluate the oncologic outcomes of pRFA and MILR based on MVI risk stratification.

Methods: This retrospective study included patients with small solitary HCC(≤ 3cm) who underwent preoperative Gd-EOB-DTPA-enhanced MRI between 2008 and 2020. A total of 99 patients underwent pRFA, and 124 underwent MILR. Two radiologists independently reviewed MRI images. Logistic regression analysis identified significant preoperative predictors of pathologic MVI in the MILR group. Patients were stratified into risk groups based on the number of risk factors, and long-term outcomes of pRFA and MILR were compared after propensity score matching for age, etiology, and platelet count.

Results: Elevated levels of α-FP(≥40 ng/mL) and two MRI features(non-smooth tumor margin, and LR-M feature) were significant predictive factors for MVI. High-risk patients(1-3 factors) showed worse overall(*P*=0.004) and recurrence-free survival(*P*=0.011) compared to the low-risk patients (no risk factors). After matching, the 2-year recurrence rate in the high-risk group was significantly lower for MILR than pRFA(17.9% vs. 54.8%, *P*=0.003). No significant difference was observed in the low-risk group, but recurrence tended to be higher with pRFA (15.7% vs. 3.0%, *P*=0.071).

Conclusions: MVI can be predicted using α-FP and MRI features, enabling better prognostic assessments. MILR appears superior to pRFA in reducing early recurrence in high-risk patients, while both treatments show comparable outcomes in low-risk patients.

Keywords: Robot Donor Hepatectomy, Anatomic Variation, Extended Criteria

Saturday, May 31, 2025, 13:10-14:30

9. HBV 2

FP-63

X/Precore Mutational Complexity and Its Impact on HBV Replicative Activity and Histological Progression in HBeAg-Positive Chronic Hepatitis B

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Aims: Genomic variants in the X/precore region of hepatitis B virus (HBV) have been implicated in chronic hepatitis B (CHB) progression. However, their impact on intrahepatic viral reservoirs, transcription, and disease phenotype remains unclear. This study aims to explore the correlation between X/precore mutational complexity, HBV replication, and CHB progression.

Methods: This study included 99 HBeAg-positive CHB patients. Twelve key X/precore mutations (G1613A, C1631T, C1653T, T1674C, T1753V, T1754V, A1762T, G1764A, C1773T, A1846T, G1896A, and G1899A) were identified in tissue-samples using an NGS-based assay. Serum HBV antigens (HBsAg, HBeAg, and HBcrAg) and intrahepatic HBV markers (cccDNA, pregenomic RNA) were quantified using commercial-assays and qPCR. Liver inflammation and fibrosis were assessed via the METAVIR scoring system.

Results: X/precore mutations were observed even during the immune-tolerant (IT) phase, with the total number of mutations significantly higher in the immune-active (IA) phase compared to the IT phase (4.5 vs. 2.1, *P*<0.05). The mutations T1753V, A1762T/G1764A (BCP mutation), A1846T, and G1896A (precore) were significantly more frequent in the IA phase, indicating their role in driving the transition from IT to IA phases. Patients with BCP mutations exhibited lower HBeAg

levels, higher aminotransferase levels, and higher histologic activity indices. The total mutational burden in HBeAg-positive patients showed a moderate-to-strong negative correlation with serum markers (HBcrAg [*r*=-0.550], HBeAg [*r*=-0.715], and HBsAg [*r*=-0.365]), and a weak negative correlation with intrahepatic markers (cccDNA [*r*=-0.357] and pgRNA [*r*=-0.263]). Furthermore, the total number of X/precore mutations was significantly associated with the progression of histological fibrosis ($P<0.01$). During follow-up, patients with precore genomic variants achieved significantly higher rates of HBeAg seroclearance compared to those without ($P<0.05$).

Conclusions: X/precore mutational complexity is closely linked to the immune phase of HBeAg-positive CHB, affecting both circulating HBV antigens and the intrahepatic reservoir. It also reflects histological grade and stage, potentially guiding antiviral strategies and management decisions for CHB patients.

Keywords: Hepatitis B Virus, Genomic Variants, Precore/X Region, Prognosis

FP-64

Prevalence of Viral Hepatitis B, D, and C among Adolescent and Adult Mongolian Migrants in Seoul, Korea: Implications for Early Screening and Intervention

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Aims: Chronic liver diseases are a significant public health concern in Mongolia, where hepatitis B virus (HBV), hepatitis D virus (HDV), and hepatitis C virus (HCV) prevalence rates are among the highest globally. Migrants from high-prevalence regions may carry this burden to host countries, with adolescents representing a critical population for early intervention. This study aimed to assess the prevalence of chronic HBV, HDV, and HCV infections among Mongolian migrants in Seoul, Korea, with particular attention to adolescents, to inform prevention strategies and improve linkage-to-care for high-risk populations.

Methods: Demographic data and blood samples were collected from Mongolian migrants in Seoul, Korea, with deliberate inclusion of both adolescent and adult populations. Serological markers for HBV, HDV, and HCV were analyzed using ELISA tests for HBsAg, anti-HDV Ab, and anti-HCV Ab, respectively.

Results: A total of 109 Mongolians (92 adolescents, 17 adults) participated. Among adolescents, HBsAg, anti-HDV Ab, and anti-HCV Ab positivity rates were 1.09% (1/92), 2.17% (2/92), and 0.00% (0/92), respectively. Among adults, these rates were 11.8% (2/17), 5.88% (1/17), and 5.88% (1/17), respectively. Two participants (1 adolescent, 1 adult) showed HBV/HDV co-infection (HBsAg+ and anti-HDV Ab+). A single case of isolated anti-HDV Ab positivity was found in adolescents.

Conclusions: The prevalence of HBsAg and anti-HDV Ab among Mongolian migrants was lower than reported rates in Mongolia but remains significant within South Korea's low-endemic context. The identification of HBV/HDV co-infection in an adolescent underscores the importance of early screening in younger migrant populations. These findings highlight the need for age-appropriate screening programs and close monitoring of individuals with HBV/HDV co-infection. Enhanced awareness, early diagnosis, and linkage-to-care efforts are essential to address the healthcare needs of migrant populations effectively, with particular attention to adolescents who may benefit most from timely intervention.

Keywords: Adolescent Migrants, Viral Hepatitis, HBV/HDV Co-Infection, Screening Programs

FP-65

Antiviral Therapy Reduces Dyslipidemia and Cardiovascular Risk in Chronic Hepatitis B: TDF as the Most Effective Agent

Hyuk Kim[1], Jae-Young Kim[2], Hyun Bin Choi[1], Ji-Soo Lee[1], Yoon E Shin[1], Jeong-Ju Yoo[1], Sang Gyune Kim[1], Young-Seok Kim[1]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital; [2]Department of Internal Medicine, Soonchunhyang University School of Medicine

Aims: Chronic hepatitis B (CHB) necessitates long-term antiviral therapy, which has raised concerns regarding its effects on dyslipidemia and associated cardiovascular risks. Notably, prior studies have predominantly focused on the impact of individual antiviral agents on lipid profiles, with limited data addressing their effects on major adverse cardiovascular events (MACE). This study aims to comprehensively evaluate the influence of antiviral therapy on both dyslipidemia and MACE.

Methods: This retrospective cohort study utilized the Health Insurance Review and Assessment (HIRA) database. A total of 445,138 CHB patients were classified into antiviral treatment (48,906) and control (396,232) groups. Propensity score matching yielded 48,906 matched pairs. Primary outcomes were dyslipidemia and MACE (ischemic heart disease, myocardial infarction, ischemic stroke).

Results: After matching, the antiviral group exhibited a lower dyslipidemia incidence (14.65 vs. 18.56 per 100,000 person-years; incidence rate ratio [IRR] 0.79, 95% CI 0.74–0.84, $P<0.001$). TDF significantly reduced dyslipidemia risk (hazard ratio [HR] 0.51, 95% CI 0.47–0.56, $P<0.001$). MACE incidence was also lower in the antiviral group (2.42 vs. 3.48 per 100,000 person-years; IRR 0.70, 95% CI 0.60–0.80, $P<0.001$). TDF and TAF reduced MACE risk, with TDF showing the strongest effect (HR 0.61, 95% CI 0.50–0.75, $P<0.001$). Subgroup analysis revealed antiviral therapy reduced dyslipidemia in non-diabetics but showed consistent MACE benefits irrespective of diabetes status.

Conclusions: Antiviral therapy reduces risks of dyslipidemia and MACE in CHB patients, with TDF demonstrating the most significant benefits. These findings highlight the extrahepatic advantages of antiviral therapy in CHB management.

Keywords: Health Insurance, Antiviral Agents, Dyslipidemia, Major Adverse Cardiac Events

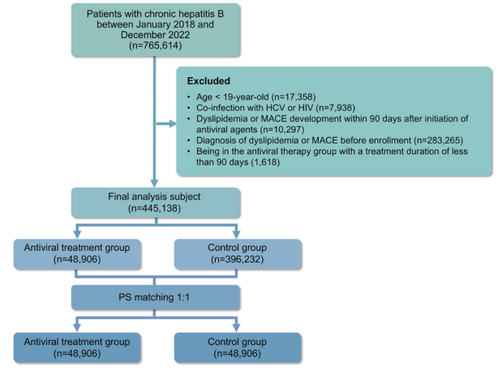

Figure 1.

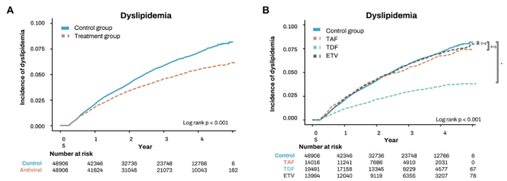

Figure 2.

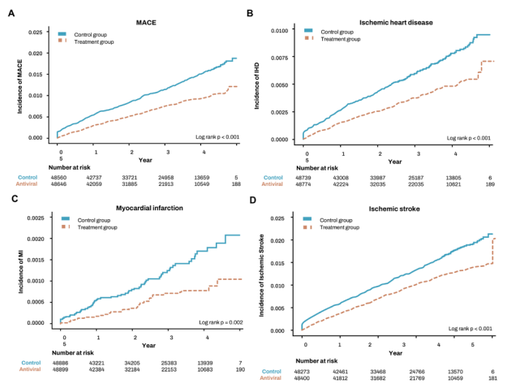

Figure 3.

FP-66

Efficacy and Safety of Switching Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in Chronic Hepatitis B Patients with Multidrug Resistance

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Aims: Tenofovir disoproxil fumarate (TDF) monotherapy effectively suppresses viral replication in patients with multidrug-resistant chronic hepatitis B (CHB). However, TDF users are at risk of kidney dysfunction and osteopenia. We conducted this randomized open-label study to compare the efficacy and safety of switching from TDF to tenofovir alafenamide (TAF) in these patients.

Methods: This prospective, open-label study was conducted at a single tertiary medical center. Current TDF users for CHB who experienced multidrug resistance (e.g., resistance to more than two non-potent nucleos(t)ide analogs or to entecavir) were enrolled between 2021 and 2023. Patients were randomized into two groups: continuing TDF (TDF group) and switching to TAF (TAF group). Virologic response was defined as HBV DNA <20 IU/mL. During the 24-month follow-up, Patients in the TAF group maintained TAF for 24 months, and patients in the TDF group switched to TAF after 12 months of TDF use. One patient who switched to TAF after only 6 months of TDF use due to osteoporosis was classified to the TAF group.

Results: We analyzed 13 patients (10 males) in the TDF group and 30 (24 males) in the TAF group. Baseline characteristics between the TDF and TAF groups were not statistically different: age (median 61.0 vs. 63.0 years, $P=0.916$), body mass index (median 22.5 vs. 23.6 kg/m^2, $P=0.209$), estimated glomerular filtration rate (eGFR) (median 96.9 vs. 86.0 mL/min/1.73^2, $P=0.070$), HBeAg positivity (61.5% vs. 70.0%, $P=0.726$), and bone mineral density of the spine (median -0.8 vs. -0.5, $P=0.615$) and femur (-1.2 vs. -1.0, $P=0.543$), respectively. Virologic responses were maintained in all patients regardless of the group. At 12 months, the TAF group showed significant improvement compared to the TDF group in the median change of eGFR (+2.2 vs. -2.4, $P=0.045$) and spine BMD (+0.3 vs. -0.0, $P=0.001$), respectively. However, compared to the TAF group, the TDF group switching to TAF after 12 months showed significant improvement in the median change of eGFR (+3.0 vs. -1.3, $P=0.022$) and a similar shift in spine BMD (-0.0 vs. -0.1, $P=0.551$) from 12 months to 24 months.

Conclusions: Switching from TDF to TAF is effective in patients with multidrug-resistant CHB and prevents kidney function and bone mineral density declines.

Keywords: Tenofovir Disoproxyl Fumarate, Tenofovir

Alafenamide, Bone Mineral Density, Kidney Function

FP-67

Comparing Liver Disease Severity and Comorbidity in Patients with HBV Mono-Infection and HBV/HDV Co-Infection: A Korean Nationwide Population-Based Study

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Aims: This study aimed to describe and compare liver disease severity, comorbidities, and antiviral treatment history for chronic hepatitis B (CHB) in patients with hepatitis B virus (HBV) mono-infection and those with HBV/hepatitis D virus (HDV) co-infection.

Methods: This nationwide study analyzed claims data from the Korea Health Insurance Review and Assessment Service database between 2013 and 2019. Eligible patients were adults with ≥1 inpatient or outpatient claims related to HBV infection between 2014 and 2018. Patients with HBV/HDV co-infection were identified by ≥1 HDV antibody test claim followed by ≥1 HDV-related claim, while patients with HBV mono-infection were identified as having no HDV-related claims, regardless of HDV antibody test claim. Comorbidities and liver-related diseases were assessed based on claims during the 12 months prior to the index date.

Results: Among 590,102 eligible patients, 589,349 (99.87%) had HBV mono-infection and 753 (0.13%) had HBV/HDV co-infection. The mean (standard deviation) age of patients with HBV mono-infection and HBV/HDV co-infection was 50.0 (13.3) years and 51.2 (11.7) years. Patients were predominantly males (56.1% of HBV mono-infection patients and 66.8% of HBV/HDV co-infection patients). Patients with HBV/HDV co-infection had greater comorbidity burdens than patients with HBV mono-infection: 91.6% vs. 74.0% had any Charlson Comorbidity Index (CCI) comorbidity, 63.2% vs. 27.7% had CCI score ≥3, 34.4% vs. 26.8% had hypertension, and 34.0% vs. 17.7% had diabetes (all P<0.0001). HBV/HDV co-infection patients showed higher rates of liver-related complications than those with HBV mono-infection: compensated cirrhosis (47.0% vs. 11.2%), decompensated cirrhosis (42.0% vs. 3.4%), and hepatocellular carcinoma (36.3% vs. 5.6%) (all P<0.0001). A higher proportion of patients with HBV/HDV co-infection was on antiviral therapy for CHB than patients with HBV mono-infection (63.1% vs. 23.1%, P<0.0001).

Conclusions: Patients with HBV/HDV co-infection had a greater burden of comorbidities and liver-related complications than those with HBV mono-infection.

Keywords: Hepatitis B, Hepatitis D, Epidemiology

FP-68

The Clinical Characteristics among HBV and HDV Co-Infected Mongolian Patients

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The Liver Center, Ulaanbaatar, Mongolia

Aims: The prevalences of Hepatitis B virus (HBV) and Hepatitis D virus (HDV) infection were respectively estimated with 11.1% of the general population, and with more than 60% of HBsAg carriers in Mongolia. Among those co-infected with HBV and HDV, 70-80% of those have a threefold increased risk of developing cirrhosis and liver cancer. In this study, we assessed the rates of chronic infection and liver cirrhosis in individuals co-infected with HBV and HDV, as well as their use of antiviral treatment.

Methods: This study involved 269 participants with HBV and HDV coinfection, who voluntarily at the Liver Center, Mongolia. The information on blood tests, antiviral drug usage, and Fibroscan, CE-MRI, AFP, and PIVKA II tests were collected from study participants. HBV-DNA level was measured using Genexpert (Cepheid, USA), and RT-PCR quantified HDV RNA.

Results: The mean age was 52.82 ± 9.0 years(19-76 age), 56.8% female respectively. Among those, 51.3% (n = 138) had chronic hepatitis (CH) and 48.7%(n=131) had liver cirrhosis (LC). Regarding the NUC status, 30.5% (n = 40) of those with CH had indications for antiviral therapy, and 69.5% (n = 91) were on NUC treatment. In contrast, 47.8% (n = 66) of the LC group had indications for NUC therapy, and 52.2% (n = 72) were receiving NUC treatment. Only 1.8% (n = 5) of the 2 groups were on antiviral treatment for HDV, including Peg-Interferon and Bulevirtide. Liver inflammation was significantly higher in the LC group compared to the CH group.

Conclusions: Our study regarding while only 1.8% of 2 group participants on antiviral treatments including peg-IFN and BLV. The elevated liver function indicators and the higher incidence of cirrhosis in HBV and HDV-infected individuals emphasize the urgent need for treatment against HDV.

Keywords: Liver Cirrhosis, Chronic Hepatitis B and D Virus, Chronic Hepatitis

FP-69

An Artificial Intelligence Model Utilizing Imaging Biomarkers on Computed Tomogram to Predict Hepatocellular Carcinoma in Patients with Chronic Hepatitis B

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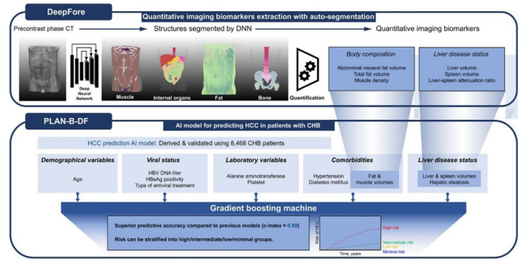
Aims: Various hepatocellular carcinoma (HCC) prediction models have been proposed for patients with chronic hepatitis B (CHB) using clinical variables. We aimed to develop an artificial intelligence (AI)-based HCC prediction model by incorporating imaging biomarkers derived from abdominal computed tomography (CT) images along with clinical variables.

Methods: An AI prediction model employing a gradient-boosting machine algorithm was developed utilizing imaging biomarkers extracted by DeepFore, a deep learning-based CT auto-segmentation software. The derivation cohort (n=5,585) was randomly divided into the training and internal validation sets at a 3:1 ratio. The external validation cohort included 2,883 patients. Six imaging biomarkers (i.e., abdominal visceral fat–total fat volume ratio, total fat–trunk volume ratio, spleen, and liver volume; liver–spleen Hounsfield unit [HU] ratio; and muscle HU) and eight clinical variables were selected as the main variables of our model, PLAN-B-DF.

Results: In the internal validation set (median follow-up duration=7.4 years), PLAN-B-DF demonstrated an excellent predictive performance with a c-index of 0.91 and good calibration function (P=0.78 by the Hosmer-Lemeshow test). In the external validation cohort (median follow-up duration=4.6 years), PLAN-B-DF showed a significantly better discrimination function compared to previous models including PLAN-B, PAGE-B, modified PAGE-B, and CU-HCC (c-index, 0.89 vs. 0.65—0.78; all P<0.001) and maintained a good calibration function (P=0.42 by the Hosmer-Lemeshow test). When patients were classified into four groups according to the risk probability calculated by PLAN-B-DF, the 10-year cumulative HCC incidence was 0.0%, 0.4%, 16.0%, and 46.2% in the minimal-, low-, intermediate-, and high-risk groups, respectively.

Conclusions: This AI prediction model, integrating deep learning-based auto-segmentation of CT images, offers improved performance in predicting HCC risk among patients with CHB compared to previous models.

Keywords: Radiologic Biomarker, Deep Learning, Visceral Fat, Myosteatosis, Segmentation



FP-70

Seroprevalence and Clinical Characteristics of Hepatitis D Virus Infection in Korean Patients with Chronic Hepatitis B, Liver Cirrhosis, and Hepatocellular Carcinoma

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Aims: Hepatitis D virus (HDV) infection worsens clinical outcomes in patients co-infected with hepatitis B virus (HBV). With the emergence of HDV-targeted therapeutics, this study aimed to assess the seroprevalence and clinical significance of anti-HDV positivity in Korean patients with chronic hepatitis B (CHB), liver cirrhosis (LC), and hepatocellular carcinoma (HCC).

Methods: Serum samples from CHB (n=100), LC (n=100), and HCC (n=337) patients were collected from Seoul National University Hospital and Seoul National University Bundang

Hospital (May 2012–Jan 2024). Anti-HDV and HDV RNA were detected using commercial kits by the central laboratory.

Results: The mean age of patients was 57.5 ± 10.8 years, with 71.1% male. Anti-HDV seroprevalence was 2.6% (14/537), while HDV RNA was detected in 0.2% (1/537). Anti-HDV positivity was 2% (2/100) in CHB, 4% (4/100) in LC, and 2.4% (8/337) in HCC (*P*=0.612). When classified by LC status, anti-HDV positivity was 1.8% (3/169) in non-LC and 3.2% (11/340) in LC patients (*P*=0.343). In HCC, seroprevalence increased with BCLC stage: 0% (0/37) in stage 0, 1.1% (1/91) in A, 1.2% (1/86) in B, 6.1% (5/82) in C, and 3.7% (1/27) in D. Anti-HDV seroprevalence was significantly higher in patients with BCLC stage C or above (*P*=0.012). Anti-HDV-positive HCC patients had a trend toward lower survival than anti-HDV-negative patients (*P*=0.08), but the difference was not statistically significant even after adjusting for age, LC, and BCLC stage (*P*=0.376). The single HDV RNA-positive patient was a 50-year-old female with LC (Child-Pugh A) and undetectable HBV DNA, not receiving antiviral therapy.

Conclusions: Anti-HDV seroprevalence in Korean HBV patients is ~2%, with HDV RNA positivity at 0.2%. The higher prevalence of advanced liver disease highlights the need for early detection efforts.

Keywords: Hepatitis D Virus, Prevalence, Anti-HDV, Hepatitis B Virus

Saturday, May 31, 2025, 13:10-14:30

10. HCV

FP-71

Changes in Healthcare Costs of Hepatitis C Patients after Introduction of Direct-Acting Antivirals (DAAs) in Korea

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Aims: Direct-Acting Antivirals (DAAs) have revolutionized hepatitis C virus (HCV) treatment. This study evaluates the economic impact of this treatment paradigm shift by analyzing changes in patient population and healthcare costs following DAA introduction in Korea.

Methods: Healthcare costs for acute and chronic HCV patients were analyzed using National Health Insurance Service data from 2016 to 2024. Costs were stratified by year, gender, age, type of medical institution, and antiviral medication. The prevalence method was employed for cost calculation. All costs were converted to US dollars (USD, $1=1,460.5 KRW, as of February 28, 2025).

Results: Over the 9-year period, 221,122 HCV patients were identified, showing a 47.0% decrease from 79,770 (2016) to 42,253 (2024). Total healthcare costs were 897 million USD, including copayments of 492 million USD (54.8%). Annual costs decreased 73.3% from 166.0 million USD to 44.4 million USD, while per-patient costs fell 49.5% from 2,081 USD to 1,051 USD. The average treatment duration was 2.5 years, with mean annual costs of 1,599 USD per patient. Costs were highest among males (4,185 USD) and patients in their 70s (3,855 USD). Tertiary and general hospitals accounted for 84.4% of total costs (757.1 million USD). Antiviral treatment patients decreased from 16,034 to 3,338, with total costs declining from 118.0 to 20.1 million USD and per-patient costs from 7,357 to 6,024 USD. The most frequently prescribed antivirals were glecaprevir/pibrentasvir (35.4%), sofosbuvir (20.1%), and daclatasvir+asunaprevir (16.9%). Cost per patient was highest for sofosbuvir+daclatasvir (14,603 USD), sofosbuvir (13,127 USD), and ledipasvir/sofosbuvir (8,517 USD). Laboratory tests constituted the largest hospital cost component (104.6 million USD, 34.6%).

Conclusions: In the 9 years post-DAA introduction, Korea saw continuous declines in HCV patient numbers and healthcare costs. This likely stems from cheaper pan-genotypic treatments and improved treatment efficiency. These findings suggest innovative treatments can reduce long-term disease burden, providing evidence for future infectious disease policy development.

Keywords: Hepatitis C Virus, Healthcare Costs, Big Data

FP-72

Cost-Effectiveness of Direct Acting-Antivirals for Chronic Hepatitis C in South Korea

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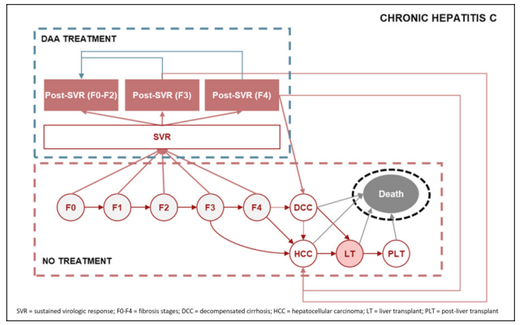
Aims: The advent of direct-acting antivirals (DAA) for treating chronic hepatitis C (CHC) has led to high sustained virologic rates (SVR) and improved outcomes for CHC patients. This study evaluated the cost-effectiveness of DAAs for treating CHC in South Korea; in particular, it investigated the cost-effectiveness of DAAs when taking into account the progression and regression of liver fibrosis.

Methods: A previously developed Markov state transition model was adapted to assess cost-effectiveness of DAA treatment, compared to no treatment, in South Korean CHC patients. Inputs consisted of direct costs, SVR after DAA treatment, state transition probabilities (progression and regression of fibrosis stages, hepatocellular carcinoma [HCC], decompensated cirrhosis, and liver transplantation) and health state utilities. Input data were sourced from the literature and publicly available databases. Fibrosis stage progression and regression were informed by the FIB-4 index. The analysis adopted a payer perspective. The incremental cost-effectiveness ratio (ICER) was calculated in terms of incremental cost (2024 US$) per quality-adjusted life year (QALY), over patients' lifetime horizon. Patients were modeled from a starting age of 59.8 years, for up to a lifetime horizon; costs and effects were discounted at 4.5%.

Results: Results showed DAA treatment to be cost saving, compared to no treatment, resulting in higher QALYs (10.5 vs. 9.3) and LYs (13.5 vs. 12.0), and lower costs ($ 9,105 vs. $ 17,051) over a lifetime horizon. Key drivers of cost-effectiveness included the starting distribution of patients between fibrosis stages, and costs and utilities associated with the non-cirrhotic and cirrhotic health states.



Conclusions: Our findings suggest that DAA treatment for CHC is cost-effective when compared to no treatment, regardless of liver fibrosis severity in South Korea. Results are in line with other comparable analyses published recently, contributing to the growing evidence base on the long-term cost-effectiveness of DAAs.

Keywords: Direct-Acting Antivirals, Cost-Effectiveness

FP-73

Advanced Fibrosis and Cardiometabolic Risk Burden Increase Atherosclerotic Cardiovascular Events in Chronic Hepatitis C Patients with Steatotic Liver Disease after Viral Eradication

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Aims: Steatotic liver disease (SLD) and cardiometabolic risk factors (CMRFs) are common in chronic hepatitis C (CHC) patients. The risk of atherosclerotic cardiovascular disease (ASCVD) in CHC patients achieving sustained virological response (SVR) remains unclear. This study aimed to assess the impact of hepatic fibrosis and CMRFs on ASCVD risk in CHC patients with SLD after achieving SVR.

Methods: A nationwide multi-center registry cohort was established in Taiwan, identifying SLD using ultrasonography and hepatic steatosis index. Metabolic dysfunction-associated SLD (MASLD) was defined as SLD with at least one CMRF. The competing risks of death and liver transplant were adjusted using Gray's cumulative incidence method and Cox sub-distribution hazards.

Results: Among 8,755 CHC patients with SLD, 624 (7.1%) developed ASCVD after SVR (181.7 per 10,000 person-years; median follow-up, 3.9 years). Patients with MASLD had a significantly higher ASCVD incidence than those with simple SLD (190.2 vs. 84.0 per 10,000 person-years, *P*<0.001). Age, chronic kidney disease (CKD, eGFR<60 ml/min/1.73m^2), advanced fibrosis (FIB-4>3.25) and MASLD were significantly associated with ASCVD. ASCVD risk increased with increased CMRF burden (adjusted hazard ratios from 1.72 for one CMRF to 2.33 for ≥ four CMRFs). The impact of CMRF on increased ASCVD risk was mainly observed in patients without advanced fibrosis and those without CKD.

Conclusions: MASLD burden, advanced liver fibrosis, and CKD increased ASCVD risk among CHC patients after SVR, with hypertension being the most contributing factor. Regular cardiovascular risk assessments and preventive measures should be prioritized for these high-risk CHC/SLD patients.

Keywords: Steatotic Liver Disease, Cardiometabolic Risk Factors, Chronic Hepatitis C, Atherosclerotic Cardiovascular Disease, Advanced Fibrosis

FP-74

Association between Hepatitis C Virus Infection and Cardiovascular Disease: A Nationwide, Population-Based Cohort Study in South Korea

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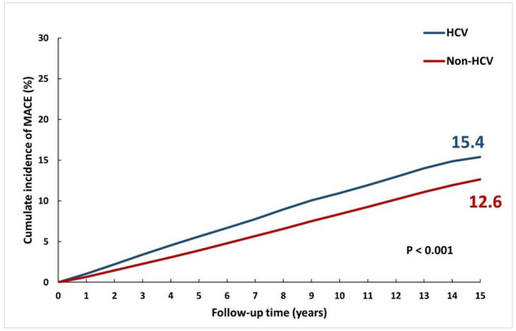
Aims: Chronic hepatitis C virus (HCV) infection has been increasingly associated with cardiovascular disease, but population-based evidence remains limited. This study aimed to evaluate the independent association between HCV infection and cardiovascular outcomes using a nationwide, population-based cohort in South Korea, with general population-matched controls.

Methods: Using the National Health Insurance Service (NHIS) database of South Korea, we identified patients newly diagnosed with HCV between 2009 and 2022 who were ≥20 years old. For each HCV patient, 10 age- and sex-matched non-HCV controls were selected from the general population. The primary outcome was the incidence of major adverse cardiovascular events (MACE), including ischemic heart disease, stroke, peripheral arterial disease, and cardiovascular-related mortality. Cox proportional hazards models and competing risk regression were used to estimate hazard ratios, adjusting for age, sex, medication use, and comorbidities, with death, liver transplantation, and decompensated cirrhosis considered as competing risks.

Results: A total of 324,850 patients were included: 41,455 HCV patients and 283,395 matched controls. The mean age was 48.8 years (± 13.4 standard deviation [SD]) in the HCV group and 45.4 years (± 12.2 SD) in the matched control group (P<0.001). The proportion of males was 51.1% in the HCV group and 52.7% in the matched control group (P<0.001). During the follow-up period, 31,679 patients developed MACE (incidence density of MACE: 11.0 per 1,000 person-years). Before adjustment for covariates, HCV infection was associated with a 37% increased risk of MACE compared to the matched control group (hazard ratio [HR] 1.37, 95% confidence interval [CI]: 1.33–1.41, P<0.001). After adjusting for age and sex differences, as well as cardiovascular risk factors including medication use and comorbidities, HCV infection remained independently associated with an increased risk of MACE (adjusted HR 1.22, 95% CI: 1.18–1.25, P<0.001, Figure 1).



Conclusions: This nationwide, general population-matched cohort study provides strong evidence that HCV infection is an independent risk factor for cardiovascular disease. These findings highlight the need for cardiovascular risk monitoring in HCV patients and further research on potential prevention strategies.

Keywords: Hepatitis C, Cardiovascular Disease, South Korea, Incidence

FP-75

Long-Term Hepatocellular Carcinoma Development Following Sustained Virologic Response in Korean Chronic Hepatitis C Patients Treated with Direct Acting Antivirals

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Aims: Direct-acting antiviral (DAA) therapy can cure chronic hepatitis C (CHC), and has been covered by insurance in Korea since August 2015. Patients who achieve sustained virologic response (SVR) after DAA treatment are expected to have good prognoses, but there was reported few long-term clinical results for Korean CHC patients who achieved SVR. Therefore, in this study, we aimed to investigate the prognosis of these patients.

Methods: Through a prospective, multicenter observational study, patients with CHC, who achieved SVR after DAA treatment, were enrolled. The primary endpoint was hepatocellular carcinoma (HCC) development, which was reviewed annually. Kaplan-Meier plots and Cox proportional hazards model were performed.

Results: A total of 1,266 patients with a median age of 60 years and 45.8% of male were enrolled. Genotype 2 and cirrhosis was presented in a half and 30% of them. Median Child-Pugh and MELD scores were 5 and 7. During a median follow-up of 36 months, HCC occurred in 51 patients. Of these, 14 patients experienced HCC beyond 5years after SVR. Cumulative probabilities of HCC development at 1 year and 8 year were 0.7% and 20.8%, respectively. There was no significant difference between Sofosbuvir-based treatment and other treatments. However, patients with cirrhosis (hazard ratio [HR] 6.7), older age (HR 1.1), male (HR 2.3), higher WBC (HR 1.1) and INR (7.3) levels, and low platelet and albumin levels were more susceptible to HCC development. Multivariable analysis revealed that age of 65 and more, male, cirrhosis, high WBC counts, low platelet counts, and low albumin levels were independent risk factors for HCC development.

Conclusions: Patients who achieved SVR had a relatively favorable prognosis. However, there is a constant risk of HCC development even five years after SVR, especially in old and cirrhotic patients. Hence, early treatment and sustained post SVR surveillance examination are essential.

Keywords: Hepatitis C, Direct-Acting Antiviral, Sustained Virologic Response, Hepatocellular Carcinoma

FP-76

Real-World Outcomes of Sofosbuvir/Velpatasvir in a Variety of Hepatitis C Patient Populations: A Retrospective Cohort Study

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Aims: Sofosbuvir/velpatasvir (SOF/VEL) has revolutionized the treatment of hepatitis C virus (HCV) by providing a promising option for virus elimination across various patient groups. However, there is a need for more comprehensive real-world studies to assess its efficacy and safety specifically in the Korean population with chronic hepatitis C (CHC), where diverse clinical scenarios and patient characteristics may influence treatment outcomes. The aim of our study was to assess the effectiveness and safety of SOF/VEL-based treatment for CHC patients in Korea.

Methods: In this real-world observational study, we recruited patients at tertiary hospital in South Korea. Patients were administered SOF/VEL (400/100mg) ± ribavirin (RBV) once daily for 12 weeks or 24 weeks. SOF/VEL with RBV for 24 weeks in HCV patients previously treated with a direct-acting antiviral (DAA) regimen. The primary efficacy endpoint was sustained virological response at post-treatment week 12 (SVR12). Adverse events (AEs) were evaluated during treatment.

Results: This study included 70 patients with HCV genotypes 1b, 2, 2b, 2a/2c, and 1b&2b, as well as seven cases of HBV coinfection and one case of HIV coinfection. 44.3% of the patients included in this study had cirrhosis, 8.6% had a Child-Pugh score of B, and 22.9% were diagnosed with hepatocellular carcinoma (HCC). Twenty-eight patients had prior treatment experience, including two with interferon based treatment, 18 with DAA treatment, and eight with DAA treatment after failing IFN therapy. Among them, 98.6% [69/70, intention to treat (ITT)] and 100% [69/69, modified ITT (mITT)] received SOF/VEL. At the end of treatment, 95.7% (ITT, 67/70) and 100% (mITT, 67/67) of patients had undetectable HCV RNA. SVR12 rates were 91.4% (ITT, 64/70) and 100% (mITT, 64/64). In the mITT analysis, SVR12 for patients with cirrhosis and HCC was 100% and 100%. Among four patients with a Child-Pugh score of B before SOF/VEL treatment, two patients improved to grade A after treatment. AEs occurred in six patients but improved with symptomatic treatment. Twenty-eight patients received SOF/VEL + RBV, and among them, eight had their RBV dose reduced; however, all achieved a 100% SVR12.

Conclusions: This study demonstrated that the SOF/VEL ± RBV achieved excellent treatment outcomes and was well tolerated in Korean patients with CHC, despite a significant proportion of patients having cirrhosis or HCC.

Keywords: Hepatitis C, Sofosbuvir-Velpatasvir (SOF/VEL), Cirrhosis, Hepatocellular Carcinoma

FP-77

Chrono-Optimal Treatments for HIV/HCV Co-Infection Yield Comparable Survival Outcomes with HCV Mono-Infection

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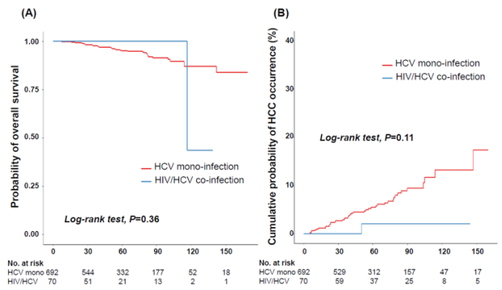
Aims: Over the past decades, treatment for human immunodeficiency virus (HIV)/hepatitis C virus (HCV) co-infection has significantly advanced. Previous studies have shown that HIV accelerates the progression of liver disease to cirrhosis, increasing liver-related complications and mortality in patients with HCV infection. With these advances, our study reassessed the effectiveness of various HCV treatments by comparing outcomes in HIV/HCV co-infection and those with HCV mono-infection patients.

Methods: We retrospectively included consecutive patients diagnosed with HCV mono-infection or HIV/HCV co-infection at 12 tertiary referral centers from January 2009 to December 2020. The primary endpoint was overall survival (OS). Secondary endpoints included achievement of a sustained virologic response (SVR), time-to-occurrence of hepatocellular carcinoma (HCC), and the changes in fibrosis-4 index (FIB-4).

Results: A total of 904 patients were included, with 792 in the HCV mono-infected group and 112 in the HIV/HCV co-infected group, of whom 97 (86.6%) had received HIV treatment before study inclusion. Among them, 741 (93.6%) of the HCV mono-infected patients and 86 (76.8%) of the HIV/HCV co-infected patients received HCV treatment. In patients treated for HCV, SVR was achieved in 93.4% of the HCV mono-infected group and 81.4% of the HIV/HCV co-infected group (P=0.11 after inverse probability of treatment weighting [IPTW] adjustment). OS and HCC occurrence showed no significant differences between the two groups, regardless of the HCV treatment method, after IPTW adjustment (hazard ratio [HR]: 0.37; 95% confidence interval [CI]: 0.05–3.07; P=0.36 for OS; Figure A, and HR: 0.19; 95% CI: 0.02–1.48; P=0.11 for HCC occurrence; Figure B). The FIB-4 index significantly improved 1 year after achieving SVR with direct-acting antiviral treatment.

Figure



Conclusions: With optimal HIV/HCV treatment regimens, HCC occurrence and mortality risks in co-infected patients have become comparable to those in patients with HCV mono-infection.

Keywords: Peginterferon, Direct-Acting Antivirals, Overall Survival, Hepatocellular Carcinoma

FP-78

Study of Safety and Efficacy of Ledipasvir + Sofosbuvir in HCV Infection in Pregnancy: A Real-Life Experience

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Aims: In India, the prevalence of prenatal HCV infection ranges from 0.3% to 2.8%, while the rate of mother-to-child transmission during pregnancy has been estimated to be between 5% and 15%. Pregnancy-related HCV treatment lowers maternal problems from HCV infection, stops transmission to the fetus, and lowers overall HCV infection in women of reproductive age. Also, an United States based study showed direct-acting antiviral medication was safe and effective when initiated in the second or third trimester.

Methods: In this prospective, single-center trial, pregnant women with chronic hepatitis C were recruited and treated with sofosbuvir and ledipasvir beyond the first trimester of pregnancy. Primary end points were sustained virologic response at 12 weeks, adverse drug reactions, and congenital malformation of the infant. The secondary end point was the transmission of HCV infection to the infant.

Results: Total 26 patients with mean age of 28±3.5 years (21–36 yrs) were enrolled in this study. All patients were non-cirrhotic and treatment-naive. The mean HCV RNA before treatment was $9.2 \times 10^5 \pm 3.6 \times 10^5$ IU/ml. Among the enrolled patients, 19 (73%) were genotype 3, 5 (19%) were genotype 1, and 2 (8%) were genotype 4. All patients achieved sustained virologic response at 12 weeks. Simple adverse reactions reported like nausea (27%), headache (27%), and fatigue (16%). All patients had institutional delivery, and no infant was found to have congenital malformations. No child had detectable HCV RNA at 6 months of age.

Conclusions: Ledipasvir and sofosbuvir were well tolerated and highly effective for both HCV treatment in the mother and elimination of mother-to-child transmission. No congenital abnormalities were detected in present study.

Keywords: Ledipasvir + Sofosbuvir, HCV Infection, Pregnancy

Baseline characteristic	Mean ± SD
Age	28±3.5 y
Bilirubin	0.9±0.3 mg/dl
Alanine transaminase	69±37 IU/L
Albumin	3.6±0.4 gm/dl
Creatinine	0.6±0.25 mg/dl
International Normalized Ratio (INR)	1.07±0.09
HCV RNA	9.2×10^5 copies/L
Baseline fibrosis by kPa (Fibroscan)	5.2±1.6 kPa
Platelets	$187 \pm 68 \times 10^3$/μL
Trimester of treatment, n (%)	
Second	15 (58)
Third	11 (42)
Genotype, n (%)	
1	5 (19)
3	19 (73)
4	2 (8)

Figure 1. Baseline charecteristics

End point	N (%)
4 wks of treatment, n/total n (%) Rapid virologic response (RVR)	26/26 (100)
12 wks of treatment, n/total n (%) End of treatment response (ETR)	26/26 (100)
12 wks Posttreatment, n/total n (%) Sustained virologic response (SVR12)	26/26 (100)

Figure 2. Virological response

End point	n (%)
Positive HCV RNA Status (Infants) 4 wks, n/total n (%)	4/26 (15)
Positive HCV RNA Status (Infants) 12 wks, n/total n (%)	0/4 (0)

Figure 3. HCV RNA status in infants

Saturday, May 31, 2025, 13:10-14:30

11. MASLD, LC and Others, Basic

FP-79

Identification of Prognostic Factors and Regulatory Pathways in Porto-Sinusoidal Vascular Disorder

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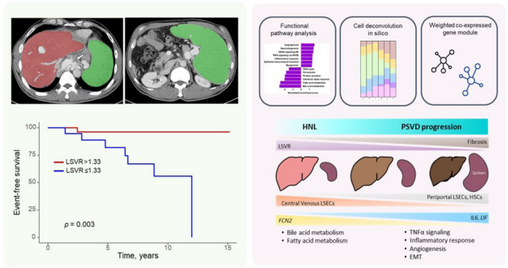
Aims: Porto-sinusoidal vascular disorder (PSVD) is a rare liver disease marked by portal hypertension in the absence of cirrhosis. This study aimed to identify prognostic factors and key regulatory pathways involved in PSVD progression by integrating clinical data with transcriptomic analysis.

Methods: The study included 114 PSVD patients, with 74 monitored longitudinally for liver-related events. RNA sequencing was performed on 21 liver samples and compared to six histologically normal controls. Clinical parameters, including the liver-to-spleen volume ratio (LSVR) and fibrosis stage, were analyzed for their association with liver outcomes. Transcriptomic profiling, encompassing co-expression networks and cell deconvolution, was conducted based on these factors.

Results: Among the 114 patients, 32 (28.1%) underwent liver transplantation at diagnosis. Fibrosis severity was a strong predictor of liver transplantation risk (adjusted odds ratio per 1-stage increase: 14.88; 95% confidence interval, 3.72–59.58) and was closely linked to LSVR. Over a median follow-up of 4.9 years, 8 (10.8%) patients in the longitudinal cohort experienced liver-related events. LSVR was identified as a reliable prognostic marker, with a threshold of 1.33 predicting these events. Transcriptomic analysis based on LSVR and fibrosis stage revealed distinct gene expression profiles and cellular alterations in PSVD, including changes in liver sinusoidal endothelial cell (LSEC) distribution, an expansion of hepatic stellate cells, and upregulation of IL-6 signaling, while immune cell composition remained unchanged throughout disease progression.

Conclusions: This study highlights LSVR as a novel prognostic marker in PSVD and suggests that IL-6 trans-signaling-induced endotheliopathy in LSECs may drive pro-inflammatory and fibrotic processes during disease progression.

Keywords: Idiopathic Non-Cirrhotic Portal Hypertension, Liver-To-Spleen Volume Ratio, Fibrosis, Il-6



FP-80

A Novel 11β-HSD1 Inhibitor Ameliorates Liver Fibrosis by Inhibiting the Notch Signaling Pathway and Increasing

NK Cell Population

Ji Eun Kim[1], Gye Ryeol Park[1], Soo Hyeon Lee[1], Jae Eun Ryu[1], In Young Kang[1], Jin Kim[1], Hye Young Kim[1], Seung Min Lee[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) regulates hepatic glucose output and is implicated in liver fibrosis. We aimed to investigate the anti-fibrotic effect of a novel 11β-HSD1 inhibitor in a thioacetamide (TAA)-induced liver fibrosis mouse model.

Methods: Mice were administered TAA for 19 weeks and treated with 11β-HSD1 inhibitor for the last 9 weeks. RNA sequencing was performed by Macrogen, Inc. (Seoul, Republic of Korea) on liver tissue from the following groups of mice per group. The analysis groups for mass cytometry included: normal control, TAA-treated, and TAA+11β-HSD1 inhibitor-treated groups. Detailed procedures are described in previous research

Results: Treatment with 11β-HSD1 inhibitor significantly reduced fibrosis area, alanine aminotransferase, and aspartate aminotransferase levels compared to the TAA-only group. Inhibition of 11β-HSD1 led to a decrease in intracellular cortisol levels, which suppressed the activation of hepatic stellate cells. RNA sequencing revealed significant downregulation of the Notch signaling pathway, including reduced expression of Notch ligands and receptors, as well as downstream genes. Furthermore, 11β-HSD1 inhibition enhanced NK cell-mediated immune responses, as indicated by the upregulation of NK cell-related genes and increased NK cell populations confirmed by mass cytometry. This increase in NK cell activity contributed to the clearance of activated HSCs and the attenuation of fibrosis.

Conclusions: These findings suggest that 11β-HSD1 inhibition alleviates liver fibrosis through Notch pathway suppression and enhancement of NK cell-mediated immune responses. Our results support the therapeutic potential of a novel 11β-HSD1 inhibitor for treating liver fibrosis.

Keywords: LIVER FIBROSIS, NOTCH SIGNALING, NK CELL, THIOACETAMIDE

FP-81

FiNi-Seq: A Quasi-Spatial Single-Cell Transcriptome Based on Physical Properties Defines Early Damage Niche of the Liver

Kwon Yong Tak[1,9], Juyeon Kim[2,3,9], Myungsun Park[1,9], Wooseok Kim[1], Seoyeong Lee[1], Narae Park[4,5], Min Jeong Kim[1], Ju-Bin Kang[2], Yongjun Koh[1], Hae Young Yang[1], Min Kyu Yum[1], Injune Kim[1,6], Yong Ryoul Yang[2,7], Won-Il Jeong[1], Jinsung Yang[8], Cheolju Lee[4], Chuna Kim[2,3], Jong-Eun Park[1,6]

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Aims: Aging is associated with the accumulation of senescent cells, which are triggered by tissue injury response and often escape clearance by the immune system. The specific traits and diversity of these cells in aged tissues, along with their effects on the tissue microenvironment, remain largely unexplored. We aim to navigate the early damaged niche of the liver to uncover age-related fibrotic microenvironment of the liver.

Methods: We utilized the physical properties of tissue to enrich the age-associated fibrotic niche and subjected them to multi-omics analysis and named this novel method Fibrotic Niche enrichment sequencing (FiNi-seq). Through this method, we were able to enrich early damage niche of the liver in both aging and damage model. Further in vitro culture and scRNA-seq unveiled the driver populations that modulate the age-related fibrotic niche.

Results: We profiled young and old livers of male mice using FiNi-seq, discovered novel Wif1 and Smoc1- producing mesenchymal cell populations showing senescent phenotypes, and investigated the early immune responses within this fibrotic niche. Spatial mapping techniques revealed that FiNi-seq-enriched cells are found around the portal vein and form interspersed patches, which expand upon chronic liver injury. Finally, FiNi-ATAC-seq revealed age-associated epigenetic changes enriched in fibrotic niche cells.

Conclusions: Our quasi-spatial, single-cell profiling method allows the detailed analysis of initial aging microenvironments, providing potential therapeutic targets for aging prevention.

Keywords: Liver Damage, Fibrosis, Aging, Single-Cell Rna-SEQ

Figure 1

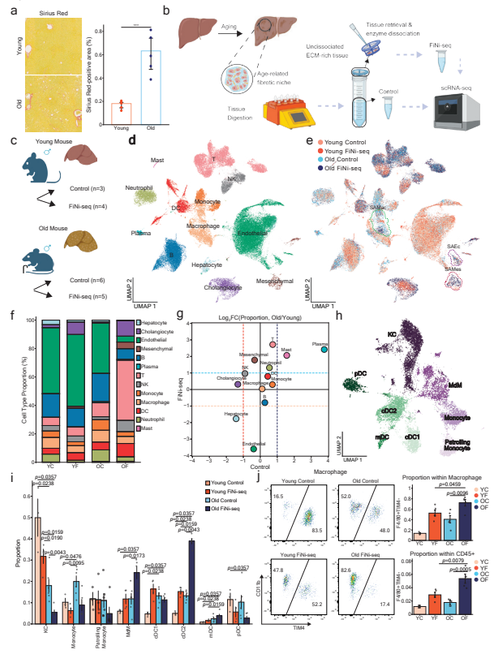
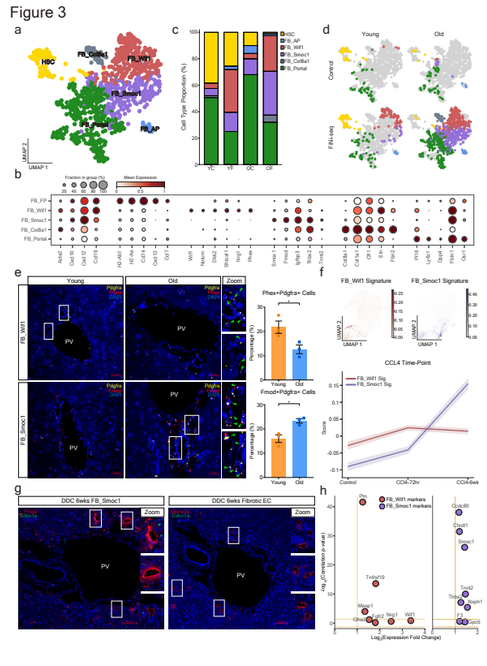
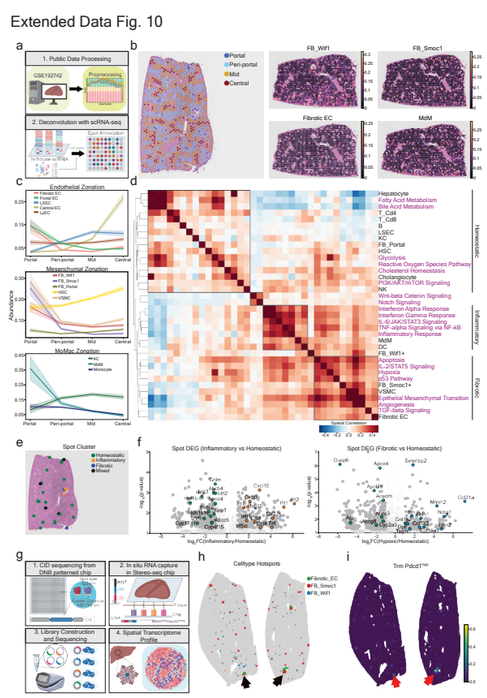


Figure 3



Extended Data Fig. 10



FP-82

Spatial Transcriptomics Reveals TAZ Signalling-Mediated Regulation of Liver Fibrosis in MASH

Young-Sun Lee, Youngwoo Lee, Eunho Choi, Ha Seok Lee, Yang Jae Yoo, Yoonseok Lee, Seong Hee Kang, Young Kul Jung, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yeon

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Aims: Although most patients with metabolic dysfunction-associated steatotic liver disease (MASLD) follow a benign clinical course, those with metabolic dysfunction-associated steatohepatitis (MASH) have worse prognoses than those with simple steatosis. This study investigates the role of TAZ signaling in the development of fibrosis associated with MASH using spatial transcriptomics.

Methods: Liver tissue and serum samples were collected from MASLD patients who underwent liver biopsies at Korea University Guro Hospital. Spatial transcriptomics analysis was performed using Xenium with preserved FFPE samples from control and MASLD patients.

Results: Spatial transcriptomics analysis was performed using FFPE samples from 3 healthy individuals, 6 patients with simple steatosis, and 6 patients with MASH. A total of 16 cell types were identified, with hepatocytes being the most abundant. The proportion of immune cells was relatively higher in the MASH group. Compared to the simple steatosis group, the MASH group exhibited activation of pathways related to endocytosis, inhibition of cell proliferation, and ECM remodeling. The expression of merlin, a known inhibitor of TAZ, was highest in the control group and lowest in the steatohepatitis group, suggesting a regulatory mechanism for TAZ activity. TAZ signaling was found to be significantly higher in hepatocytes of the MASH group compared to those in the simple steatosis group. The intensity of TAZ signaling correlated with the intensity of the Indian Hedgehog ligand, which, in turn, was associated with fibrosis signaling.

Conclusions: Spatial transcriptomics analysis revealed that TAZ signaling was significantly upregulated in hepatocytes of MASH patients, correlating with Indian Hedgehog ligand expression and fibrosis-related pathways. These findings suggest that TAZ signaling plays a crucial role in the progression of fibrosis in MASH and may serve as a potential therapeutic target.

Keywords: MASH, Fibrosis, Spatial Transcriptomics, TAZ

FP-83

Nintedanib Alleviates Metabolic Dysfuction-Associated Steatohepatitis by Suppressing THBS1 Expression in Activated Fibroblasts

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a significant global health concern, with activated fibroblasts playing a pivotal role in its progression. Targeting and eliminating these fibroblasts may represent an effective strategy for MASLD management. Nintedanib, a tyrosine kinase inhibitor approved for the treatment of idiopathic pulmonary fibrosis (IPF), has demonstrated antifibrotic properties in various models. This study aimed to investigate the therapeutic potential of nintedanib in MASLD by evaluating its effects on activated hepatic fibroblasts.

Methods: Fibroblasts were isolated from liver tissues of MASLD patients. In vitro experiments were conducted using patient-derived fibroblasts, which were treated with nintedanib, and its efficacy was compared with that of sorafenib. For in vivo analysis, a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) was used to establish a rapidly progressing fibrosis model in mice. Differences in protein expression between normal and MASLD liver tissues were analyzed via Western blotting.

Results: Western blot analysis comparing normal and MASLD patient liver tissues demonstrated increased THBS1 expression in MASLD. In vitro, nintedanib treatment significantly reduced the viability of activated fibroblasts compared to sorafenib. Western blot analysis demonstrated a decrease in phosphorylated AKT and ERK levels in nintedanib-treated fibroblasts, suggesting attenuation of inflammation and fibrosis. In the hepatic stellate cell line LX2, activation with TGF-β1 followed by nintedanib treatment resulted in downregulation of TGFBI, FN1, Col1a1, AKT, mTOR, and THBS1, as determined by bulk RNA sequencing. In the CDAHFD mouse model, nintedanib treatment eliminated FAP$^+$PD-L1$^+$ activated fibroblasts at low concentrations, indicating its potential as a therapeutic agent for MASLD. Single-cell sequencing of liver tissues from CDAHFD-fed mice revealed an upregulation of THBS1 in the CDAHFD group, which was suppressed in the nintedanib-treated group, consistent with bulk RNA sequencing findings. In LX2 cells, THBS1 knockdown via siRNA followed by TGF-β1 treatment led to a reduction in fibrosis markers, including FAP, α-SMA, and FN1, compared to TGF-β1 treatment alone. Furthermore, while the levels of the mature forms of fibrosis-associated signaling molecules (AKT, ERK, and SMAD) were elevated in the siTHBS1 + TGF-β1 co-treatment group compared to the TGF-β1 alone group, phosphorylated forms exhibited no significant differences, indicating a reduction in phosphorylation.

Conclusions: This study demonstrates the potential of nintedanib as a therapeutic agent for MASLD by targeting activated fibroblasts. Nintedanib reduced fibroblast viability, suppressed fibrosis- and inflammation-related signaling pathways, and eliminated FAP$^+$PD-L1$^+$ activated fibroblasts in vivo. Consistent findings from bulk RNA sequencing, single-cell sequencing, and Western blot analysis highlight its role in suppressing THBS1 expression in hepatic fibroblasts. These results suggest that nintedanib may be a promising strategy for attenuating fibrosis and inflammation in MASLD.

Keywords: Nintedanib, THBS1, Activated Fibroblasts, MASLD

FP-84

Targeting CD47 by Engineered Stem Cell-Derived SIRPα-Extracellular Vesicles Ameliorates Liver Fibrosis via Macrophage Reprogramming

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Aims: CD47 overexpression in hepatic inflammatory microenvironments impairs macrophage-mediated efferocytosis and tissue homeostasis. We previously demonstrated that engineered mesenchymal stem cell-derived extracellular vesicles expressing SIRPα (SIRP-EV-MSCs) efficiently ameliorate acute liver failure through dual therapeutic mechanisms (Nature Communications, 2025). Herein, we sought to elucidate their therapeutic potential in chronic liver fibrosis and metabolic dysfunction-associated steatohepatitis (MASH) models while validating scalable manufacturing parameters.

Methods: Human liver specimens from patients with fibrotic MASH underwent comprehensive profiling, revealing significant CD47 upregulation correlating with fibrosis severity. The pharmacokinetics, biodistribution, and therapeutic efficacy of intravenously administered SIRP-EV-MSCs were systematically evaluated in fibrotic liver and STAM™ MASH murine models. Fibrotic markers and inflammatory mediators were assessed through multi-modal analyses.

Results: Through patient liver tissue analysis, we confirmed significant CD47 upregulation in fibrotic MASH compared to simple steatosis, with CD47 expression strongly correlating with inflammation and fibrosis severity. Intravenously administered SIRP-EV-MSCs exhibited preferential accumulation in these pathological CD47-overexpressing hepatic regions. Mechanistically, SIRP-EV-MSCs function through dual therapeutic actions: blocking CD47 to enhance macrophage-mediated clearance of pathological cells while simultaneously delivering regenerative cargo derived from mesenchymal stem cells. This unique mechanism effectively reprogrammed hepatic macrophages from pro-inflammatory toward pro-resolving phenotypes, culminating in pronounced fibrosis regression and hepatic function restoration. In both TAA and APAP-induced liver fibrosis models, SIRP-EV-MSCs significantly attenuated hepatic fibrosis. Furthermore, in MASH models, SIRP-EV-MSCs not only reduced steatosis scores but also effectively diminished fibrotic areas.

Conclusions: This study provides compelling preclinical evidence establishing SIRP-EV-MSCs as a potent immunomodulatory therapeutic for liver fibrosis and fibrotic MASH through targeted macrophage reprogramming. These findings strongly support the clinical translation of these engineered extracellular vesicles for treating fibrotic liver diseases with limited therapeutic options.

Keywords: Macrophage Reprogramming, CD47, Mesenchymal Stem Cell Derived Extracellular Vesicle, Liver Fibrosis

FP-85

PNPLA3 I148M GG Variant Driven Immune Cell Infiltration Associates with Metabolic Dysfunction–Associated Steatotic Liver Disease Progression

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Aims: Recent evidence suggests that immune cells play a pivotal role in the progression of metabolic dysfunction-associated steatotic liver disease (MASLD). Although the patatin-like phospholipase domain-containing protein 3 (PNPLA3) I148M variant has been associated with hepatic inflammation and

fibrosis, its specific influence on intrahepatic immune cell infiltration and activation remains unclear.

Methods: Seventy patients with MASLD were prospectively enrolled. Genomic DNA was isolated from buccal swabs or liver biopsy specimens, and single nucleotide polymorphism genotyping was performed to determine the rs738409 SNP at codon 148 of PNPLA3. Immunohistochemistry using CD3 and CD68 antibodies quantified T cell and macrophage infiltration, respectively. Additionally, total RNA extracted from biopsy samples was subjected to quantitative reverse transcription polymerase chain reaction (qRT-PCR) to evaluate the expression of immune activation markers.

Results: Among the 70 patients with MASLD, 34 carried the GG genotype, while 21 and 15 had the GC and CC genotypes, respectively. The GG genotype group exhibited a trend toward a higher proportion of advanced fibrosis (F3 or F4) compared to the GC+CC group (P=0.051). Moreover, GG carriers demonstrated significantly elevated periportal $CD3^+$ and $CD68^+$ cell counts relative to GC/CC carriers (P<0.05). Transcriptomic analysis further revealed that GG carriers had increased expression of markers related to chronic antigen stimulation and immune activation, including CD8A, GZMB, CCL2, and TIMP1 (P<0.05). In addition, a consistent positive correlation was observed among inflammatory, steatosis-associated, and fibrosis-associated markers.

Conclusions: These findings indicate that the PNPLA3 I148M variant is significantly associated with enhanced immune cell infiltration and activation in the MASLD liver. Further studies are warranted to elucidate the mechanistic links between this genetic variant and liver inflammation, which may provide insights into novel therapeutic targets for MASLD progression.

Keywords: PNPLA3, Metabolic Dysfunction-Associated Steatotic Liver Disease, Liver Fibrosis, Immune Cell

FP-86

Investigating the Induction Mechanism of the Initial Aging Microenvironment in the Liver through Single-Cell Multi-Omics Analysis

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Aims: Aging is characterized by a gradual decline in physiological function. In our previous study, we identified distinct microenvironmental niches where tissue damage accumulates in a mosaic pattern within aged tissues. Here, we further investigate the underlying factors driving these alterations, with a particular focus on endothelial cells (ECs), which exhibited the most pronounced changes.

Methods: To investigate transcriptomic and epigenetic dynamics within the initial aging microenvironment, we applied multi-omics profiling combined with our in-house fibrotic niche enrichment method, Fibrotic Niche enrichment sequencing (FiNi-seq), to aged mouse livers and liver damage models.

Results: Using FiNi-seq, we identified age-associated fibrotic niches localized around the hepatic portal vein in naturally aged mice. These fibrotic regions exhibited a significant accumulation of inflammatory and scar-associated cells. A major EC subpopulation within these niches, termed Fibrotic ECs, displayed senescence-like signatures and upregulated multiple chemokines. The Fibrotic EC population expanded substantially following portal damage in a 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC) diet model, suggesting that their emergence results from chronic liver injury accumulation with age. To identify the drivers of Fibrotic EC formation, we performed single-nucleus assay for transposase-accessible chromatin using sequencing (snATAC-seq), which revealed increased chromatin accessibility at inflammation-related genes, suggesting the retention of epigenetic memory of prior tissue damage. Further, we observed enhanced accessibility to transcription factors, including HIF1α, implicating hypoxia as a key driver of endothelial senescence in liver aging.

Conclusions: Our study highlights Fibrotic ECs as key components of aging-associated fibrotic niches. Utilizing FiNi-ATAC-seq, we demonstrated that these ECs undergo epigenetic remodeling, sustaining inflammatory signaling and senescence-like characteristics. The expansion of Fibrotic ECs in both naturally aged livers and injury models suggests that chronic tissue damage plays a pivotal role in shaping the initial aging microenvironment. Together, these findings provide insights into how microenvironmental stressors, particularly hypoxia and inflammation, drive endothelial dysfunction and niche remodeling in liver aging.

Keywords: Liver Aging, Chronic Liver Damage, Endothelial Cell, Epigenetic Memory

Saturday, May 31, 2025, 13:10-14:30

12. Liver Transplantation 1

FP-87

An Increase in Regulatory B Cells Plays a Crucial Role in Achieving Tolerance in Liver Transplantation Patients

Soon Kyu Lee[1], Seon-Yeong Lee[2], Ho Joong Choi[3], Young Kyoung You[3], Jeong Won Jang[4], Pil Soo Sung[4], Ji Won Han[4], Seung Kew Yoon[4], Mi-La Cho[2], Jong Young Choi[4]

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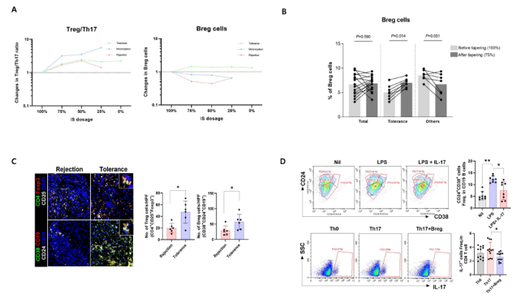
Aims: This study investigates the dynamics of regulatory B cells (Bregs) during immunosuppression (IS) tapering and their contribution to tolerance in liver transplantation (LT) patients.

Methods: We prospectively enrolled 15 LT patients who had normal liver function, no history of rejection, and had undergone LT more than five years ago. Patients were followed up every three months, and IS doses were tapered by 25% every 6–9 months. At each visit, blood samples were collected, and the proportions of T cells and B cells were analyzed by flow cytometry. Confocal microscopy and in vitro analysis were also performed to assess Breg function in LT patients.

Results: Over a median follow-up of 42 months, eight patients successfully discontinued IS without rejection (tolerance group). One patient experienced rejection (rejection group), while the remaining six patients reduced their IS dose to 25% without rejection (minimization group). During IS tapering, Treg cells and the Treg/Th17 ratio increased in the tolerance group but decreased before rejection in the rejection group (Figure A). Similarly, the tolerance group exhibited an increase in Bregs and the Breg/Th17 ratio, whereas a decrease was observed in the rejection group (Figure A, B). Moreover, a negative correlation between Bregs and Th17 cells and a significant positive association between Bregs and plasmablast B cells were identified. In liver tissue, confocal analysis showed a significant increase in Tregs and Bregs in the tolerance group compared to the rejection group (Figure C). In vitro analysis demonstrated a reduction in Th17 cells following Breg treatment, and vice versa (Figure D). Furthermore, treatment with *Faecalibacterium*, enriched in the tolerance group, led to an increase in Bregs and IL-10 levels.

Conclusions: During IS tapering, Bregs increase and contribute to the achievement of tolerance in LT patients. These findings suggest that Bregs may serve as potential biomarkers and therapeutic targets for promoting tolerance in LT.

Keywords: Liver Transplantation, Regulatory B Cells, Tolerance, Gut Microbiome



FP-88

Ferulic Acid-Loaded Liposomes Mitigate Hepatic Ischemia-Reperfusion Injury in a Rat Model Associated with Liver Transplantation via Altering Apoptosis, Mitochondrial Function and TLR-4/NF-B/NLRP3 Inflammatory Pathway

Niti Singh, **Deepika Singh**, Manvendra Singh

CSVTU, SIHAS, SHUATS, HMFA-MIET

Aims: Hepatic ischemia-reperfusion (I/R) injury is a significant challenge in liver transplantation, leading to severe oxidative stress, inflammation, and hepatocellular damage. Effective therapeutic interventions are necessary to improve transplant success and reduce post-transplant complications. In this study, we investigated the protective effects of ferulic acid-loaded liposomes (FA-LPs) against hepatic I/R injury in a rat model that is associated with liver transplantation. FA, a natural phenolic compound with potent antioxidant and anti-inflammatory properties, was encapsulated in liposomes to enhance its bioavailability and targeted delivery to liver tissues.

Methods: Ferulic acid-loaded liposomes were fabricated and characterized using sophisticated instrument. RAW 264.7 cells under the hypoxia/reoxygenation model were used and treated with FA-LPs at 1, 10, and 20 M. All the rats were split into five groups and given FA-LPs (3, 6, 9 mg/kg b.w.) for 14 days and then underwent a liver transplant. Using liver enzymes, cytokine status, hepatocyte death level, TUNEL, neutrophil and pro-inflammatory cytokines protein, and mRNA expression, the potential of FA-LPs against hepatic ischemia-reperfusion injury were estimated.

Results: FA-LPs modulates protein expression which is related with TLR-4/NF-B/NLRP3 inflammatory pathway in the RAW264.7 cells with hypoxia/reoxygenation model in dose

dependent manner. Our findings demonstrated that FA-LPs effectively attenuated liver injury by modulating inflammatory pathways and reducing oxidative damage. Histopathological analysis revealed significant reductions in hepatocellular necrosis, inflammatory cell infiltration, and tissue damage in FA-LP-treated rats compared to untreated controls. Biochemical assessments showed that FA-LPs significantly lowered serum levels of liver injury markers, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) while enhancing antioxidant enzyme activity. Additionally, FA-LPs suppressed the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, while upregulating anti-inflammatory mediators. Mechanistically, FA-LPs exerted their protective effects by inhibiting NF-κB signaling and reducing oxidative stress through the activation of the Nrf2/HO-1 pathway. These molecular interactions contributed to reduced hepatocyte apoptosis and improved mitochondrial function, thereby preserving liver architecture and function post-transplantation. It also reduced TLR-4, p-IB, p-IKK, p-IKK, p-IKK, NLRP3, p-P65MyD88, TNF-α, cleaved caspase-1, IL-1, IL-6 and IL-18.

Conclusions: Overall, our study highlights FA-LPs as a promising nanotherapeutic strategy for mitigating hepatic I/R injury in liver transplantation. By leveraging their anti-inflammatory and antioxidant properties, FA-LPs offer a potential approach to improve liver graft survival and patient outcomes. Further studies and clinical evaluations are warranted to explore their translational potential in liver transplant medicine.

Keywords: Ferulic Acid, Liposomes, Hepatic Ischemia-Reperfusion Injury, Liver Transplantation, Inflammation, Oxidative Stress, NF-K B, NRF2/HO-1 Pathway, Hepatoprotection

FP-89

Feasibility of Simultaneous Splenectomy in ABO Incompatible Living Donor Liver Transplantation with Small-for-Size Graft

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Aims: ABO incompatible living donor liver transplantation (ABOi LDLT) is breakthrough to expand living donor pool. However, immunologic problem and small-for-size graft (SFSG) is limitation of ABOi LDLT. Splenectomy is an option to resolve this limitation, but its effect remains controversial. We aimed to elucidate the feasibility of simultaneous splenectomy in ABOi LDLT with SFSG.

Methods: From June 2022 to December 2024, 24 case of ABOi LDLT was performed. Among them, cases that recipient's massive ascites or graft-recipient weight ratio (GRWR) less than 0.8 were 10. Simultaneous splenectomy with LT was 4 cases.

Results: We compared splenectomy cases to spleen-preserving cases, decrease in isoagglutinin titer was faster in splenectomy cases. Peak total bilirubin level, and PT-INR were low in splenectomy cases. Recipient's ascites after LT well controlled or lasted short period in splenectomy cases.

Conclusions: Splenectomy with LT caused greater risk of infection and portal vein thrombosis. But, in selected cases, splenectomy is prophylaxis of graft dysfunction and rejection in ABOi LT. when a small graft is predicted preoperatively, or for patients with portal hypertension, simultaneous splenectomy was recommended to prevent SFSG syndrome.

FP-90

The Impact of Everolimus Use on Incisional Hernia in Liver Transplant Patients

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Aims: Everolimus is immunosuppressive agent commonly used in liver transplantation patients. Positive effect of suppressing hepatocellular carcinoma is most common reason of choosing everolimus as post-liver transplant immunosuppressant. However Everolimus has been suggested to influence wound healing, potentially increasing the risk of incisional hernia. This study aims to evaluate the impact of Everolimus on incisional hernia development for liver transplantation patients.

Methods: A single-center retrospective cohort study was conducted for liver transplantation cases performed during 2017 to 2022. Total 812 patient was enrolled, excluding pediatric liver transplantation and retransplantation. All liver transplantations were performed in Benz incision. Patients were classified based on Everolimus usage. The incidence of incisional hernia was analyzed using Kaplan-Meier estimates and multivariable COX-regression analysis.

Results: Kaplan-Meier survival curves showed no significant difference in hernia-free survival between patients with and without pre-hernia everolimus administration (P=0.705). However, in multivariate Cox regression analysis, both pre-hernia everolimus use (HR = 4.555, 95% CI: 2.549 - 8.141, P<0.001) and higher BMI (HR = 1.164, 95% CI: 1.106 - 1.226, P<0.001) were significantly associated with an increased risk of hernia.

In contrast, longer everolimus coverage duration was associated with a decreased hernia risk (HR = 0.864, 95% CI: 0.819 - 0.911, P<0.001). However, further analysis using time-dependent covariates showed a slight increase in hernia risk over time (HR = 1.003, 95% CI: 1.001 - 1.004, P<0.001).

AUROC curve analysis for BMI demonstrated a moderate predictive value (AUC = 0.68), with an optimal cut-off value of 25.24 (Youden's index = 0.266).

Conclusions: Everolimus use before hernia onset did not appear to be significantly associated with incisional hernia occurrence. However, multivariate analysis revealed that everolimus administration was associated with an increased risk of incisional hernia. Additionally, BMI was a moderate predictor of hernia development, with higher BMI levels correlating with an increased risk.

These findings suggest that everolimus may not directly impair wound healing. However, careful monitoring for incisional hernia is warranted in patients receiving everolimus.

Keywords: Liver Trasnplantation, Everolimus, Incisional Hernia

FP-91

Transcriptomic Profiling of Personalized Immunosuppressant Modelling to Prevent Acute Cellular Rejection (ACR) in Pediatric Liver Transplant Recipients

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Aims: Acute and chronic liver rejection is a condition where the immune system mistakenly identifies the transplant organ. Acute cellular rejection (ACR) is mediated by cytotoxic T-cells, meanwhile late rejection occurs alongside the cell-mediated injury. Untreated ACR can lead to severe liver dysfunction or transplant failure. Choosing the right immunosuppressant is crucial to avoid rejection response. Limited studies have investigated potential biomarker for pediatric liver transplant. This study aimed to identify the gene expression that clinically useful to prevent ACR in pediatric liver transplant recipients.

Methods: The gene chip data GSE200340 was downloaded from the GEO expression database. Transcriptomic data from whole blood of recipients were compared to identify differentially expressed genes (DEGs) during rejection and non-rejection. At the same time, the protein-protein interaction (PPI) networks of these DEGs were established by STRING. The hub genes were identified from key and central gene.

Results: After data analysis, out of 21.668 items, TP3I13, CA1, PA2G4 were highlighted for their significant dysregulation in liver rejection cases, it potentially serving as biomarkers and therapeutic targets. The gene expression analysis showed that the gene clusters were either upregulated or downregulated in the whole blood transcriptomes patient. It could serve as a potential target in reprogrammed epigenetic and transcriptional regulation, likely resulting from the organ transplantation between individuals. This identification of blood-based module biomarkers can be implemented for modeling anti-rejection drugs.

Conclusions: This study suggests that TP3I13, CA1, PA2G4 as important research target to understand the treatment of ACR in pediatric patients.

Keywords: Acute Cellular Rejection, Immunosuppressant, Liver Transplantation, Pediatric

FP-92

Safety of Living Right Liver Donors Aged 45 and Older: Risks and Outcomes for Donors and Recipients

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Aims: The safety and viability of grafts from old aged donors remain unclear. This study aimed to compared donor and recipient outcomes in living donor liver transplantation (LDLT) using right lobe (RL) grafts from older donors (≥45 years, OD) versus younger donors (<45 years, YD).

Methods: LDLT outcomes using RL grafts from the OD group were compared to those from the YD group, both before and after propensity score matching (PSM).

Results: A total of 4,415 RL donors were analyzed, including the OD group (N=4,177) and the YD group (N=238), along with their corresponding recipients (N=4,415). Donor morbidity, including overall, major (Clavien-Dindo ≥3a), biliary, and vascular complications, were not showed in the OD group compared with YD groups. However, recipients of OD RL grafts showed significantly higher incidence of biliary stricture (9.2% vs. 6.2%; P=0.035), 1-year graft failure (5.5% vs. 1.1%; P=0.001), and reduced long-term graft survival (P=0.004) compared to the YD group. OD grafts were significantly associated with poorer graft survival in recipients with MELD score ≥20 (P<0.05). These outcomes were consistent after 1:3 PSM. Multivariate analysis identified OD grafts as a significant risk factor for 90-day biliary stricture and 1-year graft failure. No donor mortality occurred, and all donors fully recovered to their baseline activity levels.

Conclusions: LDLT using RL grafts from donors aged ≥45 years increased the risk of biliary stricture and early graft failure in recipients, particularly in those with MELD ≥20, while donor safety was not compromised. Careful donor-recipient matching is critical when considering older donors.

Keywords: Living Donor Liver Transplantation, Older Donor Age, Morbidity

FP-93

Adult-to-Adult Right Lobe Graft Living Donor Liver Transplantation for Acute-on-Chronic Liver Failure: A Single-Centre Retrospective Study in Vietnam

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Aims: Acute-on-chronic liver failure (ACLF) has a high mortality rate, and liver transplants are considered a definite treatment for patients with this condition. This study aims to evaluate the outcomes of living donor liver transplantation (LDLT) on ACLF patients in a single center.

Methods: This was a retrospective study at the 108 Military Central Hospital, enrolling 88 patients diagnosed with ACLF based on APASL criteria who underwent LDLT with the right lobe graft from December 2019 to December 2024. We utilize the MELD and AARC scores to evaluate and stratify the severity of ACLF.

Results: The average age of all patients was 44.27 ± 13.61. The average BMI was 21.78 ± 2.61. The most common underlying liver disease is chronic viral hepatitis B (85.2%). The average MELD score of the patients was 34.90 ± 5.61, with 30.2% having MELD score >= 40. In terms of ACLF severity, the average AARC score was 9.43 ± 1.68. The duration of treatment in the ICU was 8.59 ± 7.27 days, and the length of stay was 28.02 ± 13.45 days. The most common post-transplant complication was biliary complication (19.61%), with a mortality in 22 patients (25%). The survival rates at six months, one year, and three years were 84%, 81.7%, and 81.7%, respectively.

Conclusions: Living donor liver transplantation for ACLF patients is safe and has a high post-transplant survival rate. Multidisciplinary care before, during, and after surgery, and the decision to do a liver transplant early, is essential in saving the lives of ACLF patients.

Keywords: ACLF, LDLT, Liver

FP-94

Quality Score: Development of Integrative Prognostic Index for Living Donor Liver Using Multicentric Registry Data

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Aims: Donor factors significantly affect the prognosis of living donor liver transplantation (LDLT). This study aimed to develop integrative prognostic index for living donor liver using Korean Organ Transplantation Registry (KOTRY)

Methods: Data of 4802 eligible LDLT patients was randomly assigned to derivation and validation cohorts with 7:3 ratio. From derivation cohort, six donor variables were selected from 20 times repeated 10-fold cross validation. QUALITY (QUick Assessment of LIving donor liver for LDLT Yeild) score was calculated with mean value of each coefficient adjusted with recipient factors.

Results: Formula of QUALITY score was "-log10 [exp {(0.167*(Donor age-35)/5) + 0.263 if ABO-incompatible + (0.173 if GRWR 0.7~0.8 or 0.627 if GRWR <0.7) + 0.295 if Other than right lobe + 0.369 if Graft steatosis >=5%)}]*100 +100". C-indices of QUALITY score were 0.630 in derivation and 0.649 in validation cohort. In the validation cohort, 5-year graft survival was well-stratified by QUALITY score group (90.0% for QUALITY 100 [ideal donor] vs. 87.3% for QUALITY 85-99 vs. 87.1% for QUALITY 70-84 vs. 77.4% for QUALITY 55-69 vs. 68.5% for QUALITY 40-54, P<0.001). The association of QUALITY and graft survival was independent from recipient risk factors in multivariable analyses (aHR 1.28, 95% CI 1.17-1.39). Graft survival after LDLT was more precisely predicted when the QUALITY score was combined with recipient factors such as high MELD, advanced age, ICU bound, and longer cold ischemic time.

Conclusions: QUALITY score could be used for living donor selection and decision-making regarding whether to proceed with LDLT.

Keywords: Living Donor, Liver Transplantation

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FP-95

Severity and Pattern of Bile Duct Complications after Donor Right Hepatectomy: Open versus Minimally Invasive Approaches

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Aims: Bile duct division in living donor hepatectomy is a critical step that can lead to major postoperative complications. Minimally invasive donor right hepatectomy (MIDRH) has recently become popular worldwide. However, due to technical limitations, the bile duct division in MIDRH differs from that in open donor right hepatectomy (ODRH). This study aimed to compare the patterns of donor biliary complications between MIDRH and ODRH.

Methods: This retrospective, single-center study included 284 and 319 donors who underwent MIDRH and ODRH, respectively, between March 2016 and June 2024. The conventional bile duct division method is "clip and cut" in MIDH and "cut and suture" in ODRH, respectively. In MIDH, 16 donors were using "cut and suture" method during bile duct division. Bile duct complications in donors were compared between conventional MIDH and ODRH groups. The management of bile duct complications was analyzed in detai

Results: The overall biliary complication rates were similar between the groups (MIDRH 7.8% vs ODRH 6.8%, P=0.630). However, grade II or higher complications requiring management were significantly higher in MIDRH (4.9% vs 1.9%, P=0.040). MIDRH tended to have higher rates of major complications (≥ Grade III) than ODRH, though not statistically significant (3.8% vs 1.6%, P=0.093). Minor complications not requiring management were significantly higher in ODRH (1.9% vs. 6.0%, P=0.014).

Conclusions: MIDRH showed a comparable overall biliary complication rate to ODRH but with greater severity. We suggest that the current bile duct division method in MIDRH requires technical refinement in several aspects.

Keywords: Liver Donor, Biliary Complications, Minimally Invasive Donor Hepatectomy

FP-96

Prognostic Concordance between LI-RADS Imaging and Pathology for Liver Transplant Eligibility in HCC: Results from 1,059 Patients

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Aims: Due to the limited availability of pathological confirmation, imaging diagnosis is crucial for evaluating liver transplantation (LT) eligibility in patients with hepatocellular carcinoma (HCC). Using LI-RADS-based diagnosis, we examined the radiological-pathological correlation of the Milan criteria (MC) and the up-to-seven criteria (UTS), identified factors contributing to discordance, and assessed their prognostic impact.

Methods: This retrospective study included 1,059 patients from a prospective registry who had non-LR1/LR2 hepatic nodules identified on dynamic CT within three months prior to LT. Radiologic lesions were classified according to the CT/MRI LI-RADS v2018 and LI-RADS treatment response algorithm v2024, and these classifications were compared with matched pathology results. Nodules classified as LR-4, LR-5, or LR-TR-V were considered HCC for determining LI-RADS MC and UTS. HCC-related mortality was analyzed using competing risks analysis, along with overall survival. Additionally, a subgroup analysis utilizing pre-LT MRI was conducted in 203 patients.

Results: The concordance rates between CT-based LI-RADS and pathological assessments of the MC and the UTS were 85.5% and 90.7%, respectively. The primary reasons for discordance in the MC were HCCs exceeding size limits (n=51) and number limits (n=39) in liver explants. HCC-related 5-year mortality showed no significant difference in patients meeting LI-RADS MC (8.0%) versus those meeting pathological MC (6.3%; P=0.140). Prognostic performances measured by 5-year area under the precision-recall curve and integrated Brier score were comparable for LI-RADS MC and pathological MC groups (all P>0.05). Similar results were observed in UTS-based analysis, overall survival analysis, and subgroup analyses based on pre-LT treatment and MRI data.

Conclusions: LI-RADS-based transplantability criteria showed a high level of concordance with pathology-based criteria and demonstrated comparable prognostic performance. These findings suggest that LI-RADS can effectively classify suitable LT candidates for HCC.

Keywords: Liver Transplantation, LI-RADS, Milan Criteria, Up-To-Seven Criteria

FP-97

Aging in Place for Elderly Undergo Liver Transplantation: How Informal Care Could Help Maintaining Higher Quality of Life?

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Aims: The elderly (aged 60+ years) are the most vulnerable group to liver cancer due to frequent comorbidities and mortality globally. Potential curative treatment is Liver Transplantation (LT), although long-term survival is less than satisfactory. Post-operative care is crucial for the recovery and long-term well-being of patients. Informal caregiving, which includes care provided by family members or friends, plays a significant role in the post-operative phase. Understanding its impact on the quality of life of elderly liver transplant recipients can provide insights for healthcare policies and support systems.

Methods: Using Indonesia Family Life Survey (IFLS), we aim to explore how the availability of caregivers in maintaining the

elderly QoL post-LT with dementia comorbidity. Dependent variable is QoL score (WHOQOL-BREF). Independent variable include presence of a caregiver, relationship to caregiver, and caregiving hours. Control variables are age, gender, socioeconomic status, comorbidities, and time since transplantation.

Results: Sample size including 150 elderly LT recipients with mean age of 65.4 years, 60% male, and mean QoL Score of 65.2. 80% of them are having an informal caregiver which 70% received care from a family member with average caregiving hours/week was 25. Multiple linear regression show that the caregiver presence have positive impact on QoL (β=5.3, P<0.01). Relationship to caregiver was matter which family member (spouse or child) has a stronger positive impact on QoL compared to care from friends or distant relatives (β=4.8, P<0.05). Moderate caregiving hours (15-30 hours per week) are associated with higher QoL scores compared to low (<15 hours) or high (>30 hours) caregiving hours (β=3.2, P<0.05). The positive impact of informal caregiving on QoL is more pronounced in females (β=6.1, P<0.01) than in males (β=4.5, P<0.05). Higher socioeconomic status amplifies the positive effect of informal caregiving on QoL (β=5.7, P<0.01). The presence of comorbidities slightly attenuates the positive impact of caregiving on QoL (β=2.8, P<0.05).

Conclusions: Indonesia will become the second-largest Silver Economy in the world after China on 2045, informal caregiving plays a crucial role in maintaining a higher quality of life among elderly liver transplant recipients in Indonesia. Policies aimed at supporting informal caregivers can significantly contribute to the well-being of this vulnerable population.

Keywords: Elderly Post Liver Transplantation, Aging In Community, Post-Operative Care, Informal Caregiving

FP-98

Development and Optimization of Transplant Surgeon-Innovated Evmp: Validation in a Porcine DCD Liver Transplant Model

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Aims: Ex vivo machine perfusion (EVMP) is increasingly recognized as a promising technique for enhancing the preservation and viability of donor organs, especially in donation after circulatory death (DCD) liver transplantation (LT). This study validates a transplant surgeon-innovated EVMP protocol, assessing its efficacy in preserving liver function and reducing ischemic-reperfusion injury in a porcine DCD LT model.

Methods: Twenty Yorkshire pigs were used to compare static cold storage (SCS) and EVMP. In Model 1, the SCS group (n=5) underwent 5 hours of cold storage, while the EVMP group (n=9) had 1 hour of cold storage followed by 4 hours of EVMP. In Model 2, the SCS group (n=3) underwent 6 hours of cold storage, while the EVMP group (n=3) had 2 hours of cold storage followed by 4 hours of EVMP. Hemodynamic stability during perfusion, laboratory findings, and apoptosis (via TUNEL assay) after reperfusion were evaluated.

Results: The EVMP system successfully performed all 12 cases without technical complications. Hemodynamic parameters were stably maintained during perfusion. In Model 2, ALT levels were significantly lower in the EVMP group compared to SCS (e.g., 134.3 ± 27.0 vs. 48.0 ± 6.2 U/L, P=0.006 at 3 hours post-reperfusion). TUNEL staining revealed significantly reduced hepatic apoptosis in the EVMP group versus SCS at 2 and 3 hours post-reperfusion in both models.

Conclusions: This study successfully demonstrated the stability of the transplant surgeon-innovated normothermic EVMP protocol, validating its efficacy in improving organ preservation and reducing ischemic-reperfusion injury in a porcine DCD LT model.

Keywords: Ex Vivo Machine Perfusion, Donation after Circulatory Death, Ischemic-Reperfusion Injury

FP-99

Prediction of Early Risk of Patient Survival Following Liver Transplant Based on Lifestyle Factors via Machine Learning Models

Manvendra Singh[1], Deepika Singh[2]

[1]HMFA MIET, [2]SHUATS

Aims: The recommended course of treatment for those with end-stage liver disease is liver transplantation (LT). Improvements in LT have led to better posttransplant results. The Model for End-Stage Liver Disease (MELD) has been used in investigations by researchers in the past several years to see if it may predict survival following liver transplantation (LT).

The objective of this work was to build a low-cost, non-invasive, quick, and high-precision diagnostic model by employing six machine learning (ML) algorithms to classify patients into groups with high or low risk of getting patient survival following liver transplant by examining individual lifestyle characteristics.

Methods: Following liver transplant database collected in India, 1300 people's records were used in this retrospective analysis. Randomly chosen ratios of 0.7:0.3 were used to divide the data into training and test sets. Before and after utilising the relief feature selection method, six ML techniques MLP, SVM, linear kernel, SVM (RBF kernel), KNN, RF and XGBoost—were trained to create prognostic models. Test split and cross-validation were used to determine the metrics produced from the confusion matrix in order to assess the performance.

Results: This study identified 11 key risk factors for patient survival following liver transplant, including, graft failure, infection, acute renal failure, stress level, weight loss and vascular complications after transplant, as well as graft failure diagnosis interval, previous diabetes mellitus, Model for End-Stage Liver Disease score, donor inotropic support, units of packed cell received, and previous recipient dialysis, were found to be predictive factors in patient survival. The XGBoost classifier produced accuracy, sensitivity, specificity, and accuracy scores of 82.3%, 84.5%, 86.7%, 83.2%, and 82.1% when the chosen factors were incorporated into the model, according to the results. When all features were supplied into the classifiers, t model, according to the results. When all features were supplied into the classifiers, the KNN classifier for K = 7 produced results with a mean accuracy of 65.99%, a mean sensitivity of 65%, a mean specificity of 71.3%, an AUC of 65.7%, and a mean H-score of 66.15%.The XGBoost classifier's AUC and classification report; this classifier was chosen as the best one for prediction.

Conclusions: The findings, starting with basic patient baseline data, ML approaches have potential to begin the prescreening of patient survival following liver transplant and identify high-risk people who should move forward with invasive exams.

Keywords: Liver Transplant, Lifestyle Factors, Machine Learning

FP-100

Development of Immune-Evasive Meta-Soft Organ Modules through Advanced Cell Engineering and Assembly Technology

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Aims: Immune rejection and donor shortages pose challenges in liver transplantation. This study addresses these barriers by engineering immune-evasive Meta-iPSC via HLA knockout and immune checkpoint molecule knock-in to improve transplantation outcomes and advance regenerative medicine.

Methods: Using CRISPR-Cas9 genome-editing technology, TnRhipsc-4F cells were modified via HLA gene knockout and immune checkpoint molecule knock-in to generate ALC3-3 cells capable of inducing immune tolerance. These cells were differentiated into Meta-iPSC-derived hepatocytes over a 20-day period. Hepatocyte-specific gene expression was validated through RT-PCR, while immunocytochemistry confirmed the protein expression of hepatocyte markers. Albumin secretion was quantified using flow cytometry (FACS). The differentiated hepatocytes were then assembled into three-dimensional organ modules with vascular structures and transplanted into rabbit livers to evaluate in vivo biocompatibility.

Results: Pluripotency markers in the undifferentiated Meta-iPSC ALC3-3 state and hepatocyte-specific markers in Meta-iPSC-derived hepatocytes were verified via RT-PCR and immunocytochemistry. FACS analysis showed albumin and MRP2 expression in over 80% of Meta-iPSC-derived hepatocytes. Post-transplantation analyses, including DAB staining, confirmed the expression of human-specific markers such as hGAPDH and hALB in rabbit liver tissues, demonstrating successful engraftment and functional integration of the immune-evasive cells.

Conclusions: Pluripotency markers in the undifferentiated Meta-iPSC ALC3-3 state and hepatocyte-specific markers in Meta-iPSC-derived hepatocytes were verified via RT-PCR and immunocytochemistry. FACS analysis showed albumin and MRP2 expression in over 80% of Meta-iPSC-derived hepatocytes. Post-transplantation analyses, including DAB staining, confirmed the expression of human-specific markers such as hGAPDH and hALB in rabbit liver tissues, demonstrating successful engraftment and functional integration of the immune-evasive cells.

Keywords: Immune-Evasive Stem Cells, Genome-Editing Technology, Organ Transplantation

FP-101

Rehabilitation for Fatigue after Liver Transplantation: Effects of Exercise and Physical Activity Counseling

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Aims: This study aimed to investigate whether a rehabilitation program could alleviate fatigue in liver transplant recipients. Additionally, the study examined its effects on physical fitness, physical activity, and cardiovascular risk, while also evaluating adherence, satisfaction, and potential adverse events.

Methods: This was an uncontrolled intervention study conducted at an outpatient rehabilitation clinic. Eighteen fatigued liver transplant recipients participated in a 12-week rehabilitation program that included physical exercise training and counseling on physical activity. The primary outcome measure was

fatigue, while secondary measures included aerobic capacity, muscle strength, body fat, daily physical activity, lipid profile, and glycemic control. Assessments were conducted before and after the rehabilitation program, with adherence, satisfaction, and adverse events also recorded.

Results: In the study, participants experienced a significant reduction in fatigue, with the percentage of individuals reporting severe fatigue decreasing by 22% to 53%. Additionally, aerobic capacity and knee flexion strength improved significantly, while body fat decreased. Participants successfully performed physical exercises at the target training intensity, no adverse events were reported, and program adherence was high, with a 93% attendance rate and an average satisfaction score of 8.5 out of 10 (range: 7–10).

Conclusions: A rehabilitation program incorporating exercise training and physical activity counseling is well-tolerated and shows promise in reducing fatigue and enhancing fitness in liver transplant recipients.

Keywords: Fatty liver, Rehabilitation, Transplantation, Physical Activity

FP-102

Clinical Outcomes of 90 Cases of Post-Transplant Lymphoproliferative Disorder (PTLD) after Liver Transplantation: A 24-Years Single- Center Experience

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Aims: Post-Transplant Lymphoproliferative Disorder (PTLD) is a rare but severe complication following solid organ transplantation (SOT), with a mortality rate of approximately 50%. The timing of PTLD onset may influence clinical features and prognosis; however, data focusing on liver transplantation (LT) are limited. This study examines the clinical characteristics and outcomes of PTLD in LT recipients.

Methods: From January 2000 to December 2023, LT recipients diagnosed with PTLD at Asan Medical Center were retrospectively reviewed. PTLD diagnoses were pathologically confirmed, and cases were classified as early or late onset based on timing post-transplantation. Study endpoints included complete remission (CR) rates and overall survival

Results: Among 8,351 LT recipients, 90 developed PTLD, with 24(26.6%) classified as early onset and 66(73.4%) as late onset. Early onset PTLD was more frequent in pediatric recipients (45.8% vs. 15.2%, *P*=0.004). Median time to PTLD diagnosis was 3.25 years. Serum EBV DNA was detected more often in early onset cases (78.3% vs. 35.6%, *P*=0.001). CR rates were 66.7% in early onset and 80.3% in late onset PTLD (*P*=0.258), and mortality rates were similar (41.7% vs. 37.9%, *P*=0.809). In a subgroup analysis of 69 adult PTLD patients, demographic data were consistent with the overall cohort. High IPI scores (HR 5.496, 95% CI 1.529–19.762, *P*=0.009) and graft involvement (HR 2.736, 95% CI 1.096–6.828, *P*=0.031) were significant prognostic factors for survival.

Conclusions: Early and late onset PTLD in LT recipients differ clinically but show similar long-term outcomes. High IPI scores and graft involvement are poor prognostic indicators, emphasizing tailored strategies to improve outcomes.

Keywords: Liver Transplantation, PTLD

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 2: May 30 (Fri)

Oral Poster Presentation 1

OP-1~OP-6	Autoimmune Disease
OP-7~OP-12	MASLD and ALD, Basic
OP-13~OP-18	MASLD, Clinical 1
OP-19~OP-23	LC, Clinical and Liver Failure
OP-24~OP-29	Liver Transplantation 1
OP-30~OP-35	Liver Cancer, Basic 1
OP-36~OP-41	Liver Cancer, Clinical 1
OP-42~OP-47	Liver Cancer, Clinical 2
OP-48~OP-53	Liver Surgery
OP-54~OP-59	Liver Cancer, Basic 2

Friday, May 30, 2025, 16:40-17:40

1. Autoimmune Disease

OP-1

Constructing a Protein Interaction Network for Autoimmune Liver Diseases Using Protein-Protein Ratio Exposures: Insights from a Mendelian Randomization Study

Dianzhe Tian[1,2], Zuyi Yang[1], Zixuan Hu[1,2], Lvyuxing Zhao[3], Lei Zhang[2], Haitao Zhao[2], Xinting Sang[2], Yiyao Xu[2], Yunping Luo[4,5], Xin Lu[2]

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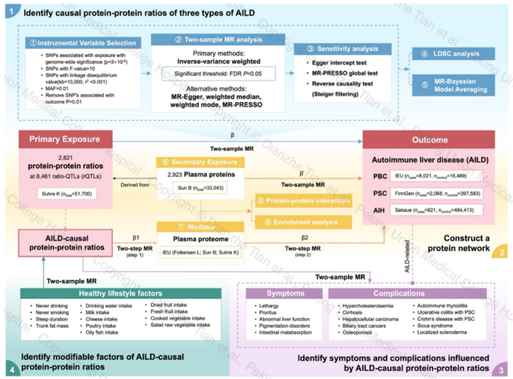
Aims: Protein-protein ratios (PPRs), representing the relative abundance between paired plasma proteins, offer a novel perspective in proteomic research by capturing functionally coupled interactions beyond absolute protein concentrations. Most existing studies focus on individual protein levels, neglecting the potential biological significance of relative protein abundance in reflecting disease-specific network disruptions. This study presents a novel computational framework that integrates PPR analysis with comprehensive proteome profiling to uncover causal relationships and therapeutic targets in autoimmune liver diseases (AILDs), including primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and autoimmune hepatitis (AIH).

Methods: By performing a two-sample MR analysis on 2,821 plasma PPRs and 1,463 proteins from the UKB-PPP Olink cohort, we identified proteins and PPRs that are causally associated with AILD. To enhance the robustness of the causal inference and assess genetic correlations, sensitivity analyses, linkage disequilibrium score regression (LDSC), and MR-Bayesian approaches were also employed. Subsequently, we conducted mediation MR analysis on the positive PPRs, followed by protein-protein interaction (PPI) via Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database and functional enrichment analysis via Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases to explore underlying mechanisms. Finally, we investigated the symptoms and complications of AILDs associated with the AILD-causal PPRs and explored the impact of several modifiable lifestyle factors on them.

Results: In PBC, the BSG/TNFRSF4 ratio demonstrated potent risk amplification (OR=3.67); for PSC, CD74-centric ratios revealed dual protective effects (CD74/NPDC1 OR=0.66; CD74/JAM2 OR=0.70) alongside CSF1/IFNGR1-mediated risk potentiation (OR=1.49). Notably, the CD74/JAM2 ratio showed cross-disease significance, exhibiting strong protection in AIH (OR=0.53) as well. Further PPI analysis in PSC revealed strong interactions among proteins like APP, CD74, and ENG, suggesting their involvement in PSC pathogenesis. GO analysis highlighted significant enrichment in processes related to synaptic plasticity, including long-term potentiation and presynaptic assembly, with proteins enriched in cellular components like the cell membrane, Golgi apparatus, and transport vesicles. Molecular functions were linked to peptide binding and metallopeptidase activity. KEGG pathways indicated roles in the renin-angiotensin system, Alzheimer's disease, and antigen processing. Simultaneously, potential symptom alleviation was observed for pruritus (CD74/NPDC1, OR=0.8307) and malabsorption (CD74/NPDC1, OR=0.9953; CD74/JAM2, OR=0.9935). Crucially, CD74-targeted ratios conferred cross-complication protection: reducing the risk of autoimmune thyroiditis (CD74/JAM2, OR=0.35; CD74/NPDC1, OR=0.33), ulcerative colitis with PSC (CD74/JAM2, OR=0.35; CD74/NPDC1, OR=0.31), and Sicca syndrome (CD74/JAM2, OR=0.54).



Conclusions: This study represents a groundbreaking approach by integrating causal proteomics with PPRs to explore AILDs. Our findings unveil mechanism-validated protein networks that offer new insights into the underlying pathogenesis of AILDs, with a particular focus on CD74 as a promising therapeutic target for PSC. Through further analysis of PPRs, we identified significant alleviation of AILD-related symptoms and complications, while our data-driven recommendations for lifestyle modifications also hold the potential to influence disease progression and management. This innovative framework not only unveils novel perspectives on mechanism and therapeutic strategies of AILDs, but also demonstrates its potential for application in exploring the pathogenesis and treatment of other diseases.

Keywords: Mendelian Randomization, Plasma Protein Ratio, Autoimmune Liver DiseaseS, CD74

OP-2

Epidemiology, Treatment Response, and Genetic Characteristics of Autoimmune Liver Diseases: A Retrospective and Prospective Cohort Study

Young Chang[1], Jae Young Jang[1], Tom Ryu[1], Soung Won Jeong[1], Jeong-Ju Yoo[2], Sae Hwan Lee[3], Sang Gyune Kim[2], Young Seok Kim[2], Hong Soo Kim[3]

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Aims: Autoimmune liver diseases, including autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC), exhibit diverse clinical presentations and treatment responses. This study aimed to establish retrospective and prospective cohorts to analyze epidemiology, treatment response, and genetic differences associated with disease severity.

Methods: A retrospective cohort included patients diagnosed with AIH or PBC between January 2005 and December 2023, while a prospective cohort was established from January 2021. Clinical characteristics, serological markers, liver biopsy findings, and treatment responses were analyzed. RNA sequencing was performed on blood samples to evaluate gene expression differences based on fibrosis stage and disease activity.

Results: The retrospective cohort comprised 266 AIH and 40 PBC patients. AIH patients had a mean diagnosis age of 57 years, while PBC patients were diagnosed at 58.5 years, with over 80% female prevalence in both groups. AIH showed significantly higher IgG levels (1758 mg/dL) compared to PBC (1506.5 mg/dL). Anti-nuclear antibody positivity exceeded 90% in both groups, while anti-mitochondrial antibody was positive in 81.6% of PBC cases. After 12 months, biochemical indicators improved significantly in both groups. Steroid treatment in AIH significantly reduced immunoglobulin G, prothrombin time, and alkaline phosphatase levels. RNA sequencing revealed significant gene expression differences in AIH patients based on fibrosis severity, particularly in pathways related to cellular detoxification, response to toxic substances, steroid hormone signaling, and inflammatory regulation. In PBC, disease activity stage was associated with alterations in immune effector regulation, particularly in pathways related to natural killer cell-mediated immunity.

Conclusions: This study highlights distinct clinical and genetic characteristics in AIH and PBC. Host factors, particularly immune-related pathways, play a crucial role in disease progression, emphasizing the need for individualized treatment approaches.

Keywords: Autoimmune Hepatitis, Primary Biliary Cholangitis, Fibrosis, Gene Expression

OP-3

Risk Factors for Predicting Incomplete Treatment Response in Patients with Primary Biliary Cholangitis: A Korean Multicenter Cohort Study

Soon Kyu Lee[1], Jeong-Ju Yoo[2], U IM Chang[3], Ahlim Lee[3], Gwang Hyeon Choi[4], Ja Kyung Kim[5], Hye Yeon Chon[5], Seung Kak Shin[6], Hae Lim Lee[7], Ji-Won Park[8], Young-Joo Jin[9], Heechul Nam[10], Jung Hyun Kwon[1], Jung Hee Kim[11], Bo Hyun Kim[12], Hyung Joon Yim[13], Sook-Hyang Jeong[4], Kyung-Ah Kim[14]

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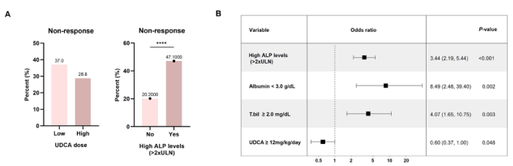
Aims: This study aimed to identify risk factors associated with an incomplete response to ursodeoxycholic acid (UDCA) therapy in patients with primary biliary cholangitis (PBC) using data from a Korean multicenter cohort.

Methods: A total of 645 newly diagnosed PBC patients from 10 Korean centers (January 2010–December 2021) were initially

enrolled. After excluding 213 patients (n=36 with follow-up <12 months; n=177 with overlap syndrome), 422 patients were included in the final analysis. The primary objective was to identify risk factors associated with an incomplete response to UDCA therapy. Treatment response was evaluated at 12 months using the POISE criteria, defined as alkaline phosphatase (ALP) <1.67× the upper limit of normal (ULN), a ≥15% reduction in ALP from baseline, and total bilirubin > ULN.

Results: The median age of the included patients was 59.0 years, with approximately 90% (n=376) being female. During a median follow-up of 56.1 months (range, 12.3-229.4 months), 21 patients died. After 12 months of UDCA treatment, 30.9% (n=130) of patients were classified as non-responders according to the POISE criteria. Patients with elevated ALP levels (>2 ×ULN) had a significantly higher rate of incomplete response compared to those with lower ALP levels (47.1% vs. 20.2%, respectively; *P*<0.001). Additionally, patients receiving a lower UDCA dose (<12 mg/kg/day) exhibited a marginally higher rate of incomplete response compared to those receiving higher doses. In multivariate logistic regression analysis, elevated ALP levels (>2×ULN; odds ratio [OR], 3.44; *P*<0.001), low albumin levels (<3.0 g/dL; OR, 8.49; *P*=0.002), and high bilirubin levels (≥2.0 mg/dL; OR, 4.07; *P*=0.003) were significantly associated with an increased risk of incomplete response at 12 months. Conversely, a higher UDCA dosage (≥12 mg/kg/day; OR, 0.60; *P*=0.048) was associated with a reduced risk of incomplete response. Based on these factors, a predictive nomogram was developed, demonstrating reliable predictive performance with an area under the receiver operating characteristic curve (AUROC) of 0.753 in 1,000 bootstrap analyses.

Conclusions: This large multicenter cohort study identifies key risk factors associated with an incomplete response to UDCA in Korean patients with PBC, providing valuable insights for early risk stratification.



Keywords: PRIMARY BILIARY CHOLANGITIS, RESPONSE, URSA, PREDICTION

OP-4

Clinical Statement for the Diagnosis and Management of PBC-AIH Overlap 2024: Japanese Experience

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Aims: Hepatologists occasionally see patients with overlapped autoimmune liver diseases (ALDs) with distinct etiologies. Among them, clinical characteristics of the primary biliary cholangitis (PBC) -autoimmune hepatitis (AIH) overlap remains elusive, with no current consensus on diagnostic and treatment strategies.

Methods: The Intractable Hepato-Biliary Disease Study Group (IHBDSG) in Japan supported by the Ministry of Health, Labor, and Welfare of Japan, assembled a Working Group to issue the clinical statement on PBC-AIH overlap for the dissemination of consensus information. Based on clinical practice guidelines for PBC and AIH published and endorsed by IHBDSG in Japan, with the introduction of the consensus recommendations for histological criteria of AIH by International AIH Pathology Group in 2022, clinical statement for the diagnosis and management of PBC-AIH overlap was established.

Results: We define first PBC-AIH overlap as a state of co-occurrence of PBC and AIH, neither as a distinct overlap syndrome nor their variants. We recommend to initiate the diagnosis process of overlap from that of clinically dominant disease. Overlap is diagnosed upon fulfillment of all of the three conditions comprising of ALT (>5xULN), IgG (>1.1xULN) and/or ANA/ASMA (>80x), and histological findings (>intermediate interface hepatitis and/or lobular hepatitis) from definite PBC, whereas those comprising of ALP(>2xULN), positive AMA or AMA-M2, and histological bile duct injury, representing typically non-suppurative destructive cholangitis, from definite AIH. In addition, we propose probable overlap when two of three above requirements were satisfied, especially in case histological evaluation is contraindicated due to overlap with acute severe AIH.

Conclusions: Comparing with stringent Paris criteria (Hepatology 1998) and quantitative Zhang criteria (Hepatol commun 2018), Japanese statement for PBC-AIH overlap 2024 encompasses atypical cases including those overlap with acute or acute severe AIH. Acknowledgement of the breadth of the phenotypic spectrum of PBC-AIH overlap could lead to the improvement of prognosis for ALDs.

Keywords: PBC-AIH Overlap, Primary Biliary Cholangitis, Autoimmune Hepatitis

OP-5

Intrahepatic Infiltration of Activated Regulatory T Cells Is Associated with the Degree of Inflammation in Autoimmune Hepatitis

Mi Hyun Kwon[1,2], Eun Ji Jang[1,2], Keungmo Yang[2,3], Jaejun Lee[2,3], Ji Won Han[2,3], Pil Soo Sung[2,3]

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Aims: Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease characterized by immune-mediated liver damage. Regulatory T cells (Tregs) are essential for maintaining immune homeostasis and preventing excessive immune responses. This study aims to investigate the role of Tregs in AIH by analyzing their function and phenotype, providing insights into their contribution to disease progression and immune dysregulation.

Methods: Peripheral blood mononuclear cells (PBMCs) and liver tissue samples were obtained from AIH patients (n= 49). Treg frequency and phenotype ($CD4^+CD25^+Foxp3^+$) were analyzed using flow cytometry with functional assessment based on subset analysis, including activated Tregs ($CD39^+$). Immunohistochemistry (IHC) was performed on liver tissue samples from AIH patients (n=24) to evaluate immune cell infiltration, including T cells, plasma cells, B cells, and macrophages. Correlation analysis was conducted to evaluate associations between Treg counts and clinical parameters such as serum ALT, necrosis, fibrosis, and immune cell populations.

Results: Treg were more abundant in liver tissues than in PBMCs, with a higher proportion of activated Tregs ($CD39^{+-}Foxp3^{high}CD45RA^-$) in tissues, while resting Tregs ($Foxp3^{low}CD45RA^+$) were more frequent in PBMCs. IHC analysis showed significant immune cell infiltration, including T cells, plasma cells, B cells, and macrophages, with distinct populations of high and low Foxp3-expressing Tregs. Correlation analysis revealed that Tregs counts negatively correlated with serum ALT levels and positively correlated with plasma cells ($CD38^+$) and B cells ($CD20^+$), but not macrophages ($CD68^+$). Tregs frequency also increased with higher fibrosis and necrosis stages.

Conclusions: This study suggests that activated Tregs are more abundant in tissues than in PBMCs, indicating their key role in regulating intrahepatic inflammation in AIH. The negative correlation between Tregs counts and serum ALT levels suggests their potential immunoregulatory role in regulating liver inflammation and preventing liver damage. The increased frequency of Tregs in advanced fibrosis and necrosis stages suggests a compensatory response to disease progression. These findings highlight the potential role of activated Tregs in modulating intrahepatic inflammation and disease severity.

Keywords: Autoimmune Hepatitis, Regulatory T Cells, FOXP3, Inflammation

OP-6

Prevalence, Incidence, and Risk Factors of Hepatic Cysts

Kang Seo[1], Yujeong Kim[2], Sang Hyuk Park[3], Nam-Joon Yi[3], Jeong Hee Yoon[4], Goh Eun Chung[5], Jeong-Moo Lee[3], Seoung Yoon Rho[6], Min Su Park[7], Eun Kyung Choe[8], Aesun Shin[1]

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Aims: Hepatic cysts are fluid-filled lesions in the liver, mostly asymptomatic, with fewer than 10-15% of patients experiencing clinically significant symptoms. The prevalence of hepatic cysts ranges from 0.06% to 71%, yet prior studies have largely focused on small populations, resulting in limited data on incidence and risk factors. This study aims to evaluate the prevalence, incidence, and risk factors for hepatic cysts in a large cohort of health screening participants.

Methods: This retrospective cohort study analyzed data from 78,676 participants in the H-PEACE cohort who underwent abdominal ultrasound (US) at Seoul National University Hospital Healthcare System Gangnam Center between 2003 and 2014. Hepatic cysts were identified from US reports using a rule-based text algorithm validated against a manually labeled dataset. Prevalence was calculated from baseline US data, while incidence was assessed from 41,179 participants who were negative for hepatic cysts at baseline and had follow-up abdominal ultrasound. Risk factors were identified using Cox proportional hazards models.

Results: The prevalence of hepatic cysts was 85.4 per 1,000 people (95% CI: 83.4–87.3) and female sex, older age, abdominal obesity, hepatitis B virus surface antigen (HBs-Ag) positive, hepatitis C virus antibody (Anti-HCV) positive, and presence of renal cyst were risk factors. The incidence was 23.4 per 1,000 person-years (95% CI: 23.0-24.0). Multivariate Cox regression analysis identified HBs-Ag positivity (HR 1.23, 95% CI: 1.02. 1.48) and the presence of renal cysts (HR 1.47, 95% CI: 1.31, 1.65) as independent risk factors, while HbA1c >6.5% (HR 0.62, 95% CI: 0.49–0.78) and high physical activity (HR 0.90, 95% CI: 0.82–1.00) appeared protective.

Conclusions: This study provides hepatic cyst prevalence and incidence, and identified risk factors. The presence of renal cysts and HBs-Ag positivity are risk factors for hepatic cyst development whereas high physical activity and diatetic status

are protective factors.

Keywords: Hepatic Cyst, Prevalence, Incidence, Risk Factor

Friday, May 30, 2025, 16:40-17:40

2. MASLD and ALD, Basic

OP-7

Liver Kinome Profiling Identifies PS1145-IKK Inhibition as a Potential Therapeutic Strategy for Systemic Inflammation in Alcohol-Associated Liver Diseases

Manisha Yadav[1], Abhishak Gupta[4], Sanju Yadav[1], Vipul Sharma[1], Yash Magar[3], Deepanshu Deepanshu, Neha Sharma[1], Nupur Sharma[1], Vasundhra Bindal[1], Sushmita Pandey[1], Gaurav Tripathi[1], Rimsha Saif[1], Babu Mathew[1], Anupama Kumari[2], Shiv Kumar Sarin[5], Jaswinder Singh Maras[1]

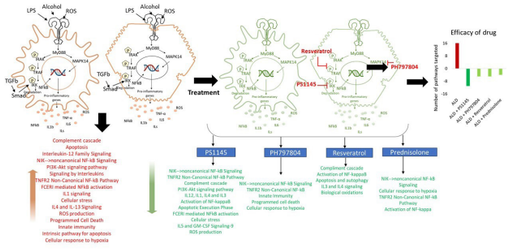
[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi; [2]Centre of Comparative Medicine, Institute of Liver and Biliary Sciences, New Delhi; [3]Amity University, Gurgaon; [4]Artemis Hospital, Gurgaon; [5]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi

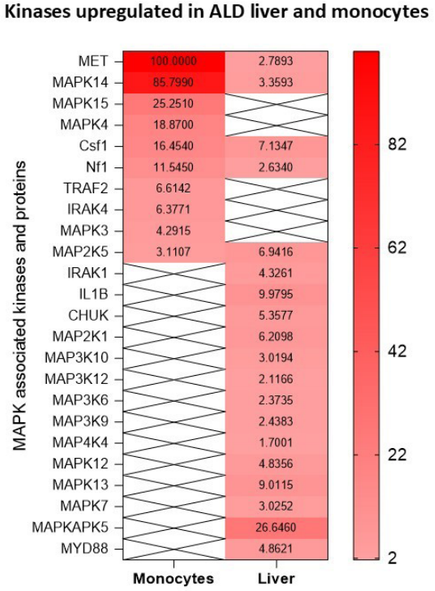
Aims: Background and aims: Alcohol-associated liver disease (ALD) has high mortality, mainly due to systemic inflammation, with no direct treatment available. We analysed the liver and monocyte kinome profiles in a chronic ethanol-exposed rat model to identify potential therapeutic targets which could ameliorate systemic inflammation and improve outcome in ALD.

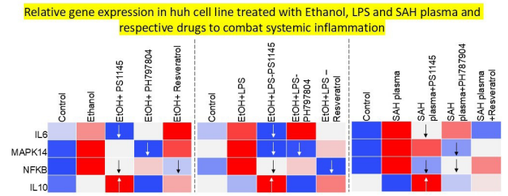
Methods: Method: ALD rat model was developed by feeding 40% ethanol (Lieber-De Carli Diet) for six months. Liver, circulating- monocytes were isolated at baseline, 8 weeks, 12 weeks, 16 weeks, 20 weeks, and 24 weeks to assess ethanol-induced pathophysiological changes temporally. Phosphoproteins were enriched and global kinome profiling was performed to outline molecular signalling and pathways that can be targeted. Pathway-specific inhibitors, including PS1145 (IKK phosphorylation inhibitor; activates IKK and suppress NFkB activation), PH-797804 (MAPK14 inhibitor), resveratrol and prednisolone were evaluated for their ability to suppress inflammation in ALD.

Results: Results: Using mass-spectrometry, ~497 kinases in liver, 345 kinases in monocytes were identified (FDR<0.01). Linear regression analysis revealed a significant and temporal increase in kinases associated with the MAPK-p38 and PI3K-AKT signalling in liver, and monocytes over time (FC>1.5, P<0.05). At 24 weeks, A total of 172 kinases in the liver and 48 kinases in monocytes were upregulated and linked to inflammatory pathways such as MyD88-TLR4, PI3K-Akt, TNF, TGFb, platelet activation, cellular senescence and others (P<0.05). Kinases linked to neurodegeneration, cellular senescence and dysregulation in complement cascade were increased specifically in liver (FC>1.5, P<0.05). Interestingly, kinases such as TGFbR, ROS production, IL1 induced phosphorylation of MAPK14 (p38)) and IKK (inhibitor of NF κ B kinase) were the major contributor of systemic inflammation in liver, and monocytes via activation of MYD88- TLR4 pathway. These kinome were targeted specifically by using IKK phosphorylation inhibitor PS1145 which effectively activated IKK and reduced inflammation by limiting the expression of NFkB *in-vitro* THP1 and HuH cell line. This observation was further validated on primary PBMCs of healthy subjects and SAH patients demonstrating the therapeutic potential of PS1145 comaptred to PH797804, resveratrol and prednisolone in ameliorating systemic inflammation in ALD.

Conclusions: Conclusion: Our study identifies the MAPK-p38 pathways as key drivers of systemic inflammation in ALD, with phosphorylated MAPK14 and IKK as potential targets. IKK phosphorylation inhibitor PS1145 ameliorate systemic inflammation and show promise for ALD treatment.







Keywords: Alcohol, Systemic Inflammation, Kinases, Signaling

OP-8

Adenosine Triphosphate-Binding Pocket Inhibitor for Mixed Lineage Kinase Domain-Like Protein Attenuated Alcoholic Liver Disease via Necroptosis-Independent Pathway

Seung Min Lee[1], Hye Young Kim[1], Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], In Young Kang[1], Jin Kim[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: Mixed lineage kinase domain-like protein (MLKL) serves as a critical mediator in necroptosis, a form of regulated cell death linked to various liver diseases. This study aims to specifically investigate the role of MLKL's adenosine triphosphate (ATP)-binding pocket in facilitating necroptosis-independent pathways that may contribute to liver disease progression. By focusing on this mechanism, we seek to identify potential therapeutic targets that can modulate MLKL activity, offering new strategies for the prevention and treatment of liver-related pathologies. We investigated the possibility of using the ATP-binding pocket-associated, necroptosis-independent MLKL pathway as a target for liver diseases.

Methods: Cell death following necroptosis stimuli was evaluated using cell proliferation assays, flow cytometry, and electron microscopy in various cells. The human liver organoid system was used to evaluate whether the MLKL ATP pocket-binding inhibitor could attenuate inflammation. Additionally, alcoholic and non-alcoholic fatty liver diseases animal models were used to determine whether MLKL ATP pocket inhibitors could attenuate liver injury.

Results: While an MLKL ATP pocket-binding inhibitor did not prevent necroptosis-induced cell death in RAW 264.7 cells, it did reduce the necroptosis-led expression of CXCL2, ICAM, and VCAM. Notably, MLKL ATP pocket inhibitor diminishes the expression of CXCL2, ICAM, and VCAM by inhibiting the I κ B kinase and nuclear factor kappa-B pathways without inducing necroptosis-induced cell death in two-dimensional cell culture as well as the human-derived liver organoid system. Although MLKL ATP-binding inhibitor was ineffective in non-alcoholic fatty liver disease animal models, MLKL ATP-binding inhibitor attenuated hepatic inflammation in the alcoholic liver disease model.

Conclusions: MLKL ATP pocket-binding inhibitor exerted anti-inflammatory effects through the necroptosis-independent MLKL pathway in an animal model of alcoholic liver disease.

Keywords: MLKL, ATP-Binding Pocket, Alcoholic Liver Disease, Necroptosis

OP-9

Polyethylene Glycol Relieves Hangover Symptoms and Protects Liver and Gut by Preventing Intestinal Absorption of Alcohol

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Aims: The harmful effects of binge drinking are well-known, including liver injury, gut barrier disruption, and behavioral impairment. This study investigates the therapeutic potential of polyethylene glycol (PEG) in alleviating hangover symptoms and mitigating tissue damage using a mouse model of acute binge drinking.

Methods: Eight-week-old male C57BL6J wild-type (WT) mice were divided into three groups: vehicle control, binge drinking (4 g/kg body weight), and binge drinking with PEG treatment (2 g/kg body weight). Behavioral tests and blood ethanol and acetaldehyde concentration measurements were performed using gas chromatography. Liver and intestine tissues were analyzed through hematoxylin and eosin (H&E) staining, immunohistochemistry, and immunofluorescence. Quantitative real-time polymerase chain reaction (qRT-PCR) was utilized to measure mRNA expression, while flow cytometry was employed to evaluate neutrophil infiltration and mononuclear cell populations.

Results: Mice in the binge drinking group exhibited elevated serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, alongside upregulated hepatic mRNA expression of *Cyp2e1* and *Tnf*. Flow cytometry and histological analyses revealed increased neutrophil infiltration and hepatocyte damage. Additionally, disrupted intestinal barriers and increased expression of cytochrome P450 2E1 (CYP2E1) and alcohol dehydrogenase (ADH) were observed in the binge drink-

ing group. Behavioral tests indicated impaired motor function, and blood concentrations of ethanol and acetaldehyde were significantly elevated. Remarkably, PEG administration post-alcohol consumption markedly reduced serum AST and ALT levels, normalized *Tnf* mRNA expression, and alleviated liver injury and neutrophil infiltration. Histological findings revealed that PEG mitigated gut barrier damage and downregulated intestinal ADH and CYP2E1 expression. Furthermore, PEG treatment reduced blood ethanol and acetaldehyde concentrations, improving motor function in binge drinking mice.

Conclusions: PEG administration after acute binge drinking demonstrates significant therapeutic potential by protecting the liver and gut, reducing systemic ethanol and acetaldehyde levels, and alleviating behavioral impairments. These findings suggest that PEG may offer a novel approach to mitigating hangover symptoms and preventing tissue damage associated with acute alcohol consumption.

Keywords: Alcohol-Associated Liver Disease, Polyethylene Glycol, Hangover, Intestinal Drinking

OP-10

GINS2 Accelerated Non-Alcoholic Fatty Liver Disease via Regulating TFEB Mediated Lipophagy

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Aims: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disorder worldwide, characterized by hepatic lipid accumulation and progressing to steatohepatitis (NASH), fibrosis, and hepatocellular carcinoma (HCC). Despite its high prevalence, no specific FDA-approved therapies exist due to its complex pathogenesis. This study aims to investigate the role of GINS2 in NAFLD pathogenesis and its potential as a therapeutic target.

Methods: Clinical databases of NAFLD patients at various stages and multiple mouse models (high-fat diet (HFD)-induced, genetically obese (db/db), and Gubra-Amylin NASH (GAN) diet-induced) were employed to evaluate the correlation between GINS2 expression and hepatic lipid accumulation. After GINS2 knockdown or overexpression, hepatic cell lines were treated with oleic acid and mice were administered HFD diet to assess its functional role. RNA sequencing (RNA-seq) and gene set enrichment analysis (GSEA) were performed to identify downstream pathways of GINS2, while co-immunoprecipitation (Co-IP) and mass spectrometry were used to identify GINS2-interacting proteins.

Results: GINS2 expression was significantly upregulated in NAFLD patient livers and mouse models. Functionally, GINS2 knockdown reduced oleic acid-induced lipid accumulation in hepatocytes, while its overexpression exacerbated HFD-induced steatosis in mice. Mechanistically, RNA-seq and GSEA revealed enrichment of the autophagy pathway in hepatocytes with GINS2 knockdown, characterized by increased LC3B expression and decreased p62 levels, enhanced autophagolysosome formation and incresed lipid droplet-autophagolysosome colocalization. Co-IP and mass spectrometry identified transcription factor EB (TFEB) as a GINS2 binding partner, with GINS2 overexpression reducing TFEB transcriptional activity in liver tissues.

Conclusions: GINS2 upregulation in response to lipid stress suppresses lipophagy by inhibiting TFEB-mediated autophagy activation, promoting hepatic lipid deposition and NAFLD progression. Targeting the GINS2-TFEB axis may represent a novel therapeutic strategy for NAFLD intervention.

Keywords: GINS2, Non-Alcoholic Fatty Liver Disease, TFEB, Lipophagy

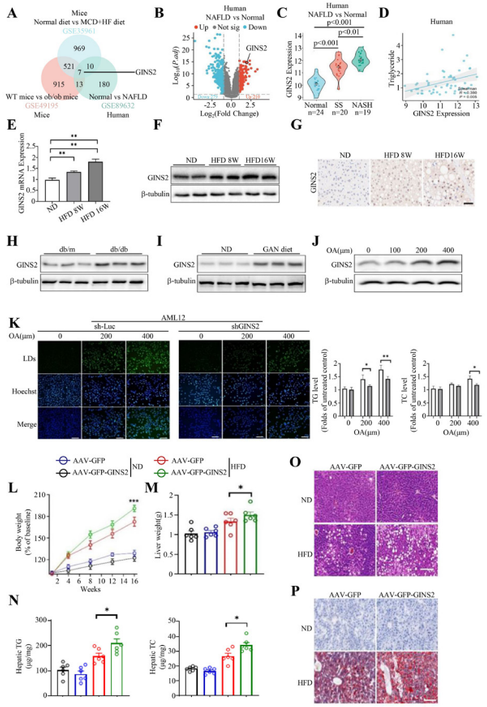

Figure 1. GINS2 is significantly upregulated in NAFLD and promotes hepatic lipid deposition.

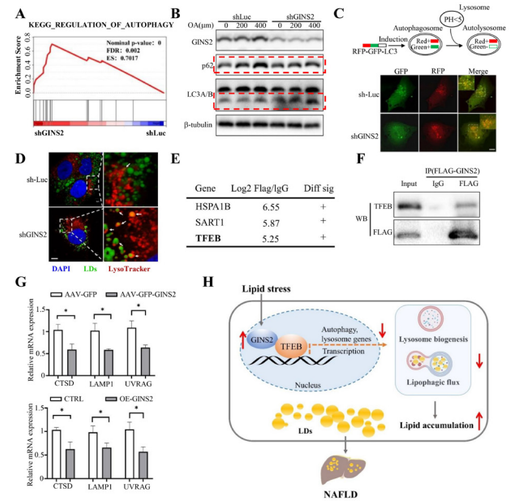

Figure 2. GINS2 suppresses lipophagy activation by regulating TFEB transcriptional activity.

OP-11

Molecular Clustering of Metabolic Dysfunction-Associated Steatotic Liver Disease Based on Transcriptome Analysis

Hye Young Kim[1], Seung Min Lee[1], Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], In Young Kang[1], Jin Kim[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a complex metabolic disorder with a diverse spectrum. This study aimed to classify patients with MASLD into molecular subtypes based on the underlying pathophysiology.

Methods: We performed high-throughput RNA sequencing on 164 liver tissue samples from healthy controls and patients with MASLD. The clustering was based on individual genes or pathways that showed high variation across the samples. Second, the clustering was based on single-sample gene set enrichment analysis.

Results: Optimal homogeneity was achieved by dividing the samples into four clusters (one healthy control and three MASLD clusters I-III) based on the top genes or pathways with differences across the samples. No significant differences were observed in waist circumference, blood pressure, glucose, alanine transaminase (ALT), or aspartate transferase (AST) levels between cluster I patients with MASLD and the healthy controls. Cluster I showed the clinical features of lean MASLD. Cluster III of MASLD demonstrated hypertension and a T2DM prevalence of 57.1% and 50.0%, respectively, with a significantly higher fibrosis burden (stage of fibrosis, liver stiffness, and FIB-4 value) than clusters I and II. Cluster III was associated with severe fibrosis and abnormal glucose homeostasis. In MASLD cluster I, the sphingolipid and GPCR pathways were upregulated, whereas the complement and phagocytosis pathways were downregulated. In MASLD cluster II, the cell cycle and NOTCH3 pathways increased, whereas the PI3K and insulin-related pathways decreased. In MASLD cluster III, increased activity occurred in the interleukin-2 and -4 and extracellular matrix pathways, coupled with decreased activity in the serotonin 2A and B pathways.

Conclusions: MASLD can be divided into three distinct molecular phenotypes, wherein each is characterized by a specific molecular pathway.

Keywords: MASLD, Transcriptome Analysis, Molecular Clustering, Phenotypes

OP-12

Treatment with IL-18 Binding Protein Biologics Inhibits Fibrotic Progression in Metabolic Dysfunction-Associated Steatohepatitis

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Aims: Metabolic dysfunction-associated steatohepatitis (MASH) is characterized by chronic liver inflammation and fibrosis, with increased IL-18 signaling playing a key role. This study aims to investigate the therapeutic potential of IL-18 binding protein (IL-18BP) biologics in suppressing fibrotic progression in MASH. Specifically, it evaluates the efficacy of a newly developed IL-18BP biologic (APB-R3) in mitigating liver inflammation and fibrosis.

Methods: To determine the role of IL-18BP in MASH progression, we measured hepatic and plasma levels of IL-18 and IL-18BP in both MASH patients and mouse models and analyzed their correlation with disease severity markers. To further investigate the functional role of IL-18BP, we used IL-18BP-deficient mice and examined their susceptibility to liver inflammation and fibrosis.

For therapeutic evaluation, we engineered APB-R3, a long-acting IL-18BP biologic, and administered it to MASH-induced mice. The pharmacological effects of APB-R3 were assessed

through histological analysis, cytokine bead arrays, flow cytometry, and Western blotting. Additionally, RNA sequencing and pathway analysis were performed to elucidate the molecular mechanisms underlying APB-R3-mediated fibrosis suppression. Finally, we compared the antifibrotic efficacy of APB-R3 with resmetirom (MGL-3196), an FDA-approved drug for MASH, in advanced fibrosis models.

Results: IL-18BP and IL-18 levels were significantly elevated in both human MASH patients and mouse models, with free IL-18 levels showing a strong positive correlation with markers of liver injury and fibrosis. In IL-18BP-deficient mice, liver inflammation and fibrosis were markedly exacerbated, confirming the protective role of IL-18BP in MASH progression.

Administration of APB-R3 in MASH-induced mice led to a significant reduction in hepatic inflammation and fibrosis. Histological analysis showed decreased collagen deposition and reduced expression of fibrotic markers. Cytokine profiling and transcriptomic analysis further revealed that APB-R3 suppressed pro-inflammatory and pro-fibrotic signaling, particularly through inhibition of IFNγ signaling and the cGMP-PKG pathway, which plays a key role in hepatic stellate cell activation.

When compared to resmetirom in severely fibrotic MASH models, APB-R3 exhibited similar or even superior antifibrotic effects, demonstrating its potential as a promising therapeutic agent for treating advanced liver fibrosis in MASH.

Conclusions: Blocking IL-18 signaling via IL-18BP biologics effectively suppresses MASH-induced fibrosis. The newly developed APB-R3 exhibits strong anti-inflammatory and antifibrotic properties, making it a promising candidate for MASH treatment. These findings highlight IL-18BP as a potential therapeutic strategy for addressing liver fibrosis in metabolic liver disease.

Keywords: IL-18BP, Fibrosis, Mash, APB-R3

Friday, May 30, 2025, 16:40-17:40

3. MASLD, Clinical 1

OP-13

Improvement of Hepatic Steatosis and Reduction in Cardiovascular Event in Patients with Diabetes Mellitus: A Prospective Study

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Aims: Patients with diabetes mellitus (DM) are at an increased risk of developing cardiovascular disease (CVD). Hepatic steatosis is common in DM, but its impact on CVD risk remains unclear. This study aimed to assess whether reducing hepatic steatosis is associated with a lower risk of CVD in patients with DM.

Methods: We prospectively enrolled 323 DM patients from January 2022, excluding those with viral hepatitis, cirrhosis, or cancer. Body weight (BW), body mass index (BMI), laboratory results, hypertension, dyslipidemia, alcohol consumption, smoking status, and anti-DM medications were collected. Hepatic steatosis was quantified using the controlled attenuation parameter (CAP) by FibroScan® at baseline and after two years. CVD was defined as ischemic heart disease or ischemic/hemorrhagic stroke

Results: A total of 277 patients completed the two-year follow-up. The mean age was 57±12 years, and 56.3% were male. The mean CAP was 274±18 dB/m. A history of CVD was present in 86(31%) patients, and 9(3.2%) developed new CVD. CAP decreased in 176 patients (d-CAP) and increased in 101 (i-CAP). The mean CAP change was -33±29 in d-CAP and +24 ±18 dB/m in i-CAP. The d-CAP was older than the i-CAP group (58±12 vs. 55±12 years, *P*=0.012). No significant differences were found in sex, BW, BMI, laboratory data, hypertension, dyslipidemia, alcohol consumption, or smoking. Insulin use was lower in d-CAP (5.1% vs. 12.9%, *P*=0.022). When stratified by CAP change, the incidence of new CVD was 0% (0/55) in patients with CAP reduction of ≤-40 dB/m, 3% (6/195) in those with changes between -40 and +40 dB/m, and 14.3% (3/18) in those with CAP increases of ≥+40 dB/m (*P*=0.007).

Conclusions: A reduction in CAP is associated with a lower risk of CVD in DM patients. CAP monitoring is a valuable tool for CVD risk assessment, and reducing hepatic steatosis may contribute to CVD prevention

Keywords: Hepatic Steatosis, Cardiovascular Event

OP-14

Sugar-Sweetened Beverage Consumption and Metabolic Dysfunction Associated Steatotic Liver Disease: Exploring Different Types of Beverages

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[1]Department of Internal medicine, Chungnam National University Sejong Hospital; [2]Department of Internal Medicine, School of Medicine, Chungnam National University; [3]Department of Internal medicine, Chungnam National University Hospital, [4]Department of Medical Science, Chungnam National University; [5]Biomedical Research Institute, Chungnam National University Hospital; [6]Department of Health Care Policy Research, Korea Institute for Health and Social Affairs

Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common liver disease. Accumulating evidence suggests a relationship between sugar-sweetened beverage (SSB) consumption and MASLD development; however, the effect of different types of SSBs on MASLD is understudied. We aimed to determine whether three different types of SSB consumption is associated with an increased risk of MASLD in Korean adults.

Methods: This study used data from the Korea National Health and Nutrition Examination Survey 2012–2016 (n=8,310, aged 40–64 years). SSB consumption (soft drinks, fruit drinks, and Korean traditional drinks) was estimated using a food frequency questionnaire. MASLD was defined as having hepatic steatosis index ≥36 and any cardiometabolic risks. Logistic regression models were used to estimate the odds ratios (ORs) with 95% confidence intervals (CIs) after adjusting for covariates.

Results: Compared to non-drinkers, soft drink consumption (≥3 servings/week) was associated with increased odds of MASLD (OR 1.36, 95% CI 1.02–1.81, *P*-trend=0.03), and Korean traditional drink consumption (≥3 servings/week) was associated with decreased odds of MASLD (OR 0.63, 95% CI 0.45–0.89, *P*-trend=0.01). No association was observed between the consumption of fruit drinks and MASLD. When stratified by sex, an inverse association between Korean traditional drinks and MASLD was observed in males (OR 0.57, 95% CI 0.34–0.95, *P*-trend=0.03) but not in females (OR 0.72, 95% CI 0.45–1.14, *P*-trend=0.17).

Conclusions: Soft drink consumption of at least 3 or more servings per week was positively associated with MASLD, whereas consumption of the same amount of Korean traditional drinks was inversely associated with MASLD.

Keywords: Sugar-Sweetened Beverage, Korean Traditional Drinks, Metabolic Dysfunction-Associated Steatotic Liver Disease, Hepatic Steatosis Index

Associations between specific types of beverage consumption and the presence of hepatic steatosis index-defined metabolic dysfunction associated steatotic liver disease, KNHANES 2012–2016

	Consumption categories [a]			
	Non-drinker	1-2 servings/wk	≥3 servings/wk	*P* trend [b]
Soft drinks				
No. of participants	5,621	2,240	449	
No. of cases (%)	1,280 (23.2)	625 (28.5)	143 (31.5)	
Multivariable-adjusted OR 1 (95% CI) [c]	1.00 (reference)	1.27 (1.10–1.48)	1.37 (1.03–1.82)	0.0193
Multivariable-adjusted OR 2 (95% CI) [d]	1.00 (reference)	1.25 (1.08–1.46)	1.36 (1.02–1.81)	0.0251
Fruit drinks				
No. of participants	5,390	2,445	475	
No. of cases (%)	1,323 (24.8)	616 (26.2)	109 (26.0)	
Multivariable-adjusted OR 1 (95% CI) [c]	1.00 (reference)	1.01 (0.88–1.16)	0.92 (0.70–1.23)	0.6079
Multivariable-adjusted OR 2 (95% CI) [d]	1.00 (reference)	1.02 (0.88–1.17)	0.95 (0.72–1.27)	0.7606
Korean traditional drinks				
No. of participants	5,569	2,398	343	
No. of cases (%)	1,406 (25.9)	569 (24.3)	73 (22.2)	
Multivariable-adjusted OR 1 (95% CI) [c]	1.00 (reference)	0.87 (0.75–1.01)	0.66 (0.47–0.93)	0.0155
Multivariable-adjusted OR 2 (95% CI) [d]	1.00 (reference)	0.87 (0.75–1.02)	0.63 (0.45–0.89)	0.0085

Abbreviation: KNHANES, Korea National Health and Nutrition Examination Survey; HSI, hepatic steatosis index; wk, week; OR, odds ratio; CI, confidence interval.
Note: Logistic regression models were used to estimate odds ratios and their corresponding 95% confidence intervals for the presence of metabolic dysfunction associated steatotic liver disease.
[a] One serving is defined as 200 mL.
[b] *P* for trends was determined by treating the median value of each type of beverage consumption as a continuous variable using the logistic regression model.
[c] Results were from the logistic regression model after adjusting for age, sex, residential area, education level, monthly household income level, marital status, current smoking, current drinking, METs/wk, and total energy intake.
[d] Results were from the logistic regression model after additionally adjusting for healthy eating index.

OP-15

Higher Age-Adjusted Skeletal Muscle Index Associated with Severe Hepatic Steatosis and Fibrosis in Male MASLD Patients

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Aims: Weight loss through diet and exercise plays a crucial role in reducing complications in metabolic dysfunction-associated steatotic liver disease (MASLD). Additionally, sarcopenia is a well-established risk factor for the development of MASLD. However, objective markers for monitoring and evaluating changes in body fat and muscle mass based on the severity of MASLD remain insufficiently studied.

Methods: A cross-sectional study of 174 Male MASLD patients assessed hepatic steatosis and fibrosis using FibroScan. Body composition was measured using bioelectrical impedance analysis(BIA). We aimed to analyze differences in body composition and identify significant factors associated with the severity of steatosis and fibrosis using appropriate statistical methods.

Results: The average age of the patients was 40.0 years, and the median body mass index (BMI) was 28.8 kg/m^2. Among the 140 patients with severe steatosis (CAP ≥ 290), compared to those with mild to moderate steatosis, the severe steatosis group had a higher BMI (29.6 kg/m^2 vs. 25.8 kg/m^2) and waist circumference (102.9 cm vs. 92.5 cm). In the body composition analysis, the severe steatosis group demonstrated significantly higher values in visceral fat area, muscle mass, fat mass, and skeletal muscle index (SMI). Mutiple regression analysis revealed a positive association between the severity of steatosis and higher age adjusted SMI along with the modest alcohol consumption and elevated triglyceride levels. For advanced fibrosis (≥10 kPa), both higher SMI Z-score and elevated AST levels were positively correlated with the outcome.

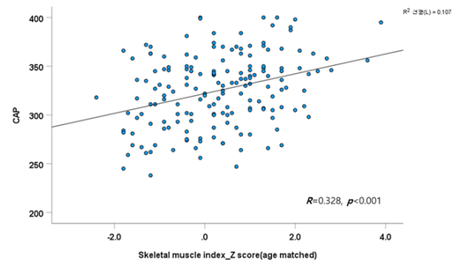

Figure 1.

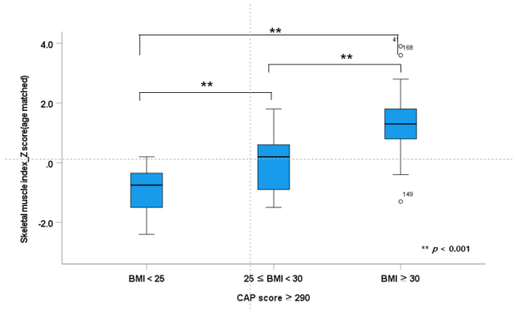

Figure 2.

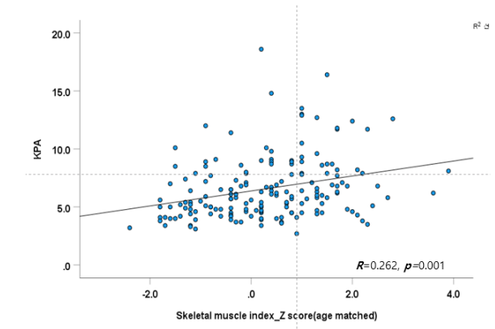

Figure 3.

Conclusions: In male patients with MASLD, age-adjusted SMI (Z score) was associated with both the severity of steatosis and advanced fibrosis. The use of body composition parameters, may be considered as a reliable objective tool for monitoring the progression and improvement of MASLD through individualized intervention strategies.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Steatosis, Fibrosis, Body Composition Analysis

OP-16

Effect of Vitamin E on Liver Stiffness in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: Current guidelines on the therapeutic efficacy of vitamin E on metabolic dysfunction-associated steatotic liver disease (MASLD) are based on limited evidence and it is not clear if vitamin E affects liver fibrosis in MASLD patients. Vibration-controlled transient elastography (VCTE) is a well-established non-invasive method for assessing liver fibrosis in MASLD. In this study, we evaluated the effect of vitamin E on the liver stiffness measured by VCTE in patients with MASLD.

Methods: In this retrospective cohort study, we identified MASLD patients who underwent serial measurements of liver stiffness by VCTE. Patients with viral hepatitis were excluded. Administration of other hepatotonics, i.e., ursodeoxycholic acid, silymarin, biphenyl dimethyl dicarboxylate, were controlled as covariates by multivariate linear regression analysis.

Results: A total of 5,055 patients with MASLD received at least 2 measurements of liver stiffness by VCTE during the period between July 2020 and March 2025. After excluding 1,206 patients with chronic hepatitis B and 105 patients with chronic hepatitis C, 3,746 patients were finally selected for analysis. 724 days (interquartile range = 549). The median change in liver stiffness measurement (LSM) was -0.2 kPa, -3.6% from baseline (interquartile range = 2.2kPa, 40%).

The median duration of vitamin E therapy was 455 days (interquartile range = 720). Multivariate logistic regression analysis showed that use of vitamin E for more than 3 months was associated with significant improvement in LSM: the odds ratio for improvement of LSM more than 50% from baseline was 2.40 (95% confidence interval, 1.68 – 3.43).

Conclusions: Use of vitamin E was associated with significant improvement of LSM in MASLD patients.

Keywords: MASLD, Vitamin E, Liver Stiffness, Transient Elastography

OP-17

Changing Prevalence and Risks Factors of Metabolic Dysfunction Associated Steatotic Liver Disease during Three Decades in Taiwan

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Aims: Metabolic dysfunction associated steatotic liver disease (MASLD) was the most rapid growing etiology of liver disease. We aimed to investigate the changes in the prevalence of MASLD in Taiwan during the past three decades.

Methods: We enrolled participants from two large cohort in Taiwan since 1996 to 2021. Participants' demographics and biochemistry data were collected. Steatotic liver disease (SLD) was defined by either abdominal ultrasound, or serum panels. MASLD was defined as SLD with at least one cardiometabolic risk factor (CMRF) accordingly. The endpoints were the changes in the prevalence of SLD, CMRF, and MASLD.

Results: A total of 729,061 participants with a mean age of 42.2 years old and 54.5% of females were enrolled. The overall prevalence of MASLD were 31.5%, and participants from Eastern Taiwan had the highest prevalence of MASLD, SLD, and CMRFs. There was a significantly increased prevalence of MASLD from 25.6% on period 1996-2000 to 37.2% on period 2016-2021. Participants of aged <40 years had a persistently increased MASLD prevalence, but a decreased prevalence was found in those aged >40 years after 2010. Males showed a significantly higher increased rate of MASLD. Similar trends of SLD and CMRF were also found in different age and gender population. Overweight/obesity was the most increased CMRF in young aged participants, and preDM/DM was the more common and increased CMRF in older aged participants. Old age, male, and living in Southern Taiwan demonstrated significantly increased risks of MASLD in all the periods. But young aged participants had a higher relatively risk across all the periods.

Conclusions: The prevalence of MASLD significantly increased in the past three decades in Taiwan, especially in those of young age, males, and living in Southern Taiwan. Future efforts in the reduction of MASLD must be done especially in these risk populations.

Keywords: Metabolic Dysfunction Associated Steatotic Liver Disease, SLD, Prevalence, Risk Factor

OP-18

Association between Smoking and Clinical Outcomes in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is an increasingly prevalent liver disorder. This study assessed the impact of smoking status on clinical outcomes in MASLD and metabolic dysfunction and alcohol-associated liver disease (MetALD).

Methods: Data from the UK Biobank were used. Primary outcomes included all-cause and liver-related mortality, while secondary outcomes comprised liver cirrhosis, cardio-cerebrovascular diseases (CVD), hepatic decompensation, and hepatocellular carcinoma (HCC). Associations were analyzed using multivariate Cox proportional hazards models, with confounders adjusted using inverse probability of treatment weighting.

Results: Never and previous smokers exhibited significantly lower hazard ratios (HRs) for mortality compared to current smokers across all cohorts. In the MASLD cohort, never smokers had HRs of 0.43 [95% confidence interval (CI): 0.41-0.44, *P*<0.001]. Never smokers also had lower rates of liver cirrhosis in the No steatotic liver disease (SLD) and MASLD cohorts, with HRs of 0.31 (95% CI: 0.22-0.43, *P*<0.001) and 0.60 (95% CI: 0.51-0.70, *P*<0.001), respectively. No significant difference was observed in MetALD. CVD incidence was also lower in never smokers across all cohorts, with HRs of 0.49 (95% CI: 0.45-0.52, *P*<0.001) in the No SLD cohort, 0.56 (95% CI: 0.53-0.59, *P*<0.001) in the MASLD cohort, and 0.60 (95% CI: 0.55-0.66, *P*<0.001) in the MetALD cohort. In MASLD, never smokers had lower risk of hepatic decompensation (HR: 0.61, 95% CI: 0.50-0.74, *P*<0.001) and HCC (HR: 0.57, 95% CI: 0.37-0.87, *P*=0.010). In contrast, smoking status was not significantly associated with hepatic decompensation or HCC in MetALD.

Conclusions: While impact of smoking was clear in MASLD, its effects in MetALD were less pronounced, likely due to the stronger influence of alcohol on liver disease. These findings emphasize smoking cessation for both MASLD and MetALD, with targeted interventions for MASLD.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Smoking, Survival, Liver Cirrhosis

Friday, May 30, 2025, 16:40-17:40

4. LC, Clinical and Liver Failure

OP-19

Impact of Cardiometabolic Risk Factors on Hepatic Fibrosis and Clinical Outcomes in MASLD: A Population-Based Multi-Cohort Study

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Aims: Evaluating five cardiometabolic risk factors (CMRFs) is crucial for diagnosing metabolic dysfunction-associated steatotic liver disease (MASLD). This study investigated the impact of CMRFs on hepatic fibrosis and long-term clinical outcomes in MASLD patients.

Methods: Two cross-sectional cohorts—Korean magnetic resonance elastography (n=6684) and United States vibration-controlled transient elastography (n=6230)—were included to assess the impact of five CMRFs and their combinations on hepatic fibrosis. Two longitudinal cohorts—United Kingdom Biobank (n=408,544; mean follow-up, 14.3 years) and Korea National Health Insurance data (n=355,640; mean follow-up, 11.7 years)—were included to evaluate long-term outcomes including liver-related events, hepatocellular carcinoma events, overall, cardiovascular, and liver-related death. The risk of MASLD associated with CMRFs was assessed using Logistic or Cox regression analysis, referencing participants without SLD.

Results: Across all four cohorts, patients with type 2 diabetes mellitus (T2DM) had the highest risk of hepatic fibrosis and long-term clinical outcomes. Among the five CMRFs, impaired fasting glucose (CMRF2) was the most significant risk factor for both hepatic fibrosis and long-term clinical outcomes. High blood pressure (CMRF3) was the second most significant risk factor for hepatic fibrosis, following CMRF2. Low high-density lipoprotein cholesterol level (CMRF5) exhibited comparable significance for long-term clinical outcomes. These clinical outcomes worsened with increasing severity of glucose abnormalities (normal and impaired fasting glucose levels and T2DM). Patients with MASLD and CMRF2 exhibited a 2–4 times higher risk than those without impaired fasting glucose levels, similar to MASLD accompanied by any four CMRFs.

Conclusions: The impact of the five CMRFs on hepatic fibrosis and long-term clinical outcomes varied across different clinical outcomes and population characteristics. However, CMRF2 consistently demonstrated the highest risk.

Keywords: Hepatic Fibrosis, Cardiometabolic Risk Factors, Cohort, T2DM

OP-20

Spleen Stiffness Measurement Using New Spleen-Dedicated Fibroscan: Intra/Interobserver Repeatability

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Aims: Bleeding from esophageal varix is one of the most life-threatening complications of portal hypertension, which is a major consequence of liver cirrhosis. The spleen stiffness measurement (SSM) by standard Fibroscan® (SSM@50Hz) has been evaluated as the non-invasive diagnostic tool for esophageal varix. Recently, the SSM using a novel spleen-dedicated Fibroscan® (SSM@100Hz) has been developed and found to have a better accuracy than SSM@50Hz. The aim of this research was to evaluate the intra- and interobserver repeatability of SSM@100Hz.

Methods: Eighty-four patients with chronic liver disease were randomly allocated to group 1 (for evaluation of intraobserver repeatability) or group 2 (for evaluation of interobserver repeatability), respectively. In group 1, both of two sessions of SSM@100Hz were performed by one radiologist. In group 2, the first session of SSM@100Hz was performed by one radiologist and the second session of SSM@100Hz was performed by another radiologist without the information about the result of the first session.

Results: Overall success rate of SSM@100Hz was 94% (79/84). Median SSM of total patients was 16.7 kPa (interquartile range [IQR] 13.2 - 19.9kPa) with 17.4 kPa (IQR 13.3 - 20.3kPa) in group 1 and 16.2 kPa (IQR 13.0 - 19.9kPa) in group 2, respectively. The intraobserver repeatability in group 1 revealed a high intra-class correlation coefficient (ICC) (0.977, 95% confidence interval [CI]: 0.955, 0.988) and, in group 2, interobserver repeatability also showed a high ICC (0.958, 95% CI: 0.919, 0.978).

Conclusions: SSM@100Hz is a feasible and highly reproducible tool in patients with chronic liver disease.

Keywords: Spleen Stiffness Measurement, Spleen-Dedicated Fibroscan, Portal Hypertension, Liver Cirrhosis

OP-21

Validation and Comparative Performance of Postoperative Risk Scores in Cirrhotic Patients: A Korean Cohort Study

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Aims: Patients with cirrhosis are at increased risk of postoperative mortality. Several models have been developed to predict postoperative risk in cirrhotic patients, including the VOCAL-Penn, Mayo risk, Model for End-Stage Liver Disease (MELD), MELD-sodium (MELD-Na), MELD-3.0, and Child-Pugh scores. However, validation of the VOCAL-Penn score and comparisons among these models in a Korean cohort remain limited. This study aimed to validate the predictive performance of the VOCAL-Penn score and compare it with the Mayo risk, MELD, MELD-Na, MELD-3.0, and Child-Pugh scores in a Korean population.

Methods: We performed a retrospective cohort study of patients with cirrhosis undergoing surgical procedures of interest at Eunpyeong St. Mary's Hospital and Uijeongbu St. Mary's Hospital from June 1, 2009, to May 1, 2024. The outcomes of interest were 30-day, 90-day, and 180-day postoperative mortality. Predictive performance was assessed using concordance statistics (C-statistics), calibration curves, Brier scores, and the Index of Prediction Accuracy (IPA).

Results: A total of 375 surgical procedures were identified. The VOCAL-Penn score had the numerically highest AUROC and C-statistic for 90-day postoperative mortality (e.g., AUROC 0.813 vs. 0.779 Mayo, 0.769 MELD-Na, 0.75 MELD, 0.794 MELD-3.0, 0.755 Child-Pugh; C-statistic 0.801 vs. 0.773 Mayo, 0.778 MELD-Na, 0.765 MELD, 0.791 MELD-3.0, 0.784 Child-Pugh), although differences were not statistically significant. The VOCAL-Penn also had the lowest Brier score and highest IPA at all time points, indicating superior overall predictive performance.

Conclusions: The VOCAL-Penn score demonstrated superior predictive accuracy for postoperative mortality in cirrhotic patients compared to established risk scores. Its higher AUROC, C-index, and lower Brier Score suggest it may be a valuable tool for perioperative risk stratification in this high-risk population. Further prospective validation is warranted to confirm these findings

Keywords: Cirrhosis, Surgery, Mortality

OP-22

Transplantation of Autologous Bone Marrow-Derived Mesenchymal Stem Cells for Decompensated Liver Cirrhosis: A Real-World Evidence Study in a Population-Based Cohort

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Aims: Despite medical advances of recent decades, the mortality rate of advanced liver cirrhosis remains high. Although liver transplantation remains the most effective treatment, candidate selection is limited by donor availability and alcohol abstinence requirements. Bone marrow-derived mesenchymal stem cells (BM-MSCs) have shown promise for the treatment of advanced cirrhosis. However, trials tend to involve small patient numbers, and long-term follow-up studies are lacking. This study assessed BM-MSC transplantation outcomes using real-world evidence (RWE) with dynamic matching to reduce bias.

Methods: A control group was selected using exposure density sampling (EDS) to reduce immortal time bias. Mortality rates were compared using Kaplan–Meier survival analysis and Cox proportional-hazard regression models, with adjustments for baseline characteristics.

Results: The cumulative incidences of 5-year mortality were 0%, 5.0%, and 11.3% at 1, 3, and 5 years in the BM-MSC group, compared with 7.0%, 10.9%, and 42.1% in the control group. The Kaplan–Meier analysis revealed no significant difference in 1-year mortality between the BM-MSC and control groups (P=0.140). However, 3- and 5-year mortality were significantly lower in the BM-MSC group (P<0.001). The adjusted hazard ratios for 5-year mortality in the BM-MSC group were 0.18 (95%CI: 0.04–0.87) and 0.14 (95%CI: 0.02–0.82) under two models, indicating a lower mortality risk compared to controls.

Conclusions: This study highlights the potential of BM-MSC transplantation in reducing long-term mortality in patients with alcoholic cirrhosis. The use of RWE provides a valuable framework for evaluating treatment efficacy and overcoming RCT limitations, setting a precedent for future clinical research.

Keywords: Stem Cell Therapy, Liver Cirrhosis

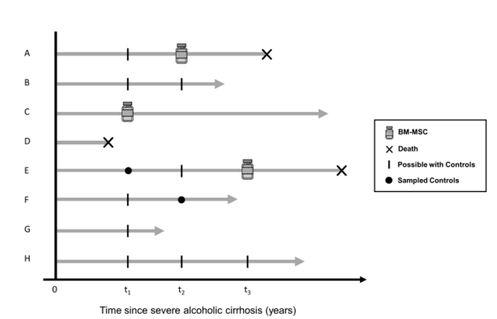

Figure 1.

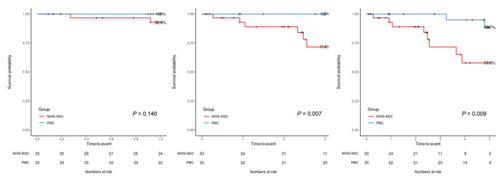

Figure 2.

OP-23

Impact of Hepatic Encephalopathy on Prognosis in Cirrhotic Patients with Acute Decompensation: The Crucial Role of Underlying Liver Function and Coagulation Failure

Jung Hee Kim[1], Sung-Eun Kim[1], Ae Jeong Jo[2], Do Seon Song[3], Hee Yeon Kim[3], Eileen L. Yoo[4], Ji Won Park[1], Young-Kul Jung[5], Ki Tae Suk[1], Hyung Joon Yim[5], Seong Hee Kang[5], Seul Ki Han[6], Sung Won Lee[3], Moon Young Kim[6], Young Chang[7],Soung Won Jeong[7], Jae-Young Jang[7], Jeong Ju Yoo[8], Sang Gyune Kim[8], Young-Joo Jin[9], Hyoungsu Kim[1], Jung Gil Park[10], Won Kim[11], Dong Joon Kim[1], on behalf of the Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

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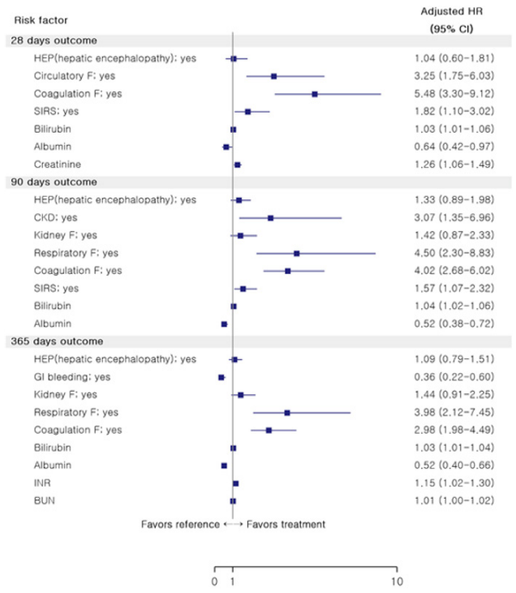
Aims: Hepatic encephalopathy (HEP) is a major complication of cirrhosis, resulting in significant impairment of the quality of life and frequent hospitalizations. HEP is considered one of the major components in the diagnosis of acute-on-chronic liver failure (ACLF), HEP is well known that it is associated with high mortality. However, there is controversial to whether HEP itself has a direct effect on the patient's prognosis and whether underlying liver function is important. This study aimed to investigate the impact of HEP on acute decompensation (AD) and adverse outcome (death or liver transplantation), utilizing real-world data.

Methods: We analyzed prospective multicenter data collected from 31 hospitals in South Korea from 2015 to 2019. We included 1,315 patients diagnosed with liver cirrhosis who were admitted due to acute decompensation. A comparative analysis was conducted to assess the risk factors and the incidence of death or liver transplantation between patients with and without HEP. Propensity score (PS) matching was employed at a 1:3 ratio for accurate comparisons. PS were computed using the following 4 variables: age; sex; etiology of cirrhosis; and MELD score

Results: The mean age of the entire cohort was 54.7 years, with 74.9% being male. HEP was noted in 14.7% of the cohort. Patients with HEP had positive correlations with ascites, jaundice and upper gastrointestinal bleeding. The median follow-up period was 8.0 months (range, 1.0–15.0 months), during which 332 patients (23.7%) either died or underwent liver transplantation. After adjusting for various factors, coexisting HEP did not increase the risk of death or liver transplantation for short-term and long-term. However, coagulation failure, underlying liver function such as prolonged prothrombin time, low serum albumin and elevated total bilirubin were revealed as major risk factors for short-term and long-term adverse outcomes.

Conclusions: In cirrhotic patients presented with HEP at admission, the presence of coagulation failure significantly increases the risk of short-term and long-term adverse outcomes. Although HEP is well-known risk factor in patients with cirrhosis with AD, the most important concept is underlying liver function, especially if coagulation failure is noted, so it is necessary to anticipate that the prognosis may be the worst and plan to early liver transplantation.

Keywords: Hepatic Encephalopathy, Liver Cirrhosis, Acute Decompensation, Acute-On-Chronic Liver Failure



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5. Liver Transplantation 1

OP-24

Renal Recovery Benefit of Living Donor Compared to Deceased Donor Liver Transplantation in High-MELD Recipients: A Propensity Score-Matched Study

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Aims: Patients with a high Model for End-Stage Liver Disease (MELD) score (>35) face significant perioperative risks, making the choice between deceased donor liver transplantation (DDLT) and living donor liver transplantation (LDLT) difficult due to differences in graft availability and patient condition. This study aimed to compare clinical outcomes between LDLT and DDLT in high-MELD recipients and identify factors influencing post-transplant survival.

Methods: We retrospectively analyzed patients with a MELD score >35 who underwent LT at Asan Medical Center from January 2000 to June 2021. Patients were divided into LDLT (n=326) and DDLT (n=386) groups, and propensity score matching (PSM) was performed (188 pairs). A subgroup analysis was conducted for patients requiring preoperative renal replacement therapy (RRT) to assess post-transplant renal recovery. The study outcomes were patient and graft survival.

Results: After PSM (188 pairs), total ischemic time was significantly longer in DDLT (347.5 vs. 38.0 min, $P<0.001$), while operation time was longer in LDLT (803.5 vs. 628.5 min, $P<0.001$). In-hospital mortality was initially higher in DDLT (20.2% vs. 8.0%, $P<0.001$) but was not significant after matching (12.2% vs. 9.0%, $P=0.332$). Overall survival at 1, 3, and 5 years was superior in LDLT (82.2% vs. 73.8%, 78.2% vs. 66.0%, and 76.3% vs. 61.3%, $P<0.001$). Graft survival also favored LDLT (81.0% vs. 71.5% at 1 year, 77.3% vs. 63.5% at 3 years, and 75.1% vs. 57.3% at 5 years, $P<0.001$). Multivariate analysis identified age >65 years (HR 1.66, $P=0.015$), re-transplantation (HR 1.98, $P<0.001$), and vasopressor use (HR 1.57, $P=0.008$) as risk factors for overall survival. Among patients requiring preoperative RRT, renal recovery was significantly higher in LDLT (56.2% vs. 30.5%, $P<0.001$).

Conclusions: LDLT was not inferior to DDLT in high-MELD patients. Timely LDLT may improve renal recovery and post-transplant outcomes, highlighting the need for individualized decision-making in LT allocation.

Keywords: MELD, LDLT, DDLT

OP-25

Impact of Radiation Therapy on Biliary Complications in Liver Transplant Hepatocellular Carcinoma Recipients Withoma: A Propensity Score-Matched Analysis

Min-Ha Choi, Sang-Hon Kim, Shin Hwang, Chul-Soo Ahn, Deok-Bog Moon, Tae-Yong Ha, Gi-Won Song, Gil-Chun Park, Ki-Hun Kim, Woo-Hyoung Kang, Young-In Yoon, Byeong-Gon Nah, Sung-Min Kim, Sung-Gyu Lee, Dong-Hwan Jung

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Aims: The role of radiation therapy (RT) in managing hepatocellular carcinoma (HCC) patients has significantly expanded. Therefore, the use of radiation therapy for pre-transplantation has also increased these days. However, its impact on post-transplant outcomes, particularly biliary complications, is not well defined This study aims to evaluate the effect of RT on biliary complications in LT recipients with HCC, utilizing propensity score-matching method for analysis.

Methods: A retrospective study was conducted on 1,008 HCC patients underwent LT between January 2018 and December 2023. Patients were classified into RT and non-RT groups. Propensity score matching was performed to ensure comparability. As the primary outcome, biliary complications were assessed. Logistic regression method was employed to analyze risk factors.

Results: RT was associated with an increased risk of biliary complications in both unmatched and matched analyses, particularly in biliary stricture($P=0.005$). Logistic regression analysis identified RT as an independent risk factor for biliary complications, with the unmatched cohort showing an OR of 1.642 ($P=0.033$) and the matched cohort demonstrating an OR of 1.960 ($P=0.015$). Other factors like separated multiple bile duct anastomosis ($P=0.019$) and dual LDLT(Living donor liver transplantation) ($P=0.004$) are also significant risk factor of bile duct complication.

Conclusions: RT in LT recipients with HCC is associated with a higher risk of biliary complications. Also, separated multiple bile duct anastomosis and dual LDLT can affect post-transplantation outcome. Future prospective studies are necessary to optimize RT protocols and improve outcomes in this population.

Keywords: Radiation Therapy, Liver Transplantation, Biliary Complication

OP-26

ABO Incompatible Dual Graft Living Donor Liver Transplantation Using Modified Extended Left Lateral Graft: Case Report

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Aims: Liver transplantation is a life-saving procedure for patients with end-stage liver disease, but the availability of suitable donor grafts remains a significant challenge. Innovative surgical techniques are essential to expand donor options while maintaining favorable outcomes for both donors and recipients.

Methods: A 54-year-old male with hepatitis B-related cirrhosis underwent an ABO-incompatible dual graft liver transplantation. The procedure involved a modified right lobe graft from one donor and a modified extended left lateral graft from an-

other donor. To minimize donor morbidity, the middle hepatic vein (MHV) was excluded from the grafts, and MHV reconstruction in the recipient was performed using a donor-derived vein allograft to ensure optimal venous outflow. Post-operative management included plasma exchange and immunosuppressive therapy to prevent rejection.

Results: The dual graft transplantation achieved a GRWR of 1.27, ensuring sufficient graft volume for the recipient. Post-operative recovery was uneventful, with no significant complications. The recipient demonstrated normalized liver function within weeks, and both donors recovered fully without long-term sequelae.

Conclusions: This case demonstrates the effectiveness of a modified dual graft technique in addressing the challenges of limited graft availability while ensuring a sufficient graft-to-recipient weight ratio (GRWR). By prioritizing donor safety and optimizing recipient outcomes, this method offers a promising strategy for managing high-risk liver transplant cases. It also highlights the potential for expanding donor options and improving the applicability of dual graft techniques in complex clinical scenarios.

Keywords: Transplantation, Dual Donor Ldlt, Liver

OP-27

Liver Transplantation Can Be a Treatment Option for Patients with Cholangiocarcinoma: A Single-Center Experience

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Department of Transplantation surgery, Samsung Medical Center, Korea

Aims: cholangiocarcinoma is not a widely accepted indication for liver transplantation. The present study describes our institutional experience with patients with both intrahepatic cholangiocarcinoma and perihilar cholangiocarcinoma who underwent transplantation for cholangiocarcinoma

Methods: Data corresponding to patients with cholangiocarcinoma were retrospectively reviewed for the purposes of this study. Data were obtained by including all patients who underwent liver transplantation for cholangiocarcinoma at Samsung Medical Center between 2000 and 2023

Results: A total of 10 patients underwent liver transplantation for cholangiocarcinoma at Samsung Medical Center. Among them, 4 patients had perihilar cholangiocarcinoma, and 6 patients had intrahepatic cholangiocarcinoma. Among the patients who underwent liver transplantation for cholangiocarcinoma, only one experienced recurrence of the disease. The one-year survival rate for these patients was 40%, respectively. Most of the deaths within the first year were due to postoperative complications, such as biliary complications leading to sepsis or complications caused by infection. The disease-free survival was 32 months, 77 months, 87 months, and 155 months, respectively, in patients who did not experience recurrence and were alive

Conclusions: Excluding postoperative complications of liver transplantation and considering the recurrence of cholangiocarcinoma, liver transplantation can be a sufficient treatment option for cholangiocarcinoma. To validate the therapeutic outcomes of liver transplantation in cholangiocarcinoma, a larger number of cases and multicenter studies will be necessary

Keywords: Cholangiocarcinoma, Liver Transplantation

OP-28

Bile Duct Complication and Impact on Outcomes after Living-Donor Liver Transplant: A Machine Learning Approach

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Aims: Liver transplantation from living donors (LDLT) has become a common practice for end-stage liver disease. However, bile duct complications are a significant challenge that can impact post-transplant outcomes. This systematic review aims to assess the role of machine learning in predicting bile duct complications and their subsequent effects on patient outcomes following LDLT.

Methods: We conducted a systematic review of studies published between 2013 and 2024 that utilized machine learning techniques to analyze bile duct complications in LDLT patients. Databases searched included PubMed, Scopus, and EBSCO. Inclusion criteria were studies that applied machine learning models to predict or analyze bile duct complications and their outcomes. Data extraction focused on study design, machine learning methods used, predictive accuracy, and clinical outcomes.

Results: Out of 14 studies reviewed, 8 employed various machine learning algorithms including decision trees, random forests, and neural networks to predict bile duct complications. The majority reported high predictive accuracy, with models achieving area under the curve values ranging from 0.75 to 0.92. Complications such as bile leak and stricture were significantly associated with poorer post-transplant outcomes, including increased reoperation rates and reduced graft survival. Machine learning models demonstrated potential in early detection and risk stratification, improving clinical decision-making.

Conclusions: Machine learning approaches show promise in predicting bile duct complications after LDLT, potentially leading to better management and improved patient outcomes. Incorporating these models into clinical practice could enhance preoperative planning and postoperative care. Further research with larger datasets is needed to confirm and optimize machine learning applications in this context.

Keywords: Bile Duct, Liver, Transplantation

OP-29

Outcomes and Risk Factors for De Novo Major Depressive Disorder after Liver Transplantation: Nested Case-Control Study

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Aims: Major depressive disorder (MDD) is a major psychiatric complication of liver transplantation (LT). Here, we aimed to analyze the impact of de novo MDD on survival post-LT and identify risk factors for this disorder among LT recipients.

Methods: A retrospective analysis was conducted on 1350 LT recipients at Severance Hospital, Korea, from July 2005 to December 2022. Patients with MDD were matched 1:5 with controls using a nested case-control design to control for immortal time bias.

Results: During follow-up post-LT, 58 patients (4.3%) were newly diagnosed with MDD. The median time from LT to MDD diagnosis was 316 (interquartile range 46–920) days. Patients with MDD had significantly lower graft survival rates than controls at 1, 3, and 5 years after matching (89.5%, 75.3%, and 66.5% vs. 95.5%, 91.5%, and 86.4%, respectively; *P*=0.003). Multivariable Cox regression identified de novo MDD as an independent risk factor for reduced graft survival (hazard ratio 2.39, 95% confidence interval [CI] 1.15–4.98, *P*=0.003). Independent risk factors for de novo MDD included female sex (odds ratio [OR] 2.29, 95% CI 1.16–4.53, *P*=0.017), alcoholic liver disease (OR 2.36, 95% CI 1.16–4.75, *P*=0.016), pre-transplant encephalopathy (OR 2.95, 95% CI 1.49–5.79, *P*=0.002), and lower hemoglobin levels (OR 0.85, 95% CI 0.73–0.98, *P*=0.025).

Conclusions: In our matched population of nested case controls, de novo MDD significantly reduced the survival of LT recipients. Screening and early intervention are required for LT recipients with risk factors for MDD.

Keywords: Major Depressive Disorder, Liver Transplantation, Nested Case-Control

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6. Liver Cancer, Basic 1

OP-30

Identification of IKBKB as a Novel Regulator of Macrophage Phagocytosis That Enhances Antitumor Immunity in Hepatocellular Carcinoma

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Aims: Phagocytosis checkpoints function as critical "don't eat me" signals that suppress immune responses in cancer immunotherapy. Given the druggable nature of protein kinases and their antitumor effects, we aim to identify key kinases involved in phagocytic evasion in hepatocellular carcinoma (HCC).

Methods: An *in vitro* CRISPR-based kinome screen targeting 713 mouse kinase genes was performed in a co-culture system, where mouse HCC cells RIL-175 interacted with RAW 264.7 macrophages. *In vitro* and *in vivo* phagocytosis assays were evaluated using a cell-based co-culture system and HCC xenograft model. Molecular pathways mediating phenotypic alterations were identified using promoter assays, western blotting, immunofluorescence staining, and flow cytometry analysis. Clinical correlation and significance were evaluated in publicly available HCC datasets.

Results: We identified *Ikbkb* (Inhibitor of kappaB kinase beta) as a novel negative regulator of phagocytosis. Perturbation of *Ikbkb* significantly enhanced cancer cell phagocytosis and promoted macrophage activation in co-culture conditions. Depletion of *Ikbkb* suppressed HCC tumor growth, accompanied by increased *in vivo*macrophage phagocytosis and infiltration. The tumor-promoting role of *Ikbkb* through its anti-phagocytic function was further demonstrated by the observation that the growth-suppressive effect in *Ikbkb* knockout cells was offset by *in vivo* depletion of macrophages using clodronate liposomes. Mechanistically, *Ikbkb*facilitates evasion from macrophage-mediated phagocytosis by driving transcriptional activation of the anti-phagocytic checkpoints CD47 and PD-L1 via canonical NF-kB signaling. Clinically, *IKBKB* overexpression in multiple HCC patient cohorts correlated with disease progression. Additionally, *IKBKB* expression was significantly associated with *CD47* and *PD-L1*, as well as reduced monocyte infiltration. These findings highlight the anti-phagocytic role of tumor-expressed IKBKB and suggest the therapeutic potential of targeting IKBKB in HCC.

Conclusions: We have identified IKBKB as a cancer-intrinsic regulator of phagocytosis, presenting a novel target to enhance

the efficacy of immune checkpoint therapies for HCC patients.

Keywords: Phagocytosis, Crispr Screen, Macrophages

OP-31

Identifying the Key Factors Contributing to the Progress of Liver Fibrosis to Cancer and the Tumor Microenvironment Immunosuppression

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Aims: Protein kinases are critical therapeutic targets for curing hepatocellular carcinoma (HCC). As a serine/threonine kinase, the potential roles of serine/threonine kinase 39 (STK39) in liver fibrosis and cancer remain to be explored.

Methods: We profile the whole kinome expression in clinical liver cancer samples and identify the overexpression of STK39. Then we established the STK39 knockout mice using the CRISPR/Case9 technology and further investigated the role of STK39 in different liver fibrosis and cancer models. The expression of STK39 was examined by RT-qPCR, western blotting and immunohistochemistry. The cell proliferation and apoptosis were detected by CCK8 and TUNEL kit. Cell migration and invasion assay were performed using a transwell system with or without Matrigel. RNA-seq, mass spectrometry and luciferase reporter assay were used to identify STK39 binding proteins.

Results: We firstly report that STK39 is highly overexpressed in clinical HCC tissues compared with adjacent tissues, high expression of STK39 was induced by transcription factor SP1 and correlates with a poor patient's survival. Gain and loss of function assays revealed that overexpression of STK39 promotes HCC cell proliferation, migration and invasion. In contrast, the depletion of STK39 attenuated the growth and metastasis of HCC cells. Moreover, knockdown of STK39 induces the HCC cell cycle arrested in the G2/M phase and promotes apoptosis. In mechanistic studies, RNA-seq revealed that STK39 positively regulates the ERK signaling pathway. Mass spectrometry identified that STK39 binds to PLK1. STK39 promotes HCC progression and activates ERK signaling pathway that was dependent on PLK1. In the STK39 knockout mice model, we found the critical role of STK39 in viral infection and the progression of liver fibrosis and cancer.

Conclusions: Our study uncovers a novel role of STK39 in viral infection and the progress of liver fibrosis and cancer and suggests STK39 as a prognosis biomarker and a promising drug target of liver fibrosis and cancer.

Keywords: Liver Fibrosis, Liver Cancer, Tumor Microenvironment, Immunosuppression

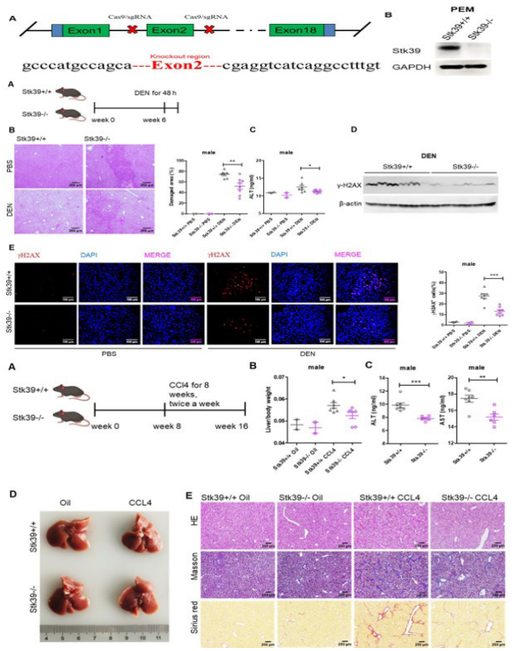

Figure 1. Establishment of the STK39 knockout mice and induced liver injury and fibrosis models-

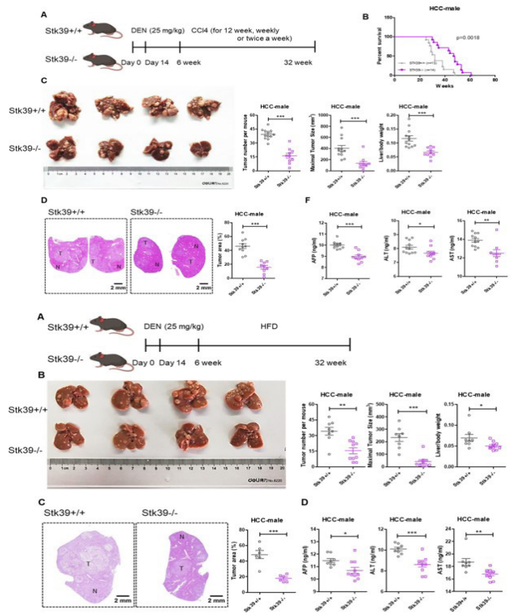

Figure 2. The different induced liver cancer models in the STK39 knockout mice.

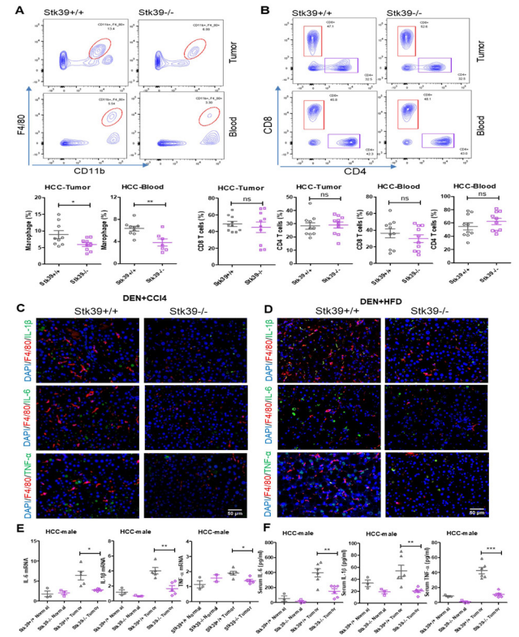

Figure 3. STK39 promotes inflammation and immune microenvironment in hepatocellular carcinoma.

OP-32

Inhibition of PLD1 Increases Apoptosis in Hepatocellular Carcinoma Cells

Ha Neul Kim[1,2,3], In Soo Kim[4], Hei Gwon Choi[1,2,3], Soon Ok Kim[3], Seok-Hwan Kim[10], Hyuk Moon[11], Simon Weonsang Ro[11], Eun-Kyeong Jo[5,6], Won-Il Jeong[7], Hyuk Soo Eun[3,8,9]

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Aims: The progression and metastasis of hepatocellular carcinoma (HCC) lead to poor prognosis in patients. The PLD1 gene is highly expressed in HCC. Additionally, while PLD1 is influenced by receptor tyrosine kinases (RTK), there has been no research to investigate the impact of PLD1 on RTK. We aimed to investigate the effect of PLD1 expression regulation on RTK and HCC.

Methods: Gene expression data of HCC patients were compared using TCGA data. The effects of PLD1 expression knockdown or overexpression in HCC cells on hepatocellular carcinoma were evaluated. In addition, HCC-specific PLD1 knockdown mice were evaluated, and RNA-sequencing was performed on mouse liver tumor tissues.

Results: In TCGA data, HCC patients with high expression of PLD1 gene showed a worse trend in disease-free survival (P=0.04) and overall survival (P=0.07). PLD1 expression was suppressed in HCC cells, and the expression of EGFR and c-MET was decreased (P=0.05). On the other hand, caspase3 (P=0.05) and Bak (P=0.04) were increased, and cell migration, proliferation, and metastasis were decreased. HCC-specific PLD1 KD mice showed a decrease in tumor number and size compared with the control group. Caspase9 (P=0.03) and Bak (P=0.04) protein expression was increased in mouse HCC tissues. RNA-seq data showed that HCC-specific PLD1 KD decreased MAPK gene expression.

Conclusions: Inhibition of PLD1 increased apoptosis of HCC cells and reduced the number and size of HCCs in mice. Modulation of PLD1 is a novel target for HCC treatment.

Keywords: Hepatocellular Carcinoma, HCC, PLD1, Apoptosis

OP-33

Genomic Analysis of Combined Hepatocellular-Cholangiocarcinoma Reveals Common Lineage of Tumor Components with Unique Gene Expression Profile

Yeshong Park[1], Seung Yeon Lim[1], Hyelim Joo[1], Boram Lee[1], Jai Young Cho[1], Yoo-Seok Yoon[1], Ho-Seong Han[1], Hee Young Na[2], Hae Won Lee[1]

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Aims: Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a rare primary liver cancer that exhibits both hepatocytic and biliary differentiation. cHCC-CCA is associated with prognosis worse than hepatocellular carcinoma (HCC) and similar to intrahepatic cholangiocarcinoma (iCCA), partly due to misdiagnosis and wrong-directed treatment. The aim of this study was to investigate genomic alterations for accurate diagnosis of cHCC-CCA.

Methods: We performed whole exome sequencing for 31 histologically defined cHCC-CCA in both hepatocytic and biliary tumor components and matched normal tissues. In total, 90 samples were analyzed. The mutational profile of hepatocytic

and biliary tumor components were compared. Identified mutations were further correlated with known hotspot mutations of HCC and iCCA.

Results: Among 58 samples of tumor components, 718 pathogenic or likely pathogenic mutations were identified. The mutation profile of hepatocytic and biliary components showed 86.6% match, suggesting a common lineage despite different phenotypic expression. The most commonly mutated genes included TP53 (25/58, 43.1%) and TERT promoter (22/58, 37.9%). Missense and stop-gained variants in RB1 (4/58, 6.9%), PIK3CA (2/58, 3.4%), PTEN (2/58, 3.4%), and frameshift mutations in ATM (2/58, 3.4%) were also identified. None of the mutations were expressed in corresponding normal tissues. The identified mutations in TP53 and TERT promoter were different from the known hotspot mutations in HCC and iCCA, suggesting a unique genomic landscape in cHCC-CCA.

Conclusions: The common mutational profile in hepatocytic and biliary components of cHCC-CCA suggests a monoclonal origin. As mutations in cHCC-CCA were not previously reported in either HCC or iCCA, they could be utilized as potential molecular markers for diagnosis.

Keywords: Combined Hepatocellular-Cholangiocarcinoma, Whole Exome Sequencing, Biomarker

OP-34

CRY2 Is an Actionable Target to Modulate Tumor Growth and Stemness in Hepatocellular Carcinoma

Regina Lo[1,2], Kristy Chan[1], Ella Au[1], Oscar Yee[1], Bernice Leung[1], Tin-Yan Koo[3], Clive Yik-Sham Chung[2,3]

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Aims: Deregulation of the circadian network has been linked to cancers. Its role in cancer stemness, however, remains poorly understood. In this study, we aimed to characterize the functional significance cryptochrome 2 (CRY2), a key factor in the repressor limb of the circadian molecular network, in regulating stemness properties of hepatocellular carcinoma (HCC).

Methods: Human HCC cell lines were adopted for functional assays. CRY2 expression was manipulated by genetic approach and pharmacological approach with CRY2 stabilizers KL001 and TH301. In vivo tumor growth was studied using subcutaneous injection mouse models. Proteomic profiling was performed by label-free liquid chromatography-mass spectrometry to explore the downstream mechanisms.

Results: CRY2 expression was downregulated in HCC tissues versus the non-tumoral liver tissues from TCGA-LIHC and GSE14520 cohorts. Low CRY2 expression was associated with worse overall survival of patients in TCGA and ICGC (LIRI-JP) cohorts. Overexpression of CRY2 by lentiviral-based approach in MHCC97L suppressed cell proliferation and tumorsphere formation in vitro, and downregulated stemness marker CD133. In vivo tumor growth and tumor incidence were attenuated upon CRY2 overexpression in MHCC97L-xenografts. Administration of KL001 or TH301 to HCC cells recapitulated the functional effects of CRY2 overexpression in cell proliferation and tumorsphere formation. Consistently, KL001 or TH301 treatment reduced tumor growth in xenografts. Proteomic profiling revealed 145 differentially expressed proteins, and pathway enrichment analysis highlighted "cell cycle" in KL001 versus mock control group. This was validated with cell cycle analysis, in which KL001 or TH301 treatment to HCC cells led to increased cell population in G1 phase and decreased cell population in S phase, accompanied by downregulation of p53 (Ser807/811), cyclin B1 and cyclin D3.

Conclusions: CRY2 underexpression is observed in HCC and associated with worse survival outcome. Enforcement of CRY2 by genetic or pharmacological approach in HCC attenuates tumor growth, self-renewal and tumor initiation, possibly through inducing cell cycle arrest.

Keywords: Liver Cancer, Self-Renewal, Molecular Target

OP-35

PNPLA3 I148M GG Variant Correlates with Poor Tumor Differentiation but Not HCC Risk in MASLD Patients

Jaejun Lee[1,2], Jung Hoon Cha[2], Hee Sun Cho[1,2], Keungmo Yang[1,2], Hyun Yang[1,2], Heechul Nam[1,2], Mi Young Byun[3], Seok Keun Cho[3], Jinsung Park[4], Hyuk Wan Ko[5], Seong Wook Yang[6], Pil Soo Sung[1,2], Si Hyun Bae[1,2]

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Aims: The patatin-like phospholipase domain-containing protein 3 (PNPLA3) I148M variant has been linked to development and progression of metabolic dysfunction-associated steatotic liver disease (MASLD). However, its role in hepatocellular carcinoma (HCC) development remains unclear. This study aims to investigate the association between the PNPLA3 I148M variant and HCC risk, as well as its potential influence on histological differentiation of HCC.

Methods: A total of 435 MASLD patients, with and without HCC, were prospectively and consecutively enrolled at a tertiary university-affiliated hospital between June 2024 and February 2025. Genomic DNA was extracted from buccal swabs or liver biopsy samples, and single nucleotide polymorphism (SNP) genotyping was performed to determine the rs738409 genotype at codon 148 of PNPLA3. The histological grade of HCC was assessed using the Edmondson-Steiner (ES) grading system in patients who underwent core-needle liver biopsy.

Results: Among 361 non-HCC patients, 153 (42.4%) had the GG genotype, 123 (34.1%) had the GC genotype, and 85 (23.5%) had the CC genotype. Similarly, among 74 HCC patients, the GG genotype was present in 34 (45.9%), while 26 (35.1%) and 14 (18.9%) had the GC and CC genotypes, respectively. The distribution of the GG variant did not significantly differ between non-HCC and HCC patients (P=0.573), and this finding was consistent across sex and age subgroups. Among the 43 HCC patients with available histological grading, 14 (32.6%) exhibited high ES grades (3–4), while 29 (67.4%) had low ES grades (1–2). Notably, HCC patients carrying the GG variant had a significantly higher proportion of high ES grades (57.1%) compared to those with GC/CC genotypes (24.1%) (P=0.003).

Conclusions: The PNPLA3 I148M GG variant was not associated with an increased risk of HCC in MASLD patients. However, it was significantly correlated with poor tumor differentiation, suggesting a potential role in HCC progression rather than initiation. These findings highlight the need for further mechanistic studies to elucidate how the PNPLA3 I148M variant contributes to tumor dedifferentiation and disease aggressiveness.

Keywords: PNPLA3, Metabolic Dysfunction-Associated Steatotic Liver Disease, Hepatocellular Carcinoma, Edmondson-Steiner Grade

Friday, May 30, 2025, 16:40-17:40

7. Liver Cancer, Clinical 1

OP-36

A New Prognostic Index for Patients with Advanced Biliary Tract Cancer Treated with Cisplatin, Gemcitabine and Durvalumab: The MAGIC-D Index

Mara Persano[1-2], M. Rimini[2], L. Fornaro[3], F. Lo Prinzi[4], L. Antonuzzo[5], F. Rossari[2], T. Satake[6], J. Lucchetti[4], J. W. Kim[7], O. Abidoye[8], I. G. Rapposelli[9], S. Tamberi[10], F. Finkelmeier[11], G. Giordano[12], H. J. Chon[13], C. Yoo[14], S. L. Chan[15], S. Camera[2], F. Vitiello[2], M. Scartozzi[1], G. Masi[3], A. Vogel[16], S. Lonardi[17], L. Rimassa[18], A. Casadei Gardini[2]

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Aims: This study aims to identify a new prognostic index for patients with biliary tract cancer (BTC) treated with cisplatin, gemcitabine and durvalumab (CGD) in first-line setting.

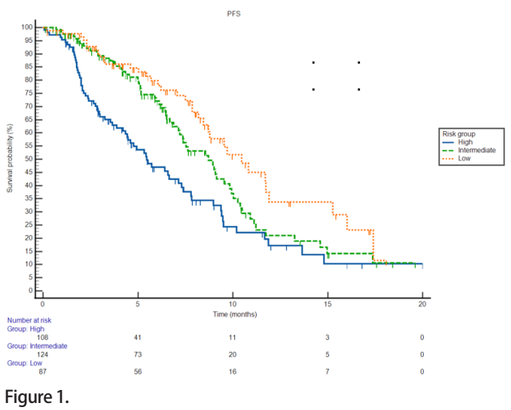
Methods: The study population consisted of 319 patients with BTC from 11 Eastern and Western Countries. Using multivariate analysis, we previously developed a prognostic model called the Metastatic disease Albumin GGT cIsplatin Carcinoembryonic antigen (CEA)-Durvalumab prognostic index "MAGIC-D index" by combining the 5 baseline positive variables and assigning a weight from 1 to 5 as follows: 1 for metastatic disease, 2 for CEA increased levels, 3 for albumin decreased levels, 4 for gamma glutamyl transferase increased levels, 5 for neutrophil-lymphocyte ratio ≥ 3. Patients were stratified into three risk-groups as follows: low risk-group (score from 0 to 5), intermediate risk-group (score from 6 to 10), and high risk-group (score from 11 to 15).

Results: Median progression-free survival was 10.5 months [95% confidence interval (CI): 8.4-11.9 months] in low risk-group (27.3%), 8.7 months (95% CI: 7.1-9.9 months) in intermediate risk-group (38.9%), and 5.5 months (95% CI: 4.4-7.4 months) in high risk-group [33.8%; low risk hazard ratio (HR): 0.44, intermediate risk HR: 0.63, high risk HR: 1, P<0.01]. Median overall survival (OS) was 17.9 months (95% CI: 13.5-17.9 months) in low risk-group,15.6 months (95% CI: 10.2-18.4 months) in intermediate risk-group, and 8.0 months (95% CI: 7.4-12.5 months) in high risk-group (low risk HR: 0.32, intermediate risk HR: 0.52, high risk HR: 1, P<0.01). There was no difference in overall response rate (low risk: 28.7%, intermediate risk: 36.3%, and high risk: 29.6%; P=0.26), while disease control rate was significantly different in the three risk-groups (low risk: 78.2%, intermediate risk: 72.6%, and high risk: 61.1%; P<0.01) as well as the rate of patients receiving a second-line therapy

(low risk: 21.8%, intermediate risk: 23.4%, and high risk: 17.6%; *P*=0.02). The safety profile was similar in the three risk-groups, except for nausea (low risk: 36.8%, intermediate risk: 42.7%, high risk: 26.8%; *P*=0.04), leukopenia (low risk: 28.7%, intermediate risk: 33.1%, high risk: 16.7%; *P*=0.01), and neutropenia (low risk: 55.2%, intermediate risk: 55.6%, high risk: 23.1%; *P*<0.01).

Conclusions: The MAGIC-D index is an easy-to-use tool able to stratify patients with BTC undergoing first-line therapy with CGD. Further studies are needed to prospectively test and validate this index.

Keywords: Biliary Tract Cancer



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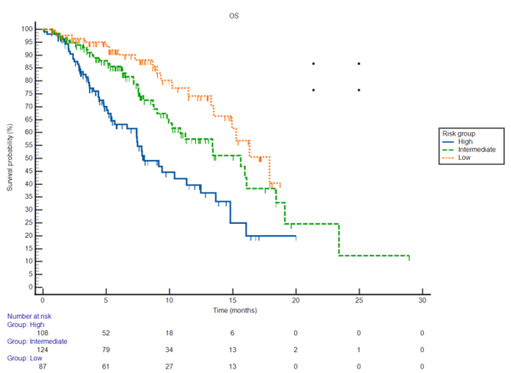

Figure 2.

OP-37

Mass Spectrometry-Based Proteomics Analysis to Discover Biomarkers in Atezolizumab and Bevacizumab Therapy for Patients with Advanced Hepatocellular Carcinoma

Eunho Choi[1], Young-Sun Lee[1], In Hee Kim[2], Jin Woo Lee[3], Jung Hwan Yu[3], Sung-Bum Cho[4], Ha Seok Lee[1], Youngwoo Lee[1], Yang Jae Yoo[1], Young Kul Jung[1], Ji Hoon Kim[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1]

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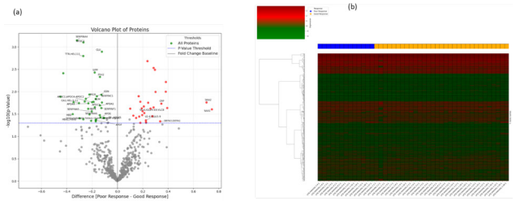
Aims: Immunotherapy, including atezolizumab and bevacizumab, as well as durvalumab and tremelimumab, is the standard first-line treatment for patients with advanced hepatocellular carcinoma. However, an effective biomarker for predicting response to this systemic therapy has not yet been identified. This study aimed to identify circulating protein biomarkers that can effectively select patients for treatment.

Methods: Serum samples were collected from patients with advanced hepatocellular carcinoma before their first cycle of atezolizumab and bevacizumab treatment at four different university hospitals. The patients were classified into two groups: the response group, which included those with stable disease, partial response, or complete response, and the non-response group, consisting of patients with progressive disease after 3 treatment cycles. Mass spectrometry-based proteomics analysis was performed on each sample. We selected proteins that showed significant differences between the two groups.

Results: Forty-eight patients were included in the analysis, with 34 in the response group and 14 in the non-response group. Analysis showed serum Amyloid A (SAA) and Neutrophil Defensin (DEFA) exhibited higher expression levels in the serum of patients with poor responses compared to those with good responses. Conversely, proteins including Kallistatin (SERPINA4), Apolipoprotein C-III (APOC3), Clusterin (CLU), Transthyretin (TTR), Lumican (LIM), Inter-alpha-trypsin inhibitor heavy chain H2 (ITIH2), Insulin-like growth factor-binding protein complex acid labile subunit (IGFALS) and Antithrombin-III (SERPINC1) showed lower expression levels in the serum of patients with poor response compared to those with a good response. Some of the significantly different proteins show a higher level of interaction than others, such as APOC3 and CLUS, indicating that these proteins may function as key hubs within the serum protein interaction network.



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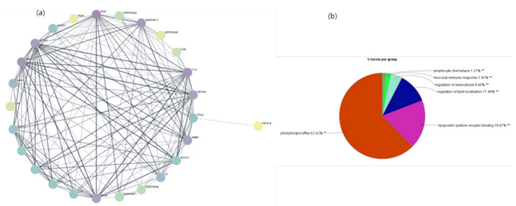

Figure 2.

Conclusions: Serum protein can be a promising biomarker for predicting response to atezolizumab and bevacizumab therapy.

Keywords: Hepatocellular Carcinoma, Atezolizumab Bevacizumab, Biomarker, Proteomics

OP-38

Development and Validation of a Risk Prediction Model for Patients with Hepatocellular Carcinoma Receiving Atezolizumab-Bevacizumab

Heechul Nam[1,2], Dong Yun Kim[3], Do Young Kim[3], Ji Hoon Kim[1,2], Chang Wook Kim[1,2], Jaejun Lee[1,4], Keungmo Yang[1,4], Ji Won Han[1,4], Pil Soo Sung[1,4], Seung Kew Yoon[1,4], Hee Sun Cho[1,5], Hyun Yang[1,5], Si Hyun Bae[1,5], Soon Kyu Lee[1,6], Jung Hyun Kwon[1,6], Soon Woo Nam[1,6], Ahlim Lee[1,7], Do Seon Song[1,7], U Im Chang[1,7], Seok-Hwan Kim[1,8], Myung Jun Song[1,8], Hae Lim Lee[1,9], Hee Yeon Kim[1,9], Sung Won Lee[1,9], Jeong Won Jang[1,4]

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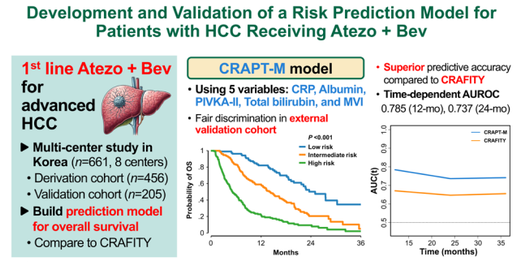
Aims: Atezolizumab plus bevacizumab (AB) has become the standard first-line treatment for advanced hepatocellular carcinoma (HCC). However, identifying reliable prognostic biomarkers remains a critical challenge. We aimed to develop a comprehensive scoring system to predict overall survival (OS) in advanced HCC patients receiving first-line AB.

Methods: We included patients with advanced HCC receiving first-line (AB) from multiple centers in Korea, forming a derivation cohort (*n*=456) and a validation cohort (*n*=205). Key prognostic factors, including tumour markers, liver function, and inflammation parameters, were analyzed. Restricted cubic spline analysis was employed to determine cut-off points for continuous variables.

Results: Multivariable analysis identified five independent prognostic factors: C-reactive protein ≥1.0 mg/dL (hazard ratio [HR] 2.06; *P*<0.001), albumin <3.5 g/dL (HR 1.60; *P*=0.002), protein induced by vitamin K absence or antagonist-II ≥1,500 mAU/mL (HR 1.60; *P*=0.002), total bilirubin ≥1.0 mg/dL (HR 1.50; *P*=0.006), and macrovascular invasion (HR 1.48; *P*=0.009). We developed the CRAPT-M model named after these factors' initial letters. Patients were categorized into low (≤4), intermediate (5-12), and high (≥13) risk groups by CRAPT-M score. Median OS differed significantly: 22.4 (95% CI, 18.6-25.0), 12.9 (95% CI, 8.7–14.8), and 6.7 (95% CI, 5.1–7.7) months for low-, intermediate-, and high-risk groups, respectively (*P*<0.001). Time-dependent area under the receiver operating characteristic for CRAPT-M demonstrated consistently higher predictive accuracy than the CRAFITY model, with values of 0.785, 0.737, and 0.742 at 12, 24, and 36 months, respectively. The model demonstrated robust predictive performance in external validation cohort, with excellent calibration and consistent discrimination across sensitivity analyses.

Conclusions: The CRAPT-M model demonstrated robust OS prediction, offering a valuable tool for prognosis estimation and clinical decision-making in advanced HCC patients receiving AB.

Keywords: Hepatocellular Carcinoma, Risk Prediction Model, Immuno-Oncology, C-Reactive Protein



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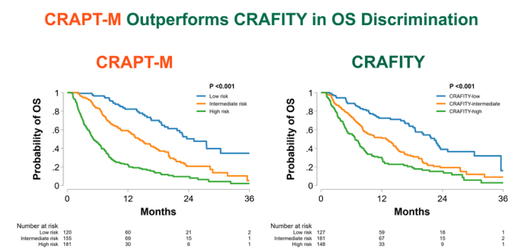

Figure 2.

OP-39

Prognostic Impact of Diabetes and Hypertension on Hepatocellular Carcinoma Survival: A 15-Year Registry-Based Analysis

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Aims: In Korea, hepatocellular carcinoma (HCC) is a major cause of cancer-related mortality, and its incidence is rising in the elderly population. Given this trend, the influence of comorbidities, such as diabetes mellitus (DM) and hypertension (HTN), on survival warrants further investigation. This study investigated the prognostic implications of these comorbidities using a 15-year, large-scale registry.

Methods: A total of 21,699 treatment-naïve HCC patients from the Asan Medical Center HCC registry (2009–2023) were analyzed. The influence of DM and HTN on overall survival (OS) was assessed according to the Barcelona Clinic Liver Cancer (BCLC) staging system. Patients were stratified into four groups based on comorbidity status: none, HTN only, DM only, and both HTN and DM. OS was estimated using the Kaplan–Meier method, with comparisons via log-rank tests. Cox proportional hazards models were used to evaluate the association between comorbidities and survival, with hazard ratios (HRs) calculated for each group.

Results: The median age of the cohort was 59 years, 80.6% were male, and hepatitis B virus infection was the most common etiology of HCC. Among all patients, 5,476 (26.5%) had DM, and 7,541 (34.8%) had HTN. When stratified by comorbidity status, the median OS was 6.0 years in patients with no comorbidities, 6.8 years in those with HTN only, 5.6 years in those with DM only, and 4.9 years in those with both DM and HTN. Patients with both DM and HTN had significantly worse survival compared to those without comorbidities (HR 1.12, P<0.001).

In patients with BCLC stage 0, OS was significantly lower in those with comorbidities. The HR for OS was 1.20 in patients with HTN, 2.02 in those with DM, and 2.17 in those with both DM and HTN (all P<0.001). A similar pattern was observed in BCLC stage A, where the HR for OS was 1.09 in patients with HTN, 1.33 in those with DM, and 1.49 in those with both comorbidities (all P<0.001). However, in BCLC stages B, C, and D, OS did not show significant differences based on comorbidity status.

Conclusions: Our findings suggest that DM is associated with poorer prognosis in HCC patients, and the presence of both DM and HTN further worsens survival outcomes, particularly in very early (BCLC 0) and early-stage (BCLC A) disease. These results highlight the need for tailored surveillance and management strategies for HCC patients with metabolic comorbidities.

Keywords: HCC, Comorbidity, Diabetes, Hypertension

OP-40

Machine Learning-Based Prediction of Clinically Significant Portal Hypertension and Future Hepatic Decompensation in Patients with BCLC-C Hepatocellular Carcinoma

Ji Won Han

The Catholic University of Korea

Aims: Clinically significant portal hypertension (CSPH) and the development of hepatic decompensation (HD) are closely associated with the survival of patients with BCLC-C hepatocellular carcinoma (HCC). We hypothesized that machine-learning (ML) algorithms using radiologic and laboratory findings could precisely predict CSPH and future HD.

Methods: A total of 2,112 BCLC-C patients from multicenter cohorts were included: 1,262 patients in the training/test set and 850 patients in the validation set. We tested various ML algorithms to predict CSPH using clinical parameters and investigated whether ML-driven prediction scores could predict HD and clinical outcomes in BCLC-C patients.

Results: Among the various algorithms, the random forest (RF) model was selected because it showed the highest area under the receiver operating characteristic curve (AUROC) of 0.840, and this performance was maintained in the independent validation set (0.786). The accuracy, precision, recall, and F1 score were 0.792, 0.827, 0.902, and 0.863, respectively. The AUROC of the RF model was significantly higher (P<0.001) than that of FIB-4 (0.725) or ALBI grade (0.680). SHAP values indicated that total bilirubin, INR, AST, albumin, largest intrahepatic tumor size, and platelets were key factors in predicting CSPH. Based on the CSPH prediction score, we classified BCLC-C HCC patients into high- and low-risk groups for future development of HD. The hazard ratio (HR) was 8.71 (P<0.001), and the optimal cutoff value was 0.62. This risk grouping also significantly predicted variceal bleeding (HR 10.43, P<0.001) and overall survival (HR 5.24, P<0.001). In the high-risk group, patients receiving atezolizumab-bevacizumab treatment had a higher risk of variceal bleeding compared with those receiving tyrosine-kinase inhibitors (HR 5.64, P=0.001), whereas there was no significant difference (P=0.100) between the two treatment groups in the low-risk group.

Conclusions: Our ML-based predictive model accurately predicts CSPH and future HD in patients with BCLC-C HCC, allowing for effective identification of high-risk patients. Notably, the model differentiates those who are at higher risk of variceal bleeding under atezolizumab-bevacizumab therapy, providing critical evidence for individualized treatment strategies.

Keywords: Machine Learning, Hepatocellular Carcinoma, Hepatic Decompensation, Variceal Bleeding

OP-41

Bleeding Complications and Survival Outcomes in HCC Patients Treated with Atezolizumab/Bevacizumab: Multicenter Real-World Study

Yu Rim Lee[1], Sung-Bum Cho[2], Hyun Young Woo[3], Jae Hyun Yoon[4], Jun Sik Yoon[5], Yeowool Kang[6], Jeong Eun Song[7], Young Mi Hong[8], Sang Youn Hwang[9], Joonho Jeong[10], Jeong Heo[3], Young Oh Kweon[11], Yang Hyun Baek[6], Soo Young Park[11], Won Young Tak[11]

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Aims: Atezolizumab/bevacizumab (atezo/bev) have been demonstrated as an effective first-line treatment for hepatocellular carcinoma (HCC). However, the risk of bleeding complications is a major concern in atezo/bev treatment. Therefore, we evaluated the efficacy and safety with a focus on bleeding events of atezo/bev in a large, multicenter real-world population.

Methods: From July 2020 to October 2024, this retrospective cohort study included 869 patients with HCC from 9 tertiary hospitals who were treated with atezo/bev.

Results: During a median follow-up of 8.4 months, 112 (12.9%) patients developed bleeding episodes at a median of 3.9 months. Of these, variceal hemorrhage occurred in 62 (7.1%) patients treated with atezo/bev at a median of 5.5 months. Grade III or IV bleeding occurred in 35 (5.1%) patients of patients, with grade V bleeding observed in 4 (0.6%) patients. Progression-free survival was not significantly different between the variceal hemorrhage and non-variceal hemorrhage groups. However, overall survival was significantly lower in patients with variceal hemorrhage (log-rank test: P=0.007). In the multivariate analysis, variceal hemorrhage was significantly associated with the presence of varices, history of variceal bleeding, and macrovascular invasion (all P<0.05).

Conclusions: Patients with advanced HCC who develop variceal bleeding during atezo/bev treatment may have a poor prognosis. It is necessary to identify high-risk group of variceal bleeding and monitor them carefully.

Keywords: Hepatocellular Carcinoma, Immunotherapy, Variceal Bleeding

Friday, May 30, 2025, 16:40-17:40

8. Liver Cancer, Clinical 2

OP-42

The State of Pediatric Malignant Neoplasm of Liver in Korea: Nationwide Cohort Study

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Aims: Pediatric liver cancer is a rare yet clinically significant malignancy, accounting for 0.8% of childhood and adolescent cancer cases. Despite its rarity, its incidence has increased by 1.7% over the past two decades. Prognosis is highly dependent on early and accurate diagnosis; however, most cases are asymptomatic and discovered incidentally. Understanding the epidemiology of pediatric liver cancer is crucial for improving early detection and therapeutic strategies. This study aimed to investigate the epidemiology of pediatric liver cancer in Korea using nationwide real-world data.

Methods: This population-based cohort study utilized health insurance claims data from the Korea National Health Insurance Service (NHIS) from 2009 to 2020. Pediatric patients aged 18 years or younger who were newly diagnosed with malignant neoplasms of the liver were included. The study analyzed the epidemiology of pediatric liver cancer, demographic characteristics, and survival. Incidence rates (IRs) were calculated per 100,000 people, and survival analyses were conducted using Kaplan-Meier estimates.

Results: A total of 345 pediatric patients were identified during the study period. The annual incidence rate ranged from 0.20

to 0.36 per 100,000 person-years. Across the entire study period, the highest incidence was observed in infants (0-2 years). Hepatoblastoma was the most common malignancy (62.9%), followed by liver cell carcinoma (17.4%). The mean age was 5.7 ± 6.1 years, and 55.7% of patients were male. A total of 26.7% of patients had a history of previous extrahepatic malignancies. During the follow-up period, 89.6% of patients received chemotherapy, while 52.5% underwent liver resection. The 5-year survival rate was 79.5%.

Conclusions: This nationwide cohort study provides valuable insights into the epidemiology and outcomes of pediatric liver cancer in Korea. Further research is needed to refine early detection and optimize therapeutic approaches to improve prognosis in affected children.

Keywords: Liver Neoplasms, Pediatrics, Epidemiology

OP-43

The Role of Transarterial Chemoembolization for Advanced Hepatocellular Carcinoma in The Era of Immune Checkpoint Inhibitor

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Aims: Transarterial chemoembolization (TACE) is still used for intrahepatic tumor control in advanced hepatocellular carcinoma (HCC), despite recent advances in systemic therapies such as immune checkpoint inhibitors (ICIs). This study evaluated the role of TACE in the treatment of advanced HCCs in the era of ICI.

Methods: We retrospectively analyzed 476 treatment-naïve patients with unresectable BCLC stage C HCC treated with either TACE or systemic therapy (atezolizumab–bevacizumab, sorafenib, or lenvatinib) between January 2021 and December 2022. Overall survival (OS) was compared using the Kaplan–Meier method. Multivariable Cox regression, propensity score matching (PSM), and inverse probability of treatment weighting (IPTW) were used to adjust for confounders.

Results: Before confounder adjustment, median OS was significantly longer in the TACE group (12.9 months) compared to the atezolizumab–bevacizumab (6.1 months), lenvatinib (6.7 months), and sorafenib (2.9 months) groups. However, after adjustment, no significant OS difference was observed between TACE and atezolizumab–bevacizumab in multivariable analysis (adjusted HR 0.90; *P*=0.49), PSM (HR 0.82; *P*=0.26), or IPTW (HR 0.92; *P*=0.66). Among patients who initially received TACE, those who subsequently received atezolizumab–bevacizumab showed the longest median OS of 17.7 months (95% CI, 15.47–23.13), which was significantly longer than that of the TACE-to-TKI group (10.1 months; 95% CI, 7.49–12.71; *P*<0.001) and the atezolizumab–bevacizumab–first group (6.1 months; 95% CI, 4.07–8.25; *P*<0.001). Subgroup analysis demonstrated a survival benefit of TACE over atezolizumab–bevacizumab in patients with none portal vein invasion (aHR 0.39; p=0.002), or branch portal vein invasion (aHR 0.64; *P*=0.04).

Conclusions: TACE may remain a viable treatment option for selected patients with advanced HCC, particularly those with none portal vein invasion or branched portal vein invasion.

Keywords: BCLC, Tyrosine Kinase Inhibitor, Atezolizumab-Bevacizumab, TACE

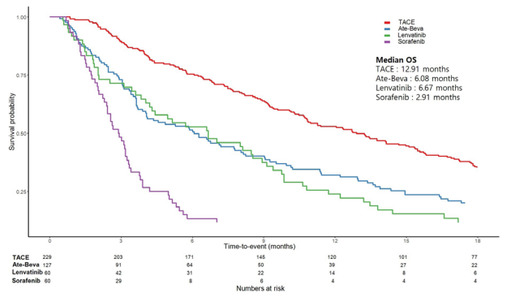

Figure. Overall survival in entire patients according to initial treatment modality.
Abbreviations: Ate-Beva, atezolizumab–bevacizumab; OS, overall survival; TACE, transarterial chemoembolization.

OP-44

15-Year Trends in Hepatocellular Carcinoma: Epidemiology, Treatment, and Outcomes from a Hospital-Based Registry

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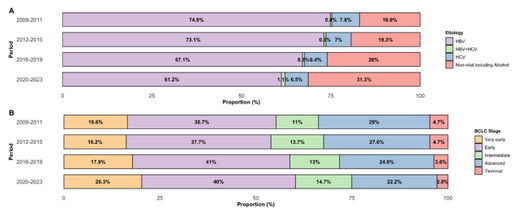
Aims: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality, particularly in South Korea. We analyzed trends in the epidemiology, tumor characteristics, treatment modalities, and outcomes of HCC over the past 15 years, using a large-scale hospital-based registry.

Methods: We examined 21,699 treatment-naïve patients with HCC from the Asan Medical Center HCC registry, diagnosed between 2009 and 2023. Patients were categorized into four periods based on their year of diagnosis: period 1 (2009–2011), period 2 (2012–2015), period 3 (2016–2019), and period 4 (2020–2023). HCC staging followed the Barcelona Clinic Liver Cancer (BCLC) system.

Results: Hepatitis B virus (HBV) declined continuously from 74.9% to 61.2%, with an increase in non-viral etiologies. The median age at diagnosis rose from 56 years in period 1 to 62 years in period 4, with increased comorbidities such as diabetes and hypertension. Early-stage HCC detection improved, with more patients diagnosed at BCLC stage 0 or A. The use of systemic therapy, particularly atezolizumab–bevacizumab, increased from 2020, especially among patients with BCLC C. The 5-year survival rate improved significantly from 44.0% in period 1 to 65.2% in period 3, with overall survival rates increasing across all stages except BCLC D. HBV-related HCC showed the best outcomes. Recurrence rates after curative treatment gradually decreased.

Conclusions: Over the past 15 years, significant advancements in the early detection and treatment of HCC in Korea have led to improved survival outcomes. These findings underscore the need for ongoing clinical strategy evolution to address the changing landscape of HCC.

Keywords: Hepatocellular Carcinoma, Epidemiology, Prognosis, Korea



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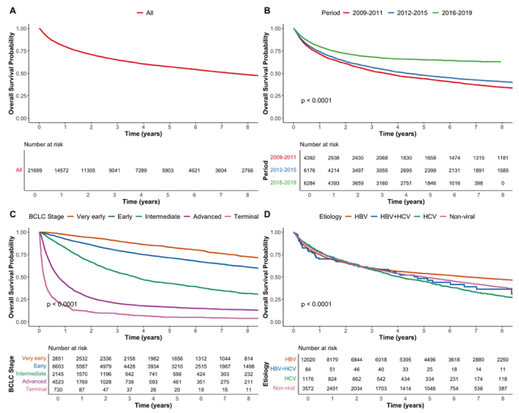

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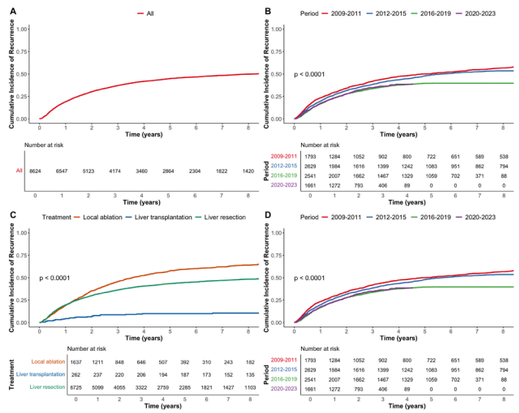

Figure 3.

OP-45

Impact of Endoscopic Retrograde Cholangiopancreatography and Radiation Therapy in Hepatocellular Carcinoma Patients with Bile Duct Invasion Receiving Atezolizumab plus Bevacizumab

Kiyoun Yi[1], Hyun Young Woo[1],Young Joo Park[1], Jeong Heo[1], Yeo Wool Kang[2], Yanghyun Baek[2], Jung Eun Song[3], Joonho Jeong[4], Yu Rim Lee[5], Soo Young Park[5], Won Young Tak[5], Jae Hyun Yoon[6], Young Mi Hong[7], Sang Youn Hwang[8], Jun Sik Yoon[9], Sung-Bum Cho[10]

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Aims: Hepatocellular carcinoma (HCC) outcomes have improved with the use of immune checkpoint inhibitors. However, the prognosis remains poor in patients with bile duct invasion due to complications like cholangitis and jaundice, often resulting in treatment discontinuation and increased mortality. This study aims to evaluate the impact of cholangiopancrea-

tography (ERCP) and radiation therapy (RT) on clinical outcomes.

Methods: This multicenter, retrospective study includes 1,179 HCC patients treated with atezolizumab and bevacizumab. These patients were divided into two groups based on the presence of bile duct invasion. Patients with bile duct invasion were further stratified based on whether they underwent ERCP and RT. Progression-free survival (PFS) and overall survival (OS) were compared between these groups.

Results: Of the 1,179 patients, those with no bile duct invasion (n=1,093) showed a significantly longer median PFS (11.9 vs. 5.26 months, *P*<0.001) and median OS (15.65 vs. 8.42 months, *P*<0.001) than those with bile duct invasion (n=86). Bivariate analysis revealed that tumor burden greater than 50% had no statistically significant association with the presence of bile duct invasion (*P*=0.487), while Vp4 showed a statistically significant relationship with bile duct invasion (*P*=0.034). Among the 86 patients with bile duct invasion, those who underwent ERCP (n = 36) showed a longer median PFS (7.92 vs. 4.54 months, *P*=0.194) and median OS (9.40 vs. 6.97 months, *P*=0.153) compared to those who did not receive ERCP (n=50). In addition, among the 36 patients who underwent ERCP, patients who received RT (n=12) had a longer median PFS (12.39 vs. 5.26 months, *P*=0.147) and median OS (15.71 vs. 8.42 months, *P*=0.141).

Conclusions: The presence of bile duct invasion in HCC patients is associated with poor prognosis and poses a challenge to treatment. This multicenter study suggests that ERCP, especially when combined with RT, may help improve clinical outcomes of patients with bile duct invasion.

Keywords: Hepatocellular Carcinoma, Bile Duct Invasion, Endoscopic Retrograde Cholangiopancreatography, Radiation Therapy

OP-46

RT Combination in Atezolizumab and Bevacizumab Benefits Hepatocellular Carcinoma with HBV Etiology

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Aims: Atezolizumab/Bevacizumab is a widely used immunotherapy for advanced hepatocellular carcinoma (HCC), with its efficacy further enhanced when combined with radiotherapy (RT). However, the precise mechanisms underlying RT's immunomodulatory effects remain incompletely understood. In this multicenter, real-world cohort study, we aimed to assess the clinical benefits of Atezolizumab/Bevacizumab in patients with HBV-related HCC and elucidate the immune-modulating effects of RT through single-cell RNA sequencing (scRNA-seq) analysis.

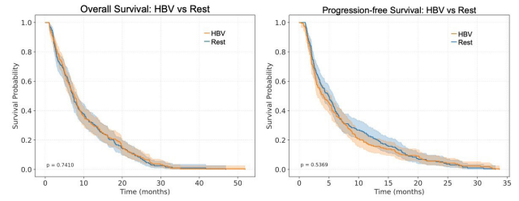
Methods: Between September 2020 and January 2025, a total of 519 hepatocellular carcinoma (HCC) patients who met the eligibility criteria and received Atezolizumab/Bevacizumab treatment were included in the study. Among them, 260 patients (50.1%) had underlying hepatitis B virus (HBV) infection, and 85 patients (32.7%) received combination therapy with RT. The primary endpoints evaluated were progression-free survival (PFS) and overall survival (OS). Single-cell RNA sequencing (scRNA-seq) datasets from GSE156625, GSE149614, and GSE151530 were obtained from publicly available repositories. Metadata were extracted from the corresponding publications, and comparative analyses were performed between the HBV and non-HBV groups.

Results: The median follow-up duration was 7.6 months. In patients receiving Atezolizumab/Bevacizumab monotherapy, no significant differences were observed in progression-free survival (PFS) and overall survival (OS) between those with HBV-related HCC and those with other etiologies (7.56 vs. 7.19 months, *P*=0.7410 and 4.04 vs. 4.93 months, *P*=0.5369, respectively). However, in the RT combination group, patients with HBV-related HCC demonstrated a trend toward improved OS compared to non-HBV patients (9.03 vs. 8.02 months, *P*=0.0300). Among HBV patients, antiviral therapy was associated with a prolonged OS (11.90 vs. 7.23 months, *P*=0.0890).

For mechanistic insights, scRNA-seq data from three datasets, comprising 43 patients and 88,572 cells, were collected and analyzed. Single-cell transcriptomic analysis revealed an increase in SPP1+ endothelial cells (ECs), suggesting enhanced non-VEGF-mediated angiogenesis in the HBV group. Consistently, pathway analysis indicated a downregulation of VEGF receptor expression in HBV-associated HCC.

Conclusions: The efficacy of Atezolizumab/Bevacizumab in HCC may be influenced by underlying etiology and treatment combination. While no significant differences in survival outcomes were observed between HBV-related and non-HBV-related HCC patients receiving monotherapy, those with HBV exhibited improved overall survival when treated with RT combination therapy. Additionally, antiviral therapy was associated with a trend toward prolonged survival in HBV patients. Mechanistic analysis using scRNA-seq revealed an increase in SPP1+ endothelial cells, suggesting a shift toward non-VEGF-mediated angiogenesis in HBV-related HCC, accompanied by downregulation of VEGF receptor expression. These findings highlight potential differences in angiogenic pathways between HBV and non-HBV HCC, which may influence responses to VEGF-targeted therapy and provide insights for optimizing treatment strategies.

Keywords: Chronic Hepatitis B, Hepatocellular Carcinoma, Atezolizumab/Bevacizumab Radiotherapy Combination, Single-Cell RNA-SEQ



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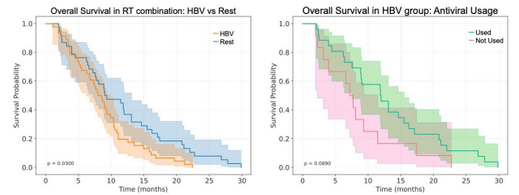

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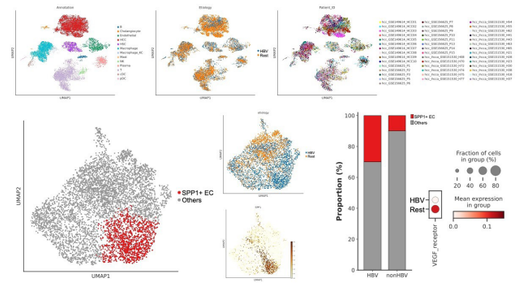

Figure 3.

OP-47

Decision Tree Modeling of Exosomal miR-30a-5p for Predicting Response to Atezolizumab and Bevacizumab in Advanced Hepatocellular Carcinoma

Eunho Choi[1], Young-Sun Lee[1], Jeong-An Gim[2], Wonhyo Seo[3], Ha Seok Lee[1], Youngwoo Lee[1], Yang Jae Yoo[1], Seong Hee Kang[1], Sun Young Yim[1], Young Kul Jung[1], Ji Hoon Kim[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1]

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Aims: Atezolizumab and bevacizumab combination therapy is the frontline treatment for advanced hepatocellular carcinoma, but identifying a reliable biomarker for predicting treatment response remains elusive. Previously we found miR-30a-5p to be a promising biomarker for treatment response. This study aimed to determine whether this exosomal miRNA retains its significance in a larger patient pool.

Methods: Blood samples were collected from patients with advanced hepatocellular carcinoma before initiating the atezolizumab and bevacizumab treatment Patients were categorized into responders (those exhibiting stable disease, partial, or complete response) and non-responders (those showing disease progression) after 3 treatment cycles. Extracellular vesicles were isolated from serum, and exosomal RNA was extracted for small RNA sequencing using next-generation sequencing (NGS). Decision tree analysis was employed to identify miRNAs that effectively differentiated between responders and non-responders.

Results: The study comprised 13 patients in responder group, and 11 patients in non-responder group. NGS yielded 1076 miRNAs, among which let7c-5p, miR-30a-5p, and miR192-5p were significantly increased in responders. As previously identified, miR-30a-5p showed significantly higher levels in responders (*P*=0.0039). Decision tree analysis indicated that miR-30a-5p levels ≥ 9.67 effectively distinguished responders from non-responders. Additionally, random forest modeling identified miR-30a-5p as the most important factor in classifying the groups.

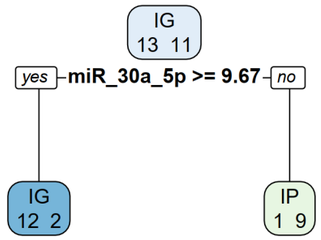

Figure 1.

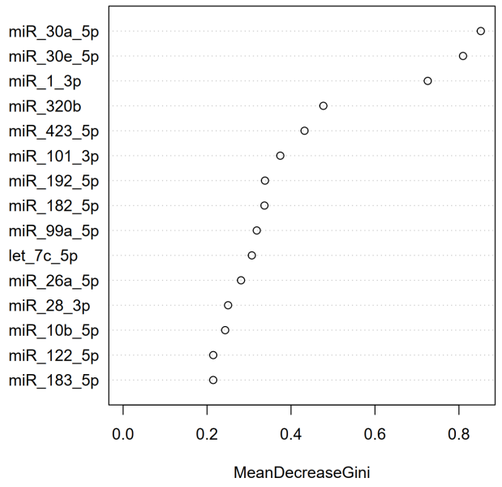

Figure 2.

Conclusions: miR-30a-5p can successfully identify the responders to atezolizumab-bevacizumab therapy.

Keywords: Hepatocellular Carcinoma, Biomarker, Mirna,

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9. Liver Surgery

OP-48

Caregiver Perception, Knowledge, and Attitude toward Postoperative Recovery among Patients with Liver Disease

Lintong Hottua Simbolon[1], Hepri Ardianson Purba[1], Yesika Simbolon[2], Helen Try Juniasti[3], Ester Marnita Purba[4], Wahyuni Kurniawati[5], Rosinta H P Purba[1]

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Aims: Postoperative recovery for patients with liver disease requires active involvement from caregivers. Their perception, knowledge, and attitude significantly impact recovery outcomes, adherence to medical advice, and quality of life (QoL). Additionally, caregiver depression levels may influence their ability to provide effective support. However, research on caregivers' roles in this context, particularly in Indonesia, remains limited.

Methods: Using the Indonesia Family Life Survey (IFLS), this study examines how these factors influence recovery outcomes, patient QoL, and caregiver depression levels. Data from primary caregivers of postoperative liver disease patients were analyzed to identify key determinants of recovery.

Results: Caregiver perception (β=0.41, P<0.01) emerged as the strongest predictor of postoperative recovery, highlighting its importance in improving adherence to medical advice and patient QoL. Knowledge (β=0.38, P<0.01) and positive attitudes (β=0.29, P<0.05) significantly enhanced recovery outcomes, while caregiver depression (β=-0.33, P<0.05) negatively impacted adherence and QoL. QoL improvements (β=0.36, P<0.01) were strongly linked to caregiver engagement and socioeconomic factors, emphasizing the interdependence of caregiver and patient well-being. Descriptive statistics revealed a mean caregiver knowledge score of 6.8 (out of 10), with moderate levels of depression (mean CES-D score=15.6). Patients' QoL averaged 68.5 out of 100, indicating moderate recovery satisfaction. Regression analysis confirmed the critical role of caregiver-related factors, controlled for socioeconomic status, age, and comorbidities.

Conclusions: This research underscores the need for caregiver-focused educational and psychological support programs to enhance recovery outcomes and patient QoL. Future studies should explore interventions to address caregiver mental health and socioeconomic barriers.

Keywords: Caregiver Perception, Postoperative Recovery, Liver Disease

OP-49

Divergent Impact of Preoperative Platelet Count Abnormalities on Long-Term Outcomes after Curative Hepatic Resection for Hepatocellular Carcinoma: A Multi-Institutional Analysis of 3,116 Patients

Jia-Hao Xu[1], Xue-Dong Wang[2], Ying-Jiang Liang[3], Hong-Wei Guo[4], Han Liu[5], Yi-Fan Wu[6], Hong Wang[7], Ya-Hao Zhou[8], Yong-Yi Zeng[9], Lei Cai[10], Tian Yang[1]

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Aims: While platelet dysfunction has been implicated in cancer progression, the clinical significance of preoperative platelet abnormalities in hepatocellular carcinoma (HCC) remains controversial. This study aimed to investigate how platelet count extremes influence long-term outcomes following curative hepatic resection and surgical decision-making.

Methods: A retrospective analysis was conducted on 3,116 HCC patients who underwent curative hepatic resection across 10 specialized hepatobiliary centers. Based on preoperative platelet counts, patients were stratified into three groups: thrombocytopenia (<100×109/L, n=655), normal range (100~299×109/L, n=2,374), and thrombocytosis (≥300×109/L, n=87). Long-term outcomes were evaluated using Kaplan-Meier survival analysis and multivariable Cox regression models, adjusting for established clinicopathological factors.

Results: Five-year overall survival rates after HCC rection demonstrated significant variation among the three groups: 52.7%, 56.0%, and 40.2% for thrombocytopenia, normal, and thrombocytosis cohorts, respectively (P<0.001). Both platelet count extremes independently predicted decreased overall survival (thrombocytopenia: HR=1.215, 95%CI: 1.045-1.413; thrombocytosis: HR=1.307, 95%CI: 1.130-1.511). Notably, thrombocytosis uniquely correlated with inferior recurrence-free survival (26.9% vs 39.3% at 5 years; HR=1.523, 95%CI: 1.196-1.939), while thrombocytopenia showed no significant impact on recurrence risk.

Conclusions: This comprehensive analysis reveals distinct prognostic patterns associated with platelet count abnormalities in HCC patients undergoing hepatic resection. The differential impact on survival and recurrence suggests distinct underlying biological mechanisms, potentially warranting tailored surveillance and adjuvant strategies for these patient subgroups. These findings may help refine preoperative risk assessment and guide personalized surgical management approaches.

Keywords: Hepatocellular Carcinoma, Thrombocytosis, Thrombocytopenia

OP-50

Superior Prognostic Performance of the AFP Model Over Milan Criteria Following Hepatic Resection for Hepatocellular Carcinoma: A Multi-Institutional Analysis

Chao Li[1], Yong-Kang Diao[1], Yi-Fan Wu[2], Xian-Ming Wang[1], Xue-Dong Wang[1], Qi-Xuan Zheng[1], Hong Wang[1], Han Liu[1], Kong-Ying Lin[1], Ying-Jian Liang[1], Ya-Hao Zhou[1], Wei-Min Gu[1], Jia-Hao Xu[1], Tian Yang[1]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Naval Medical University, China, [2] Department of Hepatobiliary Surgery, Affiliated Hospital of Nantong University, China, [3]Department of General Surgery, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, China, [4]Hepatopancreatobiliary Centre, Beijing Tsinghua Changgung Hospital, Tsinghua University, China, [5]Department of Hepatobiliary Surgery, Shandong Provincial Hospital Affiliated to Shandong University, China, [6]Department of General Surgery, Liuyang People's Hospital, China, [7]Department of Hepatobiliary And Pancreatic Surgery, General Surgery Centre, First Hospital of Jilin University, China, [8]Department of Hepatobiliary Surgery, Mengchao Hepatobiliary Hospital, Fujian Medical University, China, [9]Department of Hepatobiliary Surgery, The First Affiliated Hospital of Harbin Medical University, China, [10]Department of Hepatobiliary Surgery, Pu'er People's Hospital, China, [11]The First Department of General Surgery, The Fourth Hospital of Harbin, China, [12]Department of Surgery, Ohio State University, Wexner Medical Centre, China

Aims: While both the Milan criteria and French alpha-fetoprotein (AFP) model effectively predict outcomes after liver transplantation for hepatocellular carcinoma (HCC), their comparative value in hepatic resection remains unclear. This study evaluated the prognostic performance of the AFP model versus Milan criteria following curative resection for HCC.

Methods: A retrospective analysis of patients undergoing curative hepatic resection for HCC across multiple Chinese institutions was conducted. Recurrence and survival outcomes were compared between groups stratified by the AFP model and Milan criteria. Predictive performance was assessed using time-dependent net reclassification improvement (NRI) and area under ROC curve analyses.

Results: Analysis included 1,968 patients with median follow-up of 54.3 months. The AFP model demonstrated superior predictive ability versus Milan criteria for both recurrence and survival (5-year recurrence: 57.4% vs 33.8% for beyond/within Milan; AFP model; 58.7% vs 35.2% for beyond/within Milan; P<0.001). Time-dependent analyses confirmed better discrimination by the AFP model, particularly for early recurrence. Among patients beyond Milan criteria, the AFP model identified a high-risk subgroup with significantly worse outcomes (5-year survival: 48.1% vs 67.0%; HR=1.598; P<0.001).

Conclusions: The AFP model outperforms Milan criteria in predicting post-resection outcomes for HCC, enabling more precise risk stratification. This enhanced prognostic capability could improve patient selection and guide personalized treatment strategies, particularly for cases beyond Milan criteria.

Keywords: Alpha-Fetoprotein Model, Milan Criteria, Hepatic Resection

OP-51

Development and Validation of a Laboratory Risk Score (APASL Score) to Predict Long-Term Survival after Hepatectomy for Hepatocellular Carcinoma: A Multicenter Analysis

Bai-Dong Wang[1], Mng-Da He[1], Jia-Hao Xu[2], Lei Cai[3], Ying-Jian Liang[4], Hong-Wei Guo[5], Kong-Ying Lin[6], Han Liu[7], Zi-Qaing Li[7], Qi-Xuab Zheng[8], Ya-Hao Zhou[9], Ting-Tao Chen[10], Hong Wang[11], Yi-Fan Li[12], Tian Yang[2]

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Aims: To develop and validate a novel, purely laboratory-based risk score (APASL score) for predicting long-term survival outcomes after hepatectomy for hepatocellular carcinoma (HCC). Accurate prediction of long-term survival after hepatectomy for HCC is crucial for surgical decision-making and patient counseling. Existing staging systems that incorporate tumor characteristics may not be available preoperatively. A risk score based solely on preoperative laboratory parameters could provide valuable prognostic information.

Methods: From a multicenter database, patients who underwent hepatectomy for initially-diagnosed HCC were included. The APASL score was developed to predict long-term overall survival using five preoperative laboratory variables: alpha-fetoprotein (AFP), platelet count (PLT), albumin (ALB), aspartate aminotransferase (AST), and bilirubin (BIL). The score was validated in an independent cohort.

Results: The development cohort included 1,286 patients from 9 hospitals, and the validation cohort included 469 patients from another 2 hospitals. The APASL score demonstrated excellent discriminatory ability, with c-indices of 0.812 and 0.783 in the development and validation cohorts, respectively. The score outperformed traditional staging systems, including TNM, BCLC, CLIP, and Milan criteria. Higher APASL scores were associated with significantly worse overall survival (P<0.001). The higher APASL scores remained an independent prognostic factor in multivariate analysis (hazard ratio: 2.154, 95% confidence interval: 1.782-2.609, P<0.001).

Conclusions: The APASL score is a simple, accurate, and purely laboratory-based tool for predicting long-term survival after hepatectomy for HCC. It can facilitate preoperative risk stratification and patient counseling, without the need for tumor characteristics that may only be available postoperatively.

Keywords: Hepatocellular Carcinoma, Laboratory-Based Risk Score, Long-Term Survival Prediction

OP-52

Laparoscopic Hepatectomy for Giant Hepatic Hemangioma: A Vietnamese Center Experience

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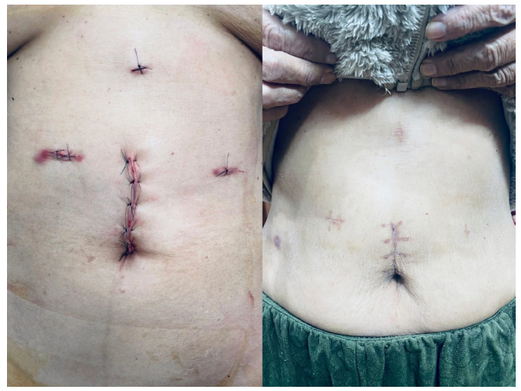
Department of HBP Surgery, 108 Military Central Hospital, Vietnam; Department of HBP Surgery, 175 Military Hospital, Vietnam; Vin University, Vietnam

Aims: Hepatic hemangiomas are the most common benign liver tumors, but giant (>10 cm) and enormous (>15 cm) hemangiomas are rare and often symptomatic, requiring surgical intervention. While laparoscopic hepatectomy poses technical challenges compared to open surgery, it offers significant advantages, including improved patient outcomes and faster postoperative recovery due to its minimally invasive nature. This study aims to present our center's experience with laparoscopic management of these complex cases, focusing on clinical outcomes and technical considerations.

Methods: This retrospective study analyzed 23 patients who underwent laparoscopic hepatectomy for giant and enormous hepatic hemangiomas at Military Central Hospital 108 from September 2015 to December 2023. Clinical and surgical data were collected and analyzed.

Results: Median tumor size was 13.5 ± 8.7 cm. Surgical indications included abdominal pain (86.9%) and rapid tumor growth (13.1%). Enucleation was performed in 43.7% of cases and anatomical resection in 56.3%. Median blood loss was 202.86 ± 211.21 ml, with transfusion required in 8.6% of patients. Median operative time was 143.13 ± 44.23 minutes. Postoperative complications occurred in 8.6% of cases, including bile leak and bleeding. Average hospital stay was 8.53 ± 1.76 days.



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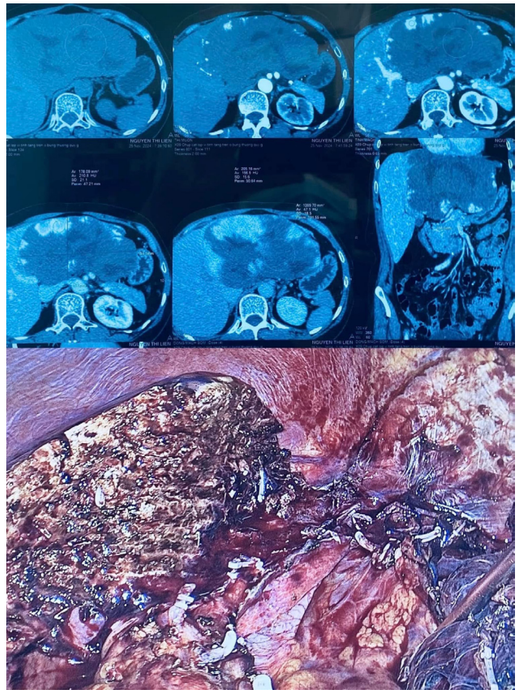

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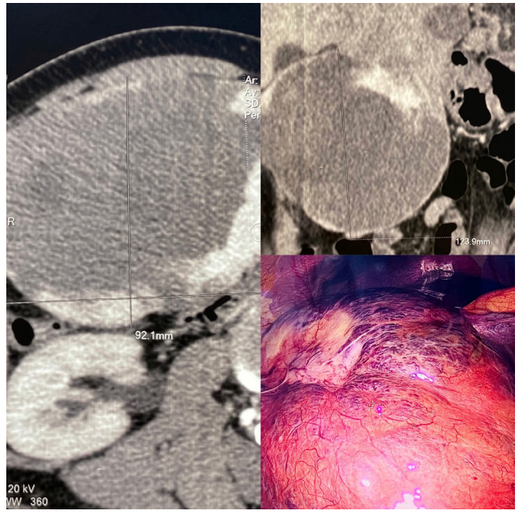


Figure 3.

Conclusions: Despite its technical demands, laparoscopic hepatectomy for giant and enormous hepatic hemangiomas is safe and effective. It offers distinct advantages over open surgery, including reduced operative trauma, faster recovery, and shorter hospital stays, making it a preferable option in suitable cases.

Keywords: Laparoscopic Hepatectomy, Giant Hepatic Hemangioma

OP-53

Surgical Approach to Supradiaphragmatic IVC Tumor Thrombosis of HCC through Abdominal Cavity by Cutting Diaphragm Vertically without Opening the Pericardium

Nyamsuren Ganbileg, Minjuur Boldbaatar, Unenbat Gurbadam, Radnaabazar Munkhbat, Dulguun Erdene-Ochir, Munkhdelger Byambaragchaa, Yerbolat Amankeyldi, Amgalantuul Batdelger, Tserendorj Demchig

Department of HPB Surgery, National Cancer Center of Mongoli

Aims: Surgical removal of tumor thrombosis of HCC in supradiaphragmatic IVC is helpful to extend lifespan and to prevent pulmonary embolism. Supradiaphragmatic IVC thrombosis can be removed through sternotomy and thoracotomy by using cardiopulmonary bypass based on extention of tumor thrombosis nevertheless those procedures have many post-operation complications. Therefore, we had to seek new approach in order to avoid the complications.

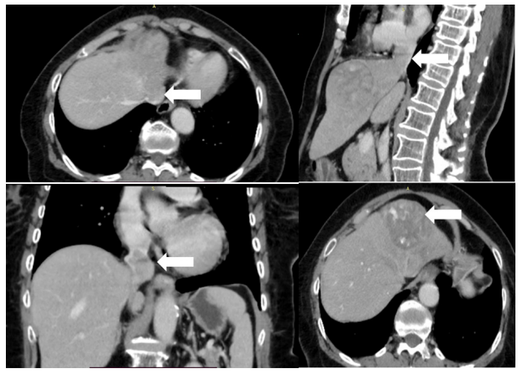
Methods: Patient who is 73 year old woman was diagnosed with Hepatocellular carcinoma in left liver with tumor thrombosis in left hepatic vein and tumor thrombosis extended into supradiaphragmatic IVC.

We performed left hepatectomy, tumor thrombectomy from supradiaphragmatic IVC through abdominal cavity by cutting diaphragm vertically without opening the pericardium.

Results: Operative time was 240 min, blood loss was 400ml and hospital stay was 7 days without any complications. Biopsy result: poorly differentiated hepatocellular carcinoma. Multiple recurrent HCC was diagnosed after operation at 14 months and she patient passed away at 16 months due to recurrent HCC.

Conclusions: However HCC related tumor thrombosis in hepatic vein, IVC and right atrium is extremely rare, incidence of tumor thrombosis of HCC is high about (44-62.2%). Median survival of tumor thrombosis in IVC is roughly 2-5 month. Our patient lived for 16 months after surgery. Removal of tumor thrombosis from supradiaphragmatic IVC by abdominal cavity by cutting diaphragm vertically without opening the pericardium may be safe, feasible and effective approach.

Keywords: Hepatocellular Cancer, Supradiaphragmatic IVC, Tumor Thrombosis, IVC Tumor Thrombosis



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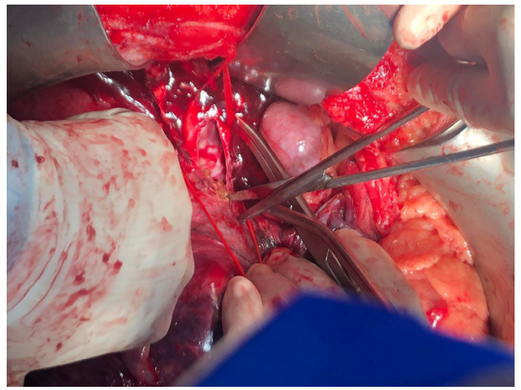

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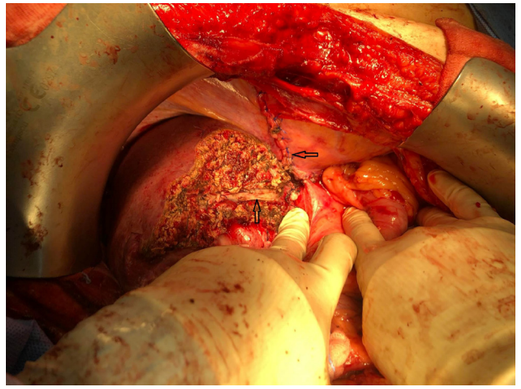

Figure 3.

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10. Liver Cancer, Basic 2

OP-54

Focal Amplification of EGFR Drives Acquired Resistance to Lenvatinib in Hepatocellular Carcinoma

Ji Young Kim[1], Jung Hyun Kim[1], Gamin Han[1], Min Jeong Kim[1], Yeup Yoon[1,2,4], Yong-Han Paik[1,3], Wonseok Kang[1,3,4]

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Aims: Hepatocellular carcinoma (HCC) is a heterogeneous malignancy with poor response to therapies. Lenvatinib, a tyrosine kinase inhibitor (TKI), is used not only as a first-line treatment for patients with unresectable HCC who are ineligible for immunotherapy, but also as a second-line treatment for patients who have progressed after immunotherapy. However, it frequently encounters resistance. This study aims to elucidate the mechanisms of lenvatinib resistance in HCC and develop strategies to overcome it.

Methods: We established lenvatinib-resistant HCC cell lines by gradually exposing sensitive lines to increasing concentrations of lenvatinib. Whole-genome sequencing (WGS) and whole-transcriptome sequencing (WTS) were performed to identify genomic alterations, including copy number variations (CNV) and gene expression alterations. Cell viability assays were conducted using CCK-8 assays to evaluate drug response.

Results: Lenvatinib-resistant HCC cell lines exhibited significantly higher IC_{50} values compared to sensitive lines. WGS revealed novel amplicons, including a notable 15-copy gain of the *EGFR* gene in resistant Huh7 cells. Co-amplified regions with EGFR showed an average size of approximately 3Mbp, with a copy count of approximately 10, indicating focal amplification. Consistent with these genomic alterations, *EGFR* gene expression was increased by 7.4-fold in resistant cells. Erlotinib, an EGFR inhibitor, treatment alone showed no differential effect, but combined treatment with lenvatinib and erlotinib synergistically inhibited cell proliferation and induced apoptosis in resistant cells.

Conclusions: Our study elucidates genomic instability contributing to Lenvatinib resistance, highlighting *EGFR* focal amplification as a key mechanism. The combined treatment strategy offers a promising approach for overcoming lenvatinib resistance, potentially improving patient outcomes.

Keywords: Hepatocellular Carcinoma, Lenvatinib, Resistance, Genomic Instability

OP-55

A Study on the Development of a Traditional Liver Cancer Mouse Model Using Hydrodynamic Injection

HyeonJi Kim, Ha Gyun Kim, Wonjae Lee, Yujin Lee, Eunjeong Kim

Kyungpook National University

Aims: Although research on genetic mutations in liver cancer patients has been ongoing, significant progress in developing effective treatments has yet to be made. Traditional transgenic mouse models for drug development require considerable time and cost due to the complex processes of genetic modification and breeding. To create a more efficient model, we collected mutation data on oncogenes and tumor suppressor genes found in liver cancer patients and engineered them into plasmids. Using the hydrodynamic injection method, we aimed to efficiently induce liver cancer in mice, providing a streamlined and cost-effective approach for research and therapeutic development.

Methods: Hydrodynamic injection is a method that facilitates the delivery and expression of genetic material in target cell through an intravenous injection. The original method of Hydrodynamic injection in small animals involves tail vein injection of plasmid DNA solution in 5-7s in a volume equal to 8% - 10% of the body weight.

The injected plasmid solution directly enters the heart, causing cardiac congestion and backflow to the inferior vena cava and hepatic veins. This solution then reaches the sinusoids; that hydrodynamic pressure expands the liver, enlarges the fenestrae of the endothelium, and forces invagination of the cell membrane of the hepatocytes to allow the DNA to move into the cytoplasm.

Results: After inducing liver cancer using hydrodynamic injection, we examined the liver condition 18 weeks later and confirmed that the injected combination effectively induced tumor formation. To assess strain-specific differences, we analyzed survival, phenotype, tumor size, tumor number, and liver weight. Additionally, histological analyses, including H&E staining and Oil Red O staining, were performed to characterize transcriptomic subtypes and histopathological features. Moving forward, we plan to conduct experiments targeting specific genes based on RNA-seq results.

Conclusions: So far, many genetic mutations that may affect liver tumorigenesis have been investigated in liver-cancer patients, but effective treatments have not yet been developed. Therefore, we try to find out the optimal mouse model by injecting oncogenes or tumor suppressor genes from liver cancer patients into mice through hydrodynamic injection to analyze the development of liver cancer and differences in mechanisms for each mouse strain. Finally, we will determine a combination of genes that is important in the development of liver cancer and how it operates in human liver cancer. Also, we will find out a new therapeutic candidate which can be developed as an anti-cancer drug.

Keywords: Liver Cancer, Hydrodynamic Tail Vain Injection, Mouse

OP-56

Prolonged Lenvatinib Treatment Affects Tumor-Neutrophil Interaction and Contributes to Compromised Immune Checkpoint Blockade Treatment in HCC

Yunong Xie[1], Linglin Liu[1], Yimiao He[1], Minghe Zhang[1], Jiahuan Cai[1], Hin Kwan Wong[1], Terence Kin-Wah Lee[2], Stephanie Ma[3], Man Tong[1]

[1]School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong; [2]Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China; [3]School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong

Aims: Hepatocellular carcinoma (HCC), the most common form of primary liver cancer, remains a major cause of cancer-related mortality worldwide. While lenvatinib is an effective treatment for unresectable HCC, its prolonged use has been associated with impaired responses to anti-PD-1 immune checkpoint blockade (ICB) therapy, but the underlying mechanisms remain poorly understood. This study aims to investigate the mechanism underlying such therapy resistance.

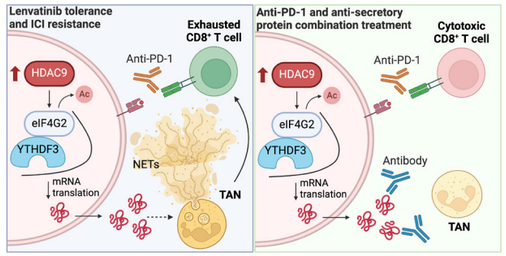
Methods: Using immunocompetent mouse models and single-cell RNA sequencing, the transcriptomic alteraction

Results: We discovered that prolonged lenvatinib treatment drives upregulation of HDAC9 expression and induces a phenotypic shift in neutrophils toward enhanced neutrophil extracellular trap (NET) formation. Immunofluorescence staining confirmed increased NET accumulation in tumor tissues with high HDAC9 expression, and neutrophils co-cultured with HDAC9-high tumor cells exhibited a similar NET phenotype. Notably, inhibiting HDAC9 expression and depleting neutrophils restored sensitivity towards anti-PD-1 therapy and enhanced the cytotoxicity of tumor-infiltrating CD8+ T cells, whereas depleting CD8+ T cells abrogated the therapeutic benefits of HDAC9 inhibition. Mechanistically, we identified that HDAC9 upregulation deacetylates key post-transcriptional modification-related proteins, potentially altering the tumor secretome. This altered secretome might mediate tumor-neutrophil interactions, promoting neutrophil phenotypic shifts, suppressing CD8+ T cell cytotoxicity, and ultimately dampening the efficacy of anti-PD-1 therapy.

Conclusions: These findings provide novel insights into the interplay between HDAC9, neutrophils, and immune evasion in

HCC, offering potential therapeutic targets to enhance therapeutic efficacy in HCC patients.

Keywords: Hepatocellular Carcinoma, Tumor-Neutrophil Interaction, Therapy Resistance



OP-57

IGF2BP1 Promotes Proliferation and Metastasis of Hepatocellular Carcinoma via m6A-Modified PEG10 mRNA

Qiongguang Huang[1,2], Zihan Zhou[3], Xiaobing Yang[2], Qian Guo[4], Binbin Jiang[2], Yan Mao[2], Lizheng Tan[2], Moqin Qiu[5], Shicheng Zhan[2], Yingchun Liu[2,6], Cunli Nong[4], Wenfeng Gong[7], Shuangdi Duan[2], Guandou Yuan[8], Hongping Yu[2,6,9]

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Aims: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related deaths worldwide. IGF2BP1 is a reader of N6-methyladenosine (m6A) on RNA and has been associated with cancer progression and metastasis. However, whether IGF2BP1 regulates proliferation and metastasis through m6A modification in HCC remains to be investigated.

Methods: We first analyzed expression levels of m6A reader in 371 HCC and 50 normal tissues from The Cancer Genome Atlas (TCGA) dataset and then performed RT-qPCR and immunohistochemical assays to validate the expression of *IGF2BP1* mRNA (n=106) and protein (n=88) in additional HCC tissues, respectively. Furthermore, we used univariate and multivariate Cox proportional hazards regression analysis to identify independent predictors of overall survival (OS) of HCC and to determine biological effects of IGF2BP1 on HCC *in vitro* and *in vivo*. Subsequently, we used RIP-qPCR, MeRIP-qPCR, RNA-stability, and dual luciferase reporter assays to screen and validate the candidate targets of IGF2BP1. Finally, we used Western blot to detect expression of proteins of the related signaling pathways and pathway inhibitors for the rescue experiments.

Results: We found that the IGF2BP1 expression was upregulated in HCC and that high expression levels of IGF2BP1 protein were an independent predictor for OS in HCC. Functionally, IGF2BP1 facilitated proliferation and metastasis of HCC both *in vitro* and *in vivo*. Furthermore, IGF2BP1 directly recognized and bound to METTL3-mediated m6A in modification on *PEG10* mRNA and maintained its stability. Meanwhile, PEG10 overexpression abolished the inhibitory effects on HCC cell proliferation, migration, invasion capacity and activation of the PI3K/AKT/mTOR signaling pathway caused by IGF2BP1 knockdown, and these effects were also abolished by the PI3K inhibitor LY294002.

Conclusions: IGF2BP1-targeted recognition and binding depend on METTL3-mediated m6A modification on *PEG10* mRNA 3′UTR, thus increasing *PEG10* mRNA stability and further activating the PI3K/AKT/mTOR signaling pathway, leading to HCC proliferation, migration and invasion. Therefore, IGF2BP1 may be a potential biomarker for the prognosis of HCC patients.

Keywords: IGF2BP1, M6A, Hepatocellular Carcinoma, PEG10, PI3K/AKT/MTOR

OP-58

Finding the Role of a Novel Oncogene in Liver Cancer through Hydrodynamic Gene Delivery

Ha Gyun Kim[1], Hyeon Ji Kim[2], Wonjae Lee, Yujin Lee, Eunjeong Kim

Kyungpook National University

Aims: Hepatocellular carcinoma (HCC) is the 4th leading cause of cancer-related mortality and the 6th most common cancer worldwide, while in South Korea, it ranks as the 2nd leading cause of cancer-related deaths.

Despite extensive studies on genetic mutations in HCC patients, the development of targeted therapies has been highly limited.

This study aims to elucidate the functional role of PLD6 in HCC and explore its potential as a novel therapeutic target.

PLD6 is known to hydrolyze cardiolipin in the outer mitochondrial membrane, promoting mitochondrial fusion, and is also involved in piRNA metabolism.

However, its role in HCC remains largely unknown, and its underlying molecular mechanisms have not been clearly defined.

Therefore, this study investigates the impact of PLD6 expression on HCC initiation and progression.

By conducting molecular and cellular analyses within the HCC microenvironment, we aim to establish PLD6 as a potential key regulator in liver cancer and propose a new therapeutic strategy based on these findings.

Methods: Hydrodynamic injection : Hydrodynamic injection is a method that facilitates the delivery and expression of genetic material in target cell through an intravenous injection.

The original method of Hydrodynamic injection in small animals involves tail vein injection of plasmid DNA solution in 5-7s in a volume equal to 8% - 10% of the body weight.

The injected plasmid solution directly enters the heart, causing cardiac congestion and backflow to the inferior vena cava and hepatic veins.

This solution then reaches the sinusoids; that hydrodynamic pressure expands the liver, enlarges the fenestrae of the endothelium, and forces invagination of the cell membrane of the hepatocytes to allow the DNA to move into the cytoplasm.

Results: Using animal models with PLD6 overexpression and deficiency, we evaluated its functional role in hepatocellular carcinoma (HCC) and found evidence suggesting that PLD6 may act as a tumor suppressor.

Even in groups injected with the same amount of HCC-inducing genes, those co-expressing PLD6 maintained liver tissue similar to the control group, with minimal tumor formation.

Additionally, survival analysis revealed a significant difference in survival rates between the HCC group and the HCC+PLD6 group, further supporting the potential role of PLD6 in suppressing HCC progression.

Further validation is currently underway using PLD6 knockout (KO) mouse models.

If the tumor-suppressive function of PLD6 is confirmed in these models, it will suggest that PLD6 exhibits a unique function distinct from other members of the PLD superfamily.

Conclusions: This study suggests that PLD6 may function as a tumor suppressor in hepatocellular carcinoma (HCC), highlighting its potential role distinct from other previously reported PLD superfamily members.

PLD6 overexpression appears to inhibit HCC progression, opening up the possibility of developing novel targeted therapeutic strategies utilizing PLD6 in liver cancer treatment.

Further research on PLD6's mitochondrial functions and its role in HCC is needed to clearly define its involvement as a key regulator of HCC initiation and progression.

This study provides a foundation for establishing PLD6 as a novel therapeutic target for HCC and is expected to serve as a valuable basis for future gene-based cancer therapy research.

Keywords: Hepatocellular Carcinoma (HCC), Hydrodynamic Tail Vein Injection, Phospholipase D Family Member 6, Tumor Suppressor Gene

OP-59

Long Non-Coding Rna TUG1 Regulates Multiple Glycolytic Enzymes in Hepatocellular Carcinoma Cells via Sponging microRNA-122-5p

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Aims: Hepatocellular carcinoma (HCC) remains the third-leading cause of cancer deaths; however, its therapeutic options are limited. To understand the molecular mechanisms of hepatocellular carcinoma (HCC) and identify potential therapeutic targets, we investigated the role of the long non-coding RNA taurine-upregulated gene 1 (TUG1) in HCC. Specifically, we aimed to determine the impact of TUG1 on HCC cell transcriptomics and its molecular function in glycolysis.

Methods: We established TUG1-knockdown and control HCC cell lines and performed RNA-sequencing (RNA-seq). KEGG pathway analysis was used to identify enriched pathways. Glucose uptake, ATP synthesis, and lactate production were measured. Clinical HCC tissue data was used to assess gene expression correlations. Bioinformatic tools and dual luciferase assays were employed to explore the competing endogenous RNA (ceRNA) model, identify microRNAs (miRNAs) interacting with TUG1, and confirm direct interactions.

Results: RNA-seq revealed glycolysis as the top-hit pathway upon TUG1 silencing. TUG1-depleted HCC cells showed impairments in glucose uptake, ATP synthesis, and lactate production. Clinical data showed positive gene expression correlations between TUG1 and glycolysis genes. To identify a molecular function of TUG1 in glycolysis, we explored the ceRNA model and used bioinformatic tools to find the five miRNAs that had the most binding sites for TUG1. MicroRNA-122-5p (miR-122-5p) displayed an inverse relationship for gene expression with most TUG1-regulated glycolysis genes. Dual luciferase assays confirmed direct interactions between TUG1 and miR-122-5p, and between miR-122-5p and the 3′ UTR of *PKM* and *ALDOA*, which encode two essential glycolytic enzymes. Inhibition of miR-122-5p alleviated the suppression of glycolysis induced by TUG1 depletion.

Conclusions: Our study demonstrates that TUG1 plays a critical role in promoting glycolysis in HCC cells by sponging miR-122-5p, which is a negative regulator of multiple glycolytic

enzymes. This suggests that TUG1 and miR-122-5p may be potential therapeutic targets for HCC.

Keywords: Hepatocellular Carcinoma, Long-Noncoding RNA, Microrna, Glycolysis

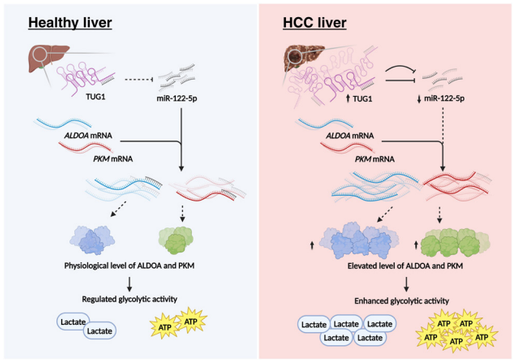

Figure 1. Mechanistic model.

THE LIVER WEEK 2025

THE A Big Welcome to the Liver Festival in Gyeongju, Korea
LIVER WEEK 2025

May 29 - 31, 2025 | HICO, Gyeongju, Korea

DAY 3: May 31 (Sat)

Oral Poster Presentation 2

OP-60~OP-65	HBV
OP-66~OP-71	MASLD, Clinical 2
OP-72~OP-77	Liver Cancer, Clinical 3
OP-78~OP-83	HBV and LC, Basic
OP-84~OP-89	Others
OP-90~OP-95	Liver Cancer, Clinical 4
OP-96~OP-101	Liver Transplantation 2
OP-102~OP-107	Liver Cancer, Basic 3
OP-108~OP-112	Liver Cancer, Clinical 5
OP-113~OP-118	Biliary and Pancreatic Surgery

Saturday, May 31, 2025, 09:30-10:30

11. HBV

OP-60

Comparative Renal Safety of Besifovir Dipivoxil Maleate and Tenofovir Disoproxil Fumarate in Chronic Hepatitis B: Insights from Nationwide Cohort Study

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Aims: Besifovir dipivoxil maleate (BSV) is a novel antiviral agent approved in Korea for chronic hepatitis B (CHB) treatment. While previous comparative studies between BSV and tenofovir disoproxil fumarate (TDF) suggested lower renal toxicity with BSV, these findings were limited by small sample sizes. This study aimed to comprehensively assess the incidence of chronic kidney disease (CKD) in CHB patients treated with BSV versus TDF using a nationwide cohort.

Methods: In this retrospective cohort study, we analyzed treatment-naïve CHB patients who initiated BSV or TDF therapy between January 2018 and December 2022. Using South Korean national health database, we created balanced cohorts of 25,849 patients each through inverse probability of treatment weighting (IPTW). The primary outcome measure was CKD incidence.

Results: The incidence rate (IR) of CKD was significantly lower in the BSV group compared to the TDF group (3.11 vs. 4.75 per 1,000 person-years; incidence rate ratio [IRR] 1.53, 95% CI 1.28-1.82, *P*<0.001). Using BSV as the reference, the adjusted hazard ratio (HR) for CKD in the TDF group was 1.26 (95% CI 1.05-1.52, *P*=0.014). In patients aged 60 years and older, TDF showed a markedly higher incidence and risk of CKD (IR 3.93 vs. 10.18 per 1,000 person-years; IRR 2.59, 95% CI 1.87-3.59, *P*<0.001; HR 2.45, 95% CI 1.74-3.47, *P*<0.001).

Conclusions: BSV is linked to a lower incidence of CKD compared to TDF, particularly in patients aged 60 and older, suggesting it may be a safer treatment option for CHB, especially in elderly patients at higher risk of renal impairment.

Keywords: Besifovir Dipivoxil Maleate, Tenofovir Disoproxil Fumarate, Chronic Hepatitis B, Chronic Kidney Disease

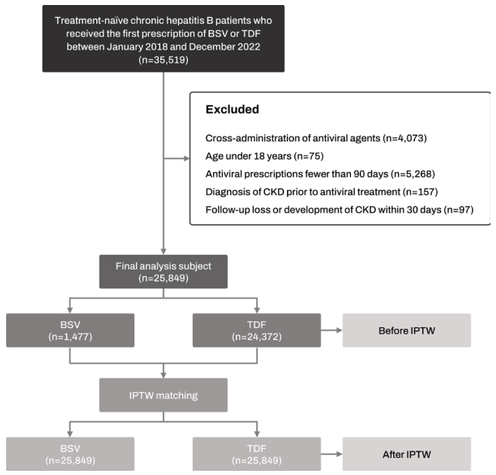

Figure 1.

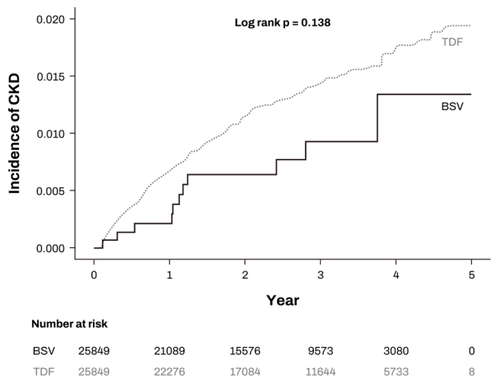

Figure 2.

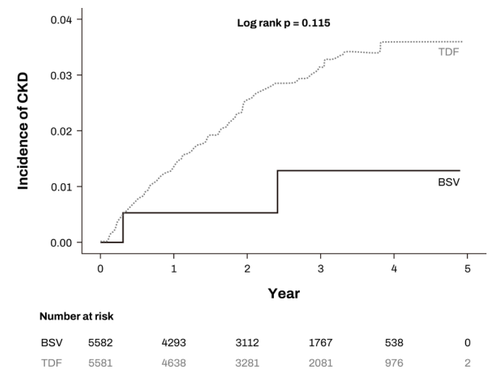

Figure 3.

OP-61

VEMLIA®(DA-2803) versus VEMLIDY® for the Treatment of Patients with Chronic Hepatitis B: A Multi-Center, Randomized, Double-Blind, Active-Controlled, Non-Inferiority Study

Jeayeon Park[1], Su Jong Yu[1], Sang Gyune Kim[2], Hyun Yang[3], Hyun Chin Cho[4], Yeon Seok Seo[5], Ji Hoon Kim[6], Young Kul Jung[7], Yang Hyun Baek[8], Jae Youn Cheong[9], Moon Young Kim[10], Yong Keun Cho[11], Hyuk Soo Eun[12], Jihyun An[13], Jeong Won Jang[14]

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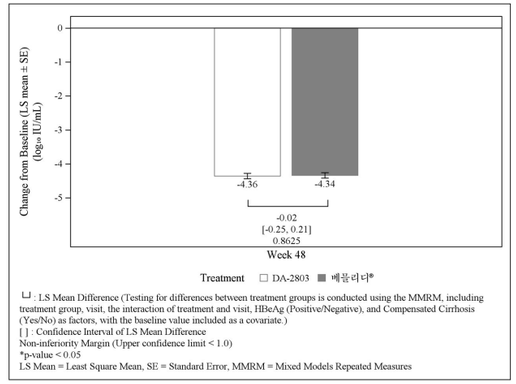
Aims: In bioequivalence study, DA-2803 developed by Dong-A ST was shown to have pharmacokinetic characteristics equivalent to VEMLIDY®. A comparative study was conducted to evaluate the antiviral activity and safety of DA-2803 compared to VEMLIDY® in patients with chronic hepatitis B (CHB).

Methods: Patients with CHB were recruited from 30 hospitals in Korea between March 2023 and September 2024 and were randomized to receive either DA-2803 or VEMLIDY® once daily for 48 weeks. The primary endpoint was the change in hepatitis B virus (HBV) DNA levels from baseline at week 48. Secondary efficacy endpoints included the mean change in HBV DNA levels from baseline to week 24, the proportion of subjects with achieving HBV DNA <69 IU/mL and <29 IU/mL at week 24 and 48, the mean change in alanine aminotransferase levels from baseline, and the proportions of HBsAg loss, HBsAg seroconversion, HBeAg loss, and HBeAg seroconversion at week 24 and 48. Adverse events, bone and renal safety were also investigated.

Results: A total of 120 patients were randomized, with 119 included in the efficacy analyses (DA-2803 group: 61 in VEMLIDY® group: 58). The least squares (LS) mean change in HBV DNA (log_{10} IU/mL) from baseline at week 48, analyzed using the Mixed Model for Repeated Measures, was -4.36 in the DA-2803 group and -4.34 in the VEMLIDY® group. The LS mean difference was -0.02 (95% confidence interval -0.25, 0.21), with the upper limit 0.21 below the non-inferiority margin of 1, supporting the non-inferiority of DA-2803 to VEMLIDY®. There were no statistically significant differences in secondary endpoints and the safety profiles between treatment groups.

Conclusions: The antiviral activity of DA-2803 was non-inferior to that of VEMLIDY® and there were no significant differences in efficacy and safety between groups. This study suggests that DA-2803 can be used as an equivalent option to VEMLIDY® in patients with CHB.

Keywords: HEPATITIS B VIRUS, TENOFOVIR ALAFENAMIDE FUMARATE, ANTIVIRAL TREATMENT, EQUIVALENCE TEST



OP-62

Comparative Risk of Osteoporosis and Fractures in Chronic Hepatitis B Patients: Tenofovir Disoproxil Fumarate versus Entecavir in a Korean Nationwide Cohort

Jisoo Lee[1], Yoon E Shin[2], Jae Young Kim[2], Hyuk Kim[1], Jeong Ju Yoo[3], Sang Gyune Kim[3], Young Seok Kim[3]

[1]Department of Internal Medicine, Soonchunhyang University School of Medicine, [2]Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital

Aims: It remains unclear whether Entecavir (ETV) should be the preferred alternative for patients with pre-existing osteoporosis risk factors. This study assesses whether TDF increases the risk of osteoporosis or fractures compared to ETV, using nationwide data from South Korea.

Methods: We analyzed data from 64,283 patients with chronic hepatitis B (CHB) who were prescribed either TDF or ETV. The primary outcome was the incidence of osteoporosis or fractures. To reduce selection bias between the TDF and ETV groups, we applied Inverse Probability of Treatment Weighting (IPTW).

Results: Patients were monitored for an average of 50.8 ± 16.8

months, during which 3,656 patients developed osteoporosis or experienced osteoporotic fractures. TDF use was associated with an increased incidence of osteoporosis across all age groups (Incidence Rate Ratio [IRR] 0.77, 95% Confidence Interval [CI] 0.73 – 0.82, *P*<0.001), but it did not significantly increase the risk of fractures (IRR 0.99, 95% CI 0.90 – 1.08, *P*=0.796). TDF was identified as a risk factor for osteoporosis (Hazard Ratio [HR] 0.749, 95% CI 0.710 – 0.790, *P*<0.001) but not for fractures (HR 0.982, 95% CI 0.899 – 1.07, *P*=0.695). In patients over 60 years old, the risk of osteoporosis and fractures was relatively lower in the ETV group, becoming evident after 1 and 3 years of treatment, respectively (HR 0.754, 95% CI 0.685 – 0.830, *P*<0.001; HR 0.825, 95% CI 0.714 – 0.954, *P*=0.010).

Conclusions: Long-term use of TDF is significantly associated with an increased risk of osteoporosis and fractures, especially in patients over the age of 60.

Keywords: Tenofovir Disoproxil Fumarate, Entecavir, Chronic Hepatitis B, Osteoporosis

OP-63

Turning LLMs into Clinical Decision Supporters: Optimizing Prompt Structures for Drug Side Effect Prediction in Chronic Hepatitis B Patients

Jihyun Moon[1], Soon Sun Kim[2], Ji Eun Han[2], Hyo Jung Cho[2], Jae Youn Cheong[2], Charmgil Hong[1]

[1]Department of Computer Science and Electrical Engineering, Handong Global University, Pohang, Korea; [2]Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Aims: *This work was supported (1) by the MSIT(Ministry of Science, ICT), Korea, under the Global Research Support Program in the Digital Field program (RS-2024-00431394) supervised by the IITP (Institute for Information & Communications Technology Planning & Evaluation) and (2) by the National IT Industry Promotion Agency (NIPA) grant funded by the MSIT, Korea, under the Development of AI Precision Medical Solution (Doctor Answer 2.0, S0252-21-1001).

Chronic hepatitis B (CHB) is a liver inflammation caused by the hepatitis B virus (HBV) that persists beyond six months. While antiviral medications effectively suppress viral replication and prevent liver damage, their long-term use can compromise renal functionality. This work proposes a novel approach to employ large language models (LLMs) for clinical prediction, specifically for forecasting creatinine clearance decline. We validate the effectiveness of our framework by comparing it with conventional data-driven approaches, such as machine learning-based predictive models. Additionally, we explore optimal strategies for effectively utilizing LLMs in clinical prediction tasks by evaluating their performance under different prompt structures.

Methods: This study analyzed electronic medical records (EMR) from 2,303 patients receiving antiviral medication over 36 months. We identified creatinine clearance decline using estimated glomerular filtration rate (eGFR), defined as a decrease from ≥60 to <60 mL/min/1.73m^2 after treatment. We compared our LLM-based approach with random forest models as a conventional baseline. To navigate optimal prompt strategies, we designed nine different prompts by combining three data presentation formats (HTML, Markdown, and Sentence) with three structural variations: basic task description, enhanced constraints, and Python code-style instructions. Performance was evaluated for all combinations.

Results: Our comparison of the LLM-based approach (using LLaMa 3.1) with random forest models showed no statistically significant performance differences, which validates LLMs as viable alternatives to traditional predictive models. Among prompt strategies, Python code-style instructions combined with Sentence format exhibited superior performance (accuracy 0.3656). This represents up to 81% improvement over other prompt structures and highlights the importance of structured reasoning instructions.

Conclusions: Our study demonstrates that properly prompted LLMs achieve clinical prediction performance comparable to machine learning models without direct training on patient data. Well-structured prompts with code-style instructions significantly enhance decision-making of LLMs, opening new possibilities for utilizing LLMs in clinical contexts.

Keywords: HBV, Drug Side Effect Prediction, Large Language Model, Machine Learning

OP-64

Longitudinal Renal Function Trajectories in Chronic Hepatitis B Patients on Entecavir or Tenofovir Alafenamide: A Nationwide Population-Based Study in Korea

Sung Kyu Choi[1], Ga Ram You[2], Sung-Bum Cho[2], Jungkuk Lee[3], Jae Hyun Yoon[1], Hyojin Song[1], Seol Hui Nam[1]

[1]Department of Gastroenterology and Hepatology, Chonnam National University Hospital and Medical School, Gwangju, South Korea; [2]Department of Gastroenterology and Hepatology, Chonnam National University Hwasun Hospital and Medical School, Hwasun, South Korea; [3]Department of Data Science, Hanmi Pharm. Co., Ltd

Aims: Patients with chronic hepatitis B (CHB) infection often require lifelong antiviral therapy with nucleot(s)ide (NUC) analogues. Prolonged use of NUC therapy may lead to a decline in renal function, the extent of which depends on the specific NUC agent administered. Tenofovir alafenamide (TAF) and entecavir (ETV) are generally regarded as having a favorable renal safety profile; however, data on their long-term effects on renal function in large patient populations remain limited. This study aims to examine the longitudinal trajectory of renal function in CHB patients undergoing treatment with TAF or ETV.

Methods: Utilizing data from the Korea National Health Insurance Service, we identified 26,427 patients treated with entecavir (ETV) and 6,789 patients treated with tenofovir alafenamide (TAF). The primary outcome was the progression of chronic kidney disease (CKD), defined as an advancement of CKD by at least one stage and the presence of overt proteinuria. Propensity score (PS) matching was employed for outcome comparisons.

Results: In the 1:1 PS-matched cohort comprising 2,712 patient pairs, after adjustment for multiple confounding variables, no statistically significant difference was observed in CKD stage progression ≥1 between the TAF and ETV groups (7.56 vs. 7.96/100 person-years [PYs]; HR 1.103, *P*=0.0703). Similarly, major renal events—defined as CKD stage progression ≥2, estimated glomerular filtration rate (eGFR) <15 mL/min/1.73m^2, kidney transplantation, or dialysis—did not differ significantly between the two groups (0.13 vs. 0.08/100 PYs; HR 0.593, *P*=0.1977). Furthermore, the incidence of hepatocellular carcinoma was comparable between the groups (1.48 vs. 1.30/100 PYs; HR 0.852, *P*=0.1541).

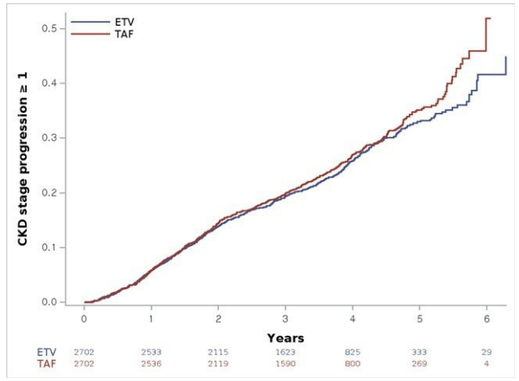


Figure 1.

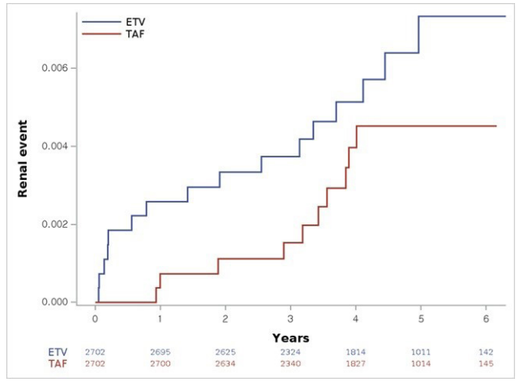


Figure 2.

Conclusions: In this large-scale, PS-matched analysis, long-term treatment with TAF showed no significant difference compared to ETV in CKD progression, major renal events, or hepatocellular carcinoma incidence. These findings suggest that TAF and ETV have comparable renal safety and oncologic outcomes in patients with CHB.

Keywords: Hepatitis B Virus, Tenofovir, Entecavir, Renal Function

OP-65

Efficacy of Prophylactic Antiviral Therapy in Preventing Hepatitis B Reactivation in Patients with Anti-HBc Antibody Undergoing Daratumumab Treatment

Jaejun Lee[1], Ji-Hoon Kim[1], Ji Won Han[1], Soon Kyu Lee[1], Jeong Won Jang[1], Jong Young Choi[1], Chang-Ki Min[2], Pil Soo Sung[1]

[1]Division of Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; [2]Division of Hematology, Department of Internal Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: Daratumumab, a monoclonal antibody targeting CD38, is currently used as a first-line therapy in patients with multiple myeloma. This study aims to investigate the risk of HBR in patients with the anti-HBc antibody and to evaluate the efficacy of prophylactic antiviral therapy in this population.

Methods: Data from 345 multiple myeloma patients treated with daratumumab between 2014 and 2024 were retrospectively collected. Patients with the anti-HBc antibody were included in the study, while those with positive HBsAg prior to daratumumab treatment were excluded. HBR was defined as HBsAg seroconversion or detection of HBV DNA until subsequent chemotherapy or 12 months after cessation of daratumumab if no subsequent chemotherapy was performed.

Results: Among the 345 patients, 109 had the anti-HBc antibody and were included in the analysis. The mean age was 64.6 years, and males were predominant (56.0%). The median duration of daratumumab treatment was 101 days, during which ten patients received prophylactic antiviral therapy (9 with entecavir and 1 with tenofovir alafenamide). Overall, 9 patients (8.3%) experienced HBR, with 3 suffering from severe hepatitis (ALT exceeding 200U/L) due to HBR, resulting in one mortality. No patient who received prophylactic antiviral therapy experienced HBR. The cumulative incidence rates of HBR in the non-antiviral treatment group were 8.0% at 12 months and 12.3% at 24 months after the start of daratumumab, while the antiviral treatment group had a cumulative incidence of 0.0%. When restricted mean survival time (RMST) was employed to compare the area under the Kaplan-Meier curve of HBR-free survival in both groups, the antiviral treatment group was significantly higher than the non-antiviral treatment group (Difference in RMST = 2.00, *P*=0.002; Ratio of RMST = 1.09, *P*=0.002). HBsAb titers less than 100 IU/L (odds ratio 7.527, *P*=0.057) and

anti-HBc antibody titer (odds ratio 1.234, *P*=0.156) showed a tendency towards an increased incidence of HBR.

Conclusions: There is a considerable risk of HBR in multiple myeloma patients with the anti-HBc antibody undergoing daratumumab treatment. The use of antiviral therapy for a sufficient duration may prevent HBR in these at-risk patients.

Keywords: Daratumumab, Hepatitis B Reactivation, Anti-HBC Antibody, Multiple Myeloma

Saturday, May 31, 2025, 09:30-10:30

12. MASLD, Clinical 2

OP-66

MEFV Dysfunction Promotes Hepatocellular Carcinoma Progression via Inflammasome Activation

Hyunjae Shin[1], Gayeon Cho[2], Chansub Lee[3,4], Ji Hyun Park[3], Seung Ho Choi[5], Eun Kyung Choe[6], Eunchae Park[3], Haeryoung Kim[7], Suk Kyun Hong[8], Youngrok Choi[8], Nam-Joon Yi[8], Kwang-Woong Lee[8], Kyung-Suk Suh[8], Moon Haeng Hur[1], Yun Bin Lee[1], Jeong-Hoon Lee[1], Su Jong Yu[1], Yoon Jun Kim[1], Jung-Hwan Yoon[1], Jong Kyoung Kim[2], Youngil Koh[3], Eun Ju Cho[1]

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Aims: Hepatocellular carcinoma (HCC) progression is closely linked to chronic inflammation, yet the role of germline mutations in this process remains unclear. We investigated the impact of rare MEFV mutations, particularly the S503C variant, on the tumor microenvironment and HCC progression through inflammasome activation.

Methods: To identify immune-related germline variants affecting HCC progression, a rare germline variant analysis was conducted using PCAWG, the 1000 Genomes Project, and a Korean HCC cohort (n=471). In vitro co-culture experiments with THP-1-derived inflammatory macrophages, single-nucleus RNA sequencing (snRNA-seq) of tumor and normal samples (each n=3), and immunohistochemistry (IHC) on surgical specimens (MEFV+, n=10; MEFV-WT, n=11) were performed.

Results: MEFV mutations were significantly associated with HCC (*P*<0.05) and linked to increased IL-18 expression and an expansion of inflammatory macrophages. snRNA-seq revealed that MEFV+ tumors exhibited enhanced macrophage-T cell interactions, with upregulation of IL-18, IL-15, and CXCL12, which facilitate CD8$^+$ T cell recruitment and activation. Ligand-receptor interaction analysis showed elevated HLA-related interactions between macrophages and CD8$^+$ T cells, suggesting increased antigen presentation. IHC confirmed increased IL-18 expression and CD8$^+$ T cell infiltration at the tumor margin in MEFV+ HCC patients. Although recurrence-free survival did not reach statistical significance (*P*=0.20), MEFV+ patients exhibited a trend toward early recurrence post-curative resection.

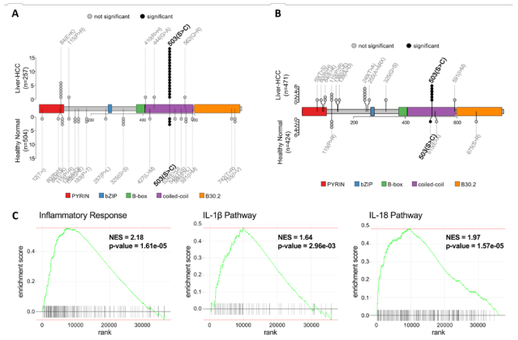

Figure 1.

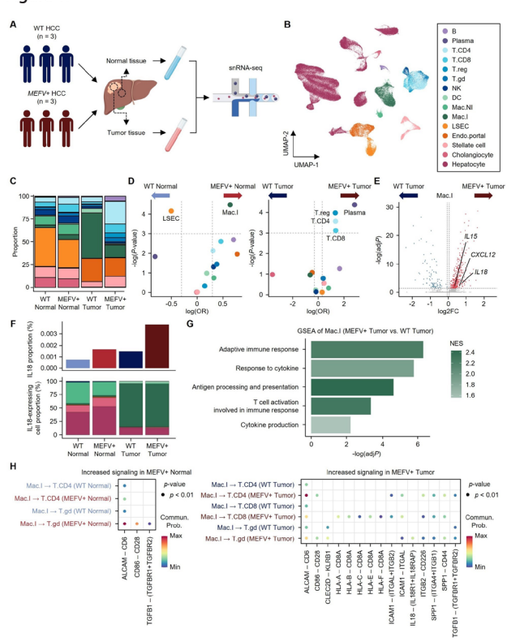

Figure 2.

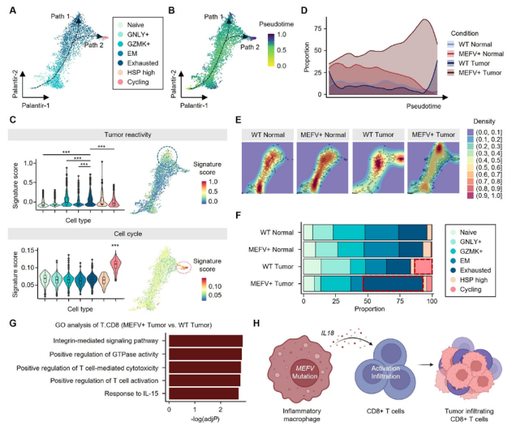

Figure3.

Conclusions: Our findings suggest that MEFV mutations remodel the tumor microenvironment through IL-18-mediated macrophage and T cell interactions, thereby promoting HCC progression. These results highlight the MEFV S503C variant as a potential prognostic factor and suggest targeting the pyrin-inflammasome axis as a novel immunologic therapy.

Keywords: PYRIN, MEFV, Inflammasome, Liver Cancer

OP-67

A Randomized Controlled Trial to Explore the Effect of Modulation of Gut Microbiota on Liver Fibrosis in Patients with Non-Alcoholic Steatohepatitis

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Aims: Non-Alcoholic Steatohepatitis (NASH), a severe form of Non-Alcoholic Fatty Liver Disease (NAFLD), can lead to liver fibrosis on progression. Recently, gut microbiota has proven to play critical role in liver fibrosis by modulating the gut-liver axis. Thus, this study was planned to explore the therapeutic potential of modulation of gut microbiota in preventing liver fibrosis in patients with NASH.

Methods: This was a placebo-controlled, parallel arm randomized controlled trial (RCT) carried out for a duration of 24 weeks at the medicine department of a tertiary care hospital in India. Biopsy confirmed cases of NASH patients with stage 2-3 fibrosis were included in the study and were randomized into two groups. The intervention group was given a synbiotic supplement (probiotics combined with prebiotics) daily while the control group received placebo. Liver elastography was performed before starting the study and after 24 weeks to assess liver fibrosis. The levels of hyaluronic acid and tissue inhibitor of metalloproteinase-1(TIMP-1) were assessed as serum biomarkers for fibrosis. The alteration in gut microbiota composition was also assessed. Relevant statistical analysis was conducted and *P*<0.01 was considered significant.

Results: The study was conducted among 60 participants, 30 in each group. There was a statistically significant reduction in liver fibrosis in the intervention group when compared with control group (-2.4 kPa vs -0.7 kPa, *P*<0.01). There was a 20% (*P*<0.01) reduction in the serum fibrosis biomarkers in intervention group, which were not significant altered in control group. There was a significant increase in the gut beneficial bacteria like Lactobacillus and reduction in the pro-inflammatory bacteria like Enterobacteriaceae in intervention group. In consequence, inflammatory markers like TNF-α and IL-6 were also decreased significantly in the intervention group (*P*<0.01).

Conclusions: Thus, in conclusion, it can be stated that gut microbiome modulation can help prevent or reduce the progression of liver fibrosis in patients with NASH. Further long term studies with larger sample size must be conducted to explore personalised theraputic regimens and treatment outcomes for gut microbiata modulation.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Microbiome

OP-68

Impaired Sensitivity to Thyroid Hormones Is Associated with Cardiovascular Outcomes in Euthyroid Subjects with Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: Thyroid hormone plays a crucial role in metabolic regulation and maintaining cardioavascular homeostasis. However, the correlation between thyroid hormone sensitivity and cardiovascular outcomes in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) remains uncertain. This study aimed to investigate the association between thyroid hormone sensitivity and cardiovascular risk in euthyroid MASLD patients.

Methods: We recruited 36,520 euthyroid adults (18-80 years) who underwent health examinations at our center and who were not previously diagnosed with cardiovascular or thyroid disease. Cardiovascular risk was defined as > 100 calcium score or 50% diameter stenosis on coronary computed tomography. Associations were estimated using a multivariable Cox model. Sensitivity analyses were performed by defining the cardiovas-

cular risk using the PREVENT scores.

Results: Impaired sensitivity to thyroid hormone was associated with cardiovascular risk in patients with MASLD after adjustments for age, sex, body mass index, smoking, hypertension, diabetes, total cholesterol, low-density lipoprotein, and triglycerides as follows: TT4RI - adjusted hazard ratio [aHR], 2.09; 95% confidence interval [CI], 1.09-4.00; *P*=0.005, TSHI - aHR, 2.24; 95% CI, 1.15-4.36; *P*=0.008, TFQI - aHR, 2.01; 95% CI, 1.04-3.89; *P*=0.003, PTFQI - aHR, 2.16; 95% CI, 1.12-4.17; *P*=0.006. Similar findings were observed in the analysis of subgroups stratified by age, sex, diabetes status, and hypertension status. Sensitivity analyses showed consistent results.

Conclusions: Impaired sensitivity to thyroid hormone, centered on variations in the typical pituitary response to thyroid hormones, was associated with cardiovascular risk in patients with MASLD.

Keywords: Parametric Thyroid Feedback Quantile Index, Cardiovascular Risk, Euthyroid Population, Thyroid Hormone Sensitivity

OP-69

Cancer Risk and Its Non-Invasive Predictors in MASLD, MetALD, and ALD: A Longitudinal Analysis

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Aims: The new classification of steatotic liver disease (SLD) includes metabolic dysfunction-associated steatotic liver disease (MASLD), MASLD with increased alcohol intake (MetALD) and alcohol-related liver disease (ALD), which were previously excluded from the NAFLD definition. Although alcohol is known to be a carcinogen, studies on the development of cancer in alcohol-related SLD disease defined by the new classification are needed.

Methods: We analyzed data from 66,332 participants who underwent a health checkup between 2010 and 2011. Liver steatosis was diagnosed by sonography. We investigated whether the Fibrosis-4 Index (FIB-4) and the Steatosis-Associated Fibrosis Estimator (SAFE) score could be used to predict cancer incidence.

Results: Of the 43,994 people included in the study, 66% did not have SLD, while 28%, 4.0%, and 1.4% had MASLD, MetALD and ALD. During the median follow-up of 10.5 years (398,202 person-years), cancers were developed in a total of 3,619 cases (7.2%). Compared to the non-SLD group (762.4 per 100,000 person-years), the cancer incidence rates for MASLD (843.2), MetALD (861.9), and ALD (1197.4) were significantly different (*P*<0.001). In men, the incidence of liver cancer and stomach cancer was higher for all SLD subgroups, and the incidence of esophageal cancer was higher for both MetALD and ALD. In women, liver cancer, pancreaticobiliary cancer, and colon cancer were more frequently developed in the MASLD group than non-SLD group. The more number of cardiovascular metabolic risk factor (CMRF) was significantly associated with the greater cancer risk (HR 1.27 [95% CI 1.14-1.41] for 2-3 CMRFs; and 1.41 [95% CI 1.25-1.59] for 4-5 CMRFs). BMI <25 kg/m^2 reduced a risk of liver cancer in the overall study population (HR 0.38 [95% CI 0.22-0.68]), and this trend was also observed in the MetALD group (0.61 [0.13-2.97]: *P*=0.05). The FIB-4 and SAFE score strata significantly differentiated the incidence of all types of cancer including liver cancer in all SLD subgroups.

Conclusions: This study highlights the differential cancer risks among individuals with MASLD, MetALD, and ALD. These findings underscore the need for tailored cancer surveillance strategies using effective noninvasive markers in the SLD subgroups, particularly in those with alcohol-related components.

Keywords: Steatotic Liver Disease, Alcohol-Related Liver Disease, Cancer Risk, Non-Invasive Predictors

OP-70

Aspirin and HCC Risk in MASLD: Nationwide Cohort Study with Genetic Risk Analysis

Juhee Ahn[1], Moon Haeng Hur[2], Hyunjae Shin[2], **Min Kyung Park**[3], Sungho Won[1,4,5,6], Jeayeon Park[2], Yunmi Ko[2], Youngsu Park[2], Yun Bin Lee[2], Eun Ju Cho[2], Jeong-Hoon Lee[2], Su Jong Yu[2], Jung-Hwan Yoon[2], Yoon Jun Kim[2]

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Aims: Evidence on the association between aspirin use and hepatocellular carcinoma (HCC) risk in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) remains insufficient. This study investigated the effect of aspirin on HCC development in MASLD patients using the Korean National Health Insurance Service (NHIS) and UK Biobank (UKB) databases.

Methods: A retrospective cohort analysis of the NHIS database included a 3-year landmark approach, balancing baseline characteristics through inverse probability of treatment weighting (IPTW) or 1:3 propensity score matching (PSM). In parallel, a one-sample genomic risk score (GRS)-based Mendelian randomization (MR) analysis was performed in the UKB cohort. GRS for salicylic acid levels was calculated utilizing single nucleotide polymorphisms related to aspirin metabolism. Accordingly, an increased GRS was assumed to serve as a genetic proxy for aspirin use.

Results: In the NHIS cohort, 6,584,155 eligible patients were included, of whom 1,723,435 had MASLD. After applying PSM, aspirin use was associated with a significantly lower risk of HCC compared to no aspirin use, both in the overall population (adjusted hazard ratio [aHR]=0.86, 95% confidence interval [CI]=0.78–0.95, *P*=0.002) and in the MASLD group (aHR=0.86, 95% CI=0.75–0.99, *P*=0.036). Similar results were reproduced in the IPTW-balanced population, as well as in several sensitivity and subgroup analyses. In the UKB cohort, individuals in the top 95% of GRS had a significantly lower risk of HCC compared to those in the bottom 5% of GRS, in both the overall population (aHR=0.61, 95% CI=0.39–0.95, *P*=0.028) and the MASLD group (aHR=0.47, 95% CI=0.29–0.76, *P*=0.002).

Conclusions: Both the population-based cohort study and the MR analysis suggest that aspirin use is associated with a reduced risk of HCC in MASLD patients.

Keywords: Fatty Liver, Aspirin, Salicylic ACID, Liver Cancer

OP-71

PNPLA3 p.I148M Polymorphism Increases Risk of Liver Fibrosis in Breast Cancer Patients Receiving Tamoxifen Therapy

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Aims: Estrogen upregulates PNPLA3 gene expression and activates energy-consuming hepatic metabolism. Recent studies suggest that estrogen may induce metabolic dysfunction-associated steatotic liver disease (MASLD) in women carrying the PNPLA3 p.I148M variant. Tamoxifen, a selective estrogen receptor modulator, is widely used for the prevention and treatment of estrogen receptor-positive breast cancer but is associated with steatotic liver disease (SLD). However, the relationship between PNPLA3 genotypes and tamoxifen-associated SLD remains unexplored. We aimed to investigate the prevalence and progression of MASLD in breast cancer patients receiving tamoxifen therapy, stratified by PNPLA3 genotype, to identify high-risk populations who may benefit from enhanced monitoring and personalized treatment strategies.

Methods: This retrospective analysis utilized a prospective cohort of breast cancer patients from Samsung Medical Center between January 2015 and May 2020. Of 909 women screened, 328 breast cancer patients treated with tamoxifen for ≥2 years were included in the final analysis. PNPLA3 genotyping was performed using the TaqMan SNP Genotype Assay. Patients were classified into low-risk (CC/CG types, n=243) and high-risk (GG type, n=85) groups. Data were analyzed over five years using FIB-4 scores to detect fibrosis progression, with patients stratified by baseline liver fibrosis status.

Results: In multivariable analysis, the PNPLA3 GG genotype had a significantly increased risk of fibrosis progression (HR 2.69, 95% CI 1.18-6.11; *P*=0.018) compared to CC/CG genotype. In patients with low baseline fibrosis risk (FIB-4 <1.3), the GG genotype was associated with a 5.08-fold increased risk (HR 5.08, 95% CI 1.85-14.0; *P*=0.002) compared to CC/CG genotypes, with cumulative incidence curves diverging after 24 months of treatment. In patients with moderate baseline fibrosis risk, no significant association was found (HR: 0.60; 95% CI: 0.07-4.94; *P*=0.600). Subgroup analysis revealed significantly elevated fibrosis risk associated with GG genotype in patients aged ≥65 years (HR 3.73, 95% CI 1.25-11.20), those without diabetes mellitus (HR 3.27, 95% CI 1.18-9.07), patients with pre-existing MASLD (HR 2.53, 95% CI 1.01-6.35), and postmenopausal status (HR: 3.10; 95% CI: 1.26-7.61).

Conclusions: The PNPLA3 GG genotype is associated with accelerated liver fibrosis in breast cancer patients undergoing tamoxifen therapy, particularly in those with low baseline fibrosis risk. Our findings suggest that PNPLA3 genotyping could serve as a valuable risk stratification tool, especially for older, postmenopausal women with pre-existing MASLD, who may benefit from enhanced liver monitoring during tamoxifen therapy.

Keywords: PNPLA3, Tamoxifen, MASLD, Breast Cancer

Saturday, May 31, 2025, 09:30-10:30

13. Liver Cancer, Clinical 3

OP-72

Impact of Metformin Administration on Clinical Outcomes in Patients with Hepatocellular Carcinoma Treated with Atezolizumab plus Bevacizumab

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Aims: Although the recent use of immunotherapy in hepatocellular carcinoma (HCC) has improved the clinical outcomes, finding ways to further enhance the treatment efficacy is a good strategy to improve patient survival rates. Metformin has been suggested to increase anticancer effects by regulating T cell function. The aim of our study was to investigate the favorable factors on clinical outcomes and the role of metformin in HCC patients treated with atezolizumab plus bevacizumab

Methods: This retrospective study enrolled 65 patients (81.5% males, mean age 63.1) receiving ATE/BEV for unresectable HCC at Gachon University Gil Medical Center between March 2022 and November 2024. Clinical, laboratory and radiological findings were collected and analyzed. Objective response rate (ORR), progression free survival (PFS) and overall survival (OS) were evaluated by Kaplan-Meier method and log-rank tests. Univariate and multivariate analyses were conducted to explore the favorable factors on clinical outcomes.

Results: In total of 65, 47 patients (72.3%) had viral HCC (CHB 44, CHC 3), and 18 patients had non-viral HCC (alcohol 8, MASLD 2, Cryptogenic 8). In the total of 65 patients, 22 were diabetic, of which 18 (27.7%) were taking metformin. During median follow-up of 10 months, the median PFS was 12.8 months (95% CI: 9.6 to 16.1), and the median OS was 18.2 months (95% CI: 15.1 to 21.7). ORR was 36.8%. Keplan–Meier analysis revealed that viral etiology affected OS. Patients with HCC caused by viral hepatitis had better OS. (P=0.013). Multivariate Cox regression analysis revealed that the decrease of A-FP after 1st cycle treatment is independently correlated with PFS (P=0.017). Especially, In particularly, the use of metformin was associated with a statistically significant reduction in AFP with treatment. (P=0.04). Baseline radiologic findings such as signal intensity at hepatobiliary phase, arterial phase enhancement pattern, intratumoral steatosis were not associated with clinical outcomes in our study.

Conclusions: Patients with HCC caused by viral hepatitis responded better to ATE/BEV treatment than patients with non-viral etiologies. AFP reduction with 1st cycle treatment was significantly associated with PFS. This study suggests that the use of metformin may be associated with a reduction in AFP.

Keywords: Hepatocellular Carcinoma, Immunotherapy, Metformin

OP-73

Comparative Analysis of Therapeutic Strategies in Combined Hepatocellular-Cholangiocarcinoma

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Aims: Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare and aggressive malignancy with limited therapeutic options, particularly in advanced stages. This study aimed to compare the efficacy of different therapeutic strategies, including hepatic arterial infusion chemotherapy (HAIC) and systemic chemotherapy, in patients with cHCC-CC.

Methods: A retrospective analysis was conducted on 100 patients with pathologically confirmed cHCC-CC, classified into three treatment groups: curative treatment (liver transplantation, resection, or radiofrequency ablation), transarterial therapy, and chemotherapy. Among patients with advanced-stage cHCC-CC, two treatment groups were further defined: HAIC (n = 19) and systemic chemotherapy (n = 33). Baseline characteristics, treatment responses, overall survival (OS), and progression-free survival (PFS) were analyzed. Univariate and multivariate Cox regression analyses were performed to identify prognostic factors associated with survival outcomes.

Results: Patients who underwent curative treatment demonstrated the most favorable survival outcomes, while among non-surgical options, transarterial treatments provided better disease control than chemotherapy. In advanced-stage cHCC-CC patients receiving chemotherapy, the HAIC group showed significantly improved OS (HR = 0.44, 95% CI: 0.20-0.69, P=0.044) and PFS (HR = 0.54, 95% CI: 0.20-0.99, P=0.048) compared to the systemic chemotherapy group. Furthermore, the objective response rate and disease control rate were significantly higher in the HAIC group than in the systemic chemotherapy group (P=0.004 and P<0.001, respectively). Multivariate analysis identified extrahepatic metastasis (HR = 7.17, 95% CI: 2.90-17.7, P<0.001) and maximum tumor diameter > 5 cm (HR = 2.19, 95% CI: 1.09-4.43, P=0.028) as independent risk factors for OS.

Conclusions: The optimal treatment strategy for cHCC-CC depends on disease stage and tumor burden. Surgical treatment provides the best survival benefit for eligible patients. Among advanced-stage patients, HAIC demonstrated superior tumor response and survival outcomes compared to systemic chemotherapy. These findings highlight the need for individualized treatment approaches to improve patient outcomes in cHCC-CC.

Keywords: Combined Hepatocellular-Cholangiocarcinoma, Hepatic Arterial Infusion Chemotherapy, Systemic Chemotherapy, Survival Analysis

OP-74

Cytokine-Induced Killer Cell Immunotherapy Reduces Recurrence in Patients With Early-Stage Hepatocellular Carcinoma

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Aims: Hepatocellular carcinoma (HCC) has a high recurrence rate despite curative treatments such as resection or radiofrequency ablation (RFA). Cytokine-induced killer (CIK) cell immunotherapy has shown potential in reducing recurrence. This study evaluates the efficacy and safety of adjuvant CIK therapy in early-stage HCC patients in a real-world setting.

Methods: A retrospective cohort study was conducted on 49 patients who received CIK cell therapy after curative resection or RFA, compared to 49 propensity score-matched control patients without adjuvant therapy. Recurrence-free survival (RFS) was the primary endpoint, and overall survival (OS) was the secondary endpoint. Changes in tumor markers, including alpha-fetoprotein (AFP) and protein induced by vitamin K absence-II (PIVKA-II), were analyzed before and after CIK therapy. Kaplan-Meier analysis and Cox proportional hazards models were used to assess survival outcomes.

Results: The median follow-up was 19.1 months for the CIK group and 67.7 months for the control group. CIK therapy significantly improved RFS compared to the control (hazard ratio [HR], 0.32; 95% CI, 0.15–0.71; log-rank P=0.001). The median RFS was not reached in the CIK group but was 48.62 months in the control group. Multivariable analysis confirmed CIK therapy as an independent factor for reduced recurrence risk (adjusted HR, 0.32; P=0.005). No significant OS differences were observed (P=0.082). In patients with elevated post-treatment markers, AFP levels significantly decreased from 15.3 ng/mL to 1.3 ng/mL (P=0.002), while PIVKA-II levels decreased from 42.0 mAU/mL to 27.0 mAU/mL (P=0.019). No Grade 3 or 4 adverse events were reported.

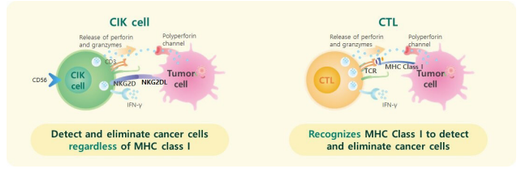
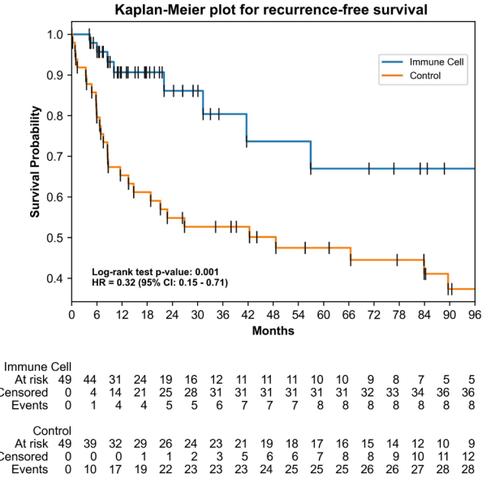


Figure 1.



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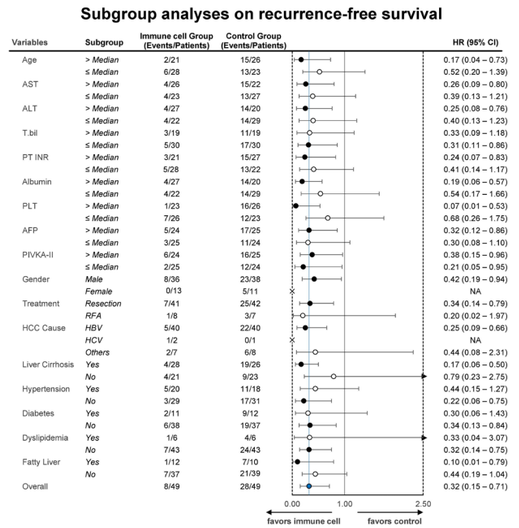

Figure 3.

Conclusions: Adjuvant CIK cell immunotherapy significantly prolongs RFS in early-stage HCC and reduces tumor marker levels in high-risk patients without severe adverse events. Further research is needed to evaluate long-term survival benefits and broader clinical applications.

Keywords: Hepatocellular Carcinoma, Cytokine-Induced Killer Cell, Recurrence, Immunotherapy

OP-75

Effect of Combining Serum Alpha-Fetoprotein with LI-RADS v2018 on Gadoxetate-Enhanced MRI in the Diagnosis and Prognostication of Hepatocellular Carcinoma

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Aims: While serum alpha-fetoprotein (AFP) can provide additional diagnostic information, there are no previous studies that applied AFP in CT/MRI Liver Imaging Reporting and Data System (LI-RADS). We aimed to evaluate the performance of combining AFP with LI-RADS (LI-RADS+AFP) on gadoxetate-enhanced magnetic resonance imaging (MRI) for diagnosing hepatocellular carcinoma (HCC) ≤3.0 cm and predicting post-surgical patient outcomes, compared to LI-RADS v2018.

Methods: Patients with hepatic observations ≤3.0 cm who underwent preoperative gadoxetate-enhanced MRI and surgical resection were retrospectively analyzed. In LI-RADS+AFP, LR-4 (probably-HCC), LR-M (probably or definitely-malignant but not HCC specific), or LR-TIV (definite-tumor-in-vein) by LI-RADS v2018 was upgraded to LR-5 (definitely-HCC) if they met AFP criteria based on three different cut-offs (≥20, ≥200, ≥400 ng/mL). The sensitivity, specificity, and accuracy of LI-RADS v2018 LR-5 and LI-RADS+AFP LR-5 were compared using generalized estimating equations. Recurrence-free survival (RFS) and overall survival (OS) in the two groups (LR-4/5 vs. LR-M) of LI-RADS v2018 and LI-RADS+AFP were compared using log-rank tests.

Results: In 520 observations from 414 patients (mean age, 60± 9 years; 328 men), LI-RADS+AFP ≥20 ng/mL (LI-RADS+AFP20) showed the highest accuracy among the three cut-offs. Compared to LI-RADS v2018, LI-RADS+AFP20 showed significantly higher sensitivity in diagnosing HCC (79.9% [95% confidence interval, 75.7–83.6] vs. 71.8% [67.2–76.1], *P*<0.001) and accuracy (82.7% [79.2–85.9] vs. 76.9% [73.1–80.5], *P*<0.001) without difference in specificity (93.5% [87.1–97.4] vs. 96.3% [90.8–99.0], *P*=0.083). Unlike LI-RADS v2018, showing no difference in RFS between LR-4/5 and LR-M (50.6 vs. 42.6 months; *P*=0.078), LI-RADS+AFP20 showed significant differences in RFS (50.6 vs. 35.0 months; *P*<0.001) and OS (67.6 vs. 54.8 months, *P*=0.008).

Conclusions: Combining AFP and LI-RADS v2018 resulted in better diagnostic performance and superior post-surgical prognostication compared to LI-RADS v2018 alone.

Keywords: Liver, Liver Neoplasms, Magnetic Resonance Imaging, Diagnosis, Prognosis

OP-76

Association between Young Age and Prognosis of Hepatocellular Carcinoma: A Large Single-Center Matched Study

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Aims: Hepatocellular carcinoma (HCC) in young patients is rare, and its postoperative prognosis remains uncertain. This study aimed to compare recurrence rates and long-term outcomes between young and older HCC patients.

Methods: We retrospectively analyzed 5,465 patients who underwent hepatectomy for HCC at Asan Medical Center from 2008 to 2019. Patients were categorized into young (<40 years, N=265) and older (≥40 years, N=5,200) groups. Postoperative recurrence rates, overall survival (OS), and recurrence-free survival (RFS) were compared before and after 1:10 propensity score matching (PSM). Multivariate logistic regression identified significant factors for early recurrence.

Figure1. Overall survival (OS) and recurrence-free survival (RFS) in patients with hepatocellular carcinoma within the Milan criteria. OS (A) and RFS (B) in the entire cohort. OS (C) and RFS (D) in the propensity score-matched cohort.

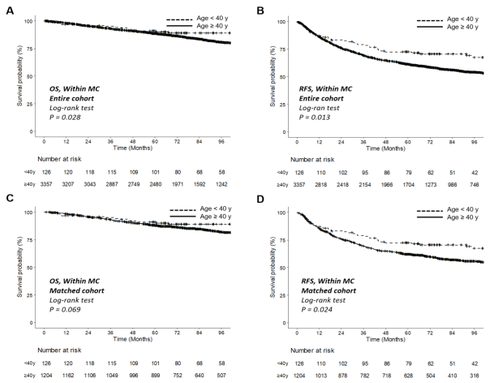

Figure 1.

Results: Young patients had a higher 2-year recurrence rate than older patients (39.6% vs. 31.7%, *P*=0.007). OS was significantly worse in young patients (*P*=0.003), while RFS did not differ between the groups (*P*=0.150). Among patients with HCC within the Milan criteria (MC), young patients had better OS (*P*=0.028) and RFS (*P*=0.013). However, in cases beyond MC, young patients had worse OS (*P*=0.028) and RFS (*P*=0.013). This observed trend remained consistent after PSM. Multivariate analysis identified age <40 years as a significant predictor of 2-year recurrence in the beyond-MC cohort, but not in the within-MC cohort.

Figure 2. Overall survival (OS) and recurrence-free survival (RFS) in patients with hepatocellular carcinoma beyond the Milan criteria. OS (A) and RFS (B) in the entire cohort. OS (C) and RFS (D) in the propensity score-matched cohort.

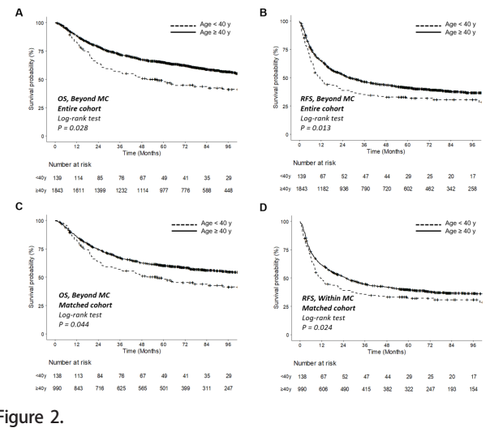

Table Risk factor analyses for early recurrence within 2-year in matched cohort with HCC in beyond Milan criteria.

	Univariate			Multivariate		
	OR	95 % CI	*p*	OR	95% CI	*p*
Sex, male	0.892	0.667 – 1.193	0.411			
Age > 40 years	1.773	1.240 – 2.535	0.002	1.499	1.008 – 2.229	**0.046**
BMI, kg/m^2	0.945	0.908 – 0.985	0.007			
DM	1.462	0.673 – 3.180	0.337			
Underlying liver disease						
HBV		Reference				
HCV	3.671	1.029 – 13.101	0.045			
NBNC	0.612	0.438 – 0.855	0.004			
AFP (ng/mL)						
≤ 20 ng/mL		Reference			Reference	
20 – 500 ng/mL	1.54	1.110 – 2.139	0.010	1.435	0.999 – 2.061	0.051
> 500 ng/mL	2.035	1.529 – 2.709	<0.001	1.521	1.101 – 2.102	**0.011**
Preoperative needle biopsy	1.795	0.900 – 3.581	0.097			
Pre-HCC treatment	0.246	0.167 – 0.362	<0.001	0.250	0.162 – 0.386	**<0.001**
Anatomical resection	1.004	0.711 – 1.419	0.982			
Multiple resection	1.632	1.010 – 2.638	0.046			
Combined BDR	2.007	0.601 – 6.704	0.257			
Tumor size, cm	1.090	1.057 – 1.125	<0.001	1.072	1.035 – 1.110	**<0.001**
Tumor number						
1		Reference				
2	0.912	0.667 – 1.246	0.562			
≥3	1.321	0.897 – 1.944	0.158			
Combined HCC-CCC	2.258	1.235 – 4.128	0.008	2.594	1.341 – 5.018	**0.005**
E-S grade, 1-2 vs. 3-4	1.374	1.081 – 1.746	0.009			
Totally necrotic mass	0.191	0.079 – 0.462	<0.001			
Microvascular invasion	3.276	2.554 – 4.202	<0.001	1.765	1.331 – 2.342	**<0.001**
Portal vein invasion	3.169	2.133 – 4.709	<0.001	2.092	1.292 – 3.185	**0.002**
Bile duct invasion	1.109	0.447 – 2.750	0.823			
Capsular invasion	2.392	1.751 – 3.269	<0.001	1.454	1.026 – 2.062	**0.036**
Satellite nodules	3.692	2.539 – 5.367	<0.001	2.628	1.744 – 3.960	**<0.001**
Cirrhosis	1.443	1.130 – 1.844	0.003	1.441	1.087 – 1.911	**0.011**
R1 resection	4.659	2.572 – 8.440	<0.001	2.753	1.453 – 5.217	**0.002**

OR, odds ratio; **CI**, confidence interval; **BMI**, body mass index; **DM**, diabetes mellitus; **HBV**, hepatits B virus; **HCV**, hepatitis C virus; **NBNC**, non-B and non-C; **AFP**, alpha-fetoprotein; **HCC**, hepatocelluar carcinoma; **BDR**, bile duct resection; **CCC**, cholangiocarcinoma; **E-S**, Edmondson-Steiner

Conclusions: Young HCC patients have a higher risk of early recurrence, particularly in cases beyond MC, leading to worse long-term outcomes. These findings suggest that younger patients with advanced HCC may need closer surveillance and tailored treatment to improve prognosis.

Keywords: Hepatocellular Carcinoma, Early Recurrence, Overall Survival, Recurrence-Free Survival

OP-77

Real-World Incidence and Predictive Factors of Variceal Bleeding in Hepatocellular Carcinoma Patients Treated with Atezolizumab-Bevacizumab

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Aims: The combination therapy of Atezolizumab and Bevacizumab improves survival in hepatocellular carcinoma (HCC) patients but increases the risk of variceal bleeding, especially in those with pre-existing varices. Current real-world data on the incidence and risk factors associated with variceal bleeding in this group is lacking. This study aims to address this gap by investigating the real-world incidence and predictors of variceal bleeding among HCC patients receiving this treatment.

Methods: This retrospective study was conducted across nine tertiary hospitals in the Daegu-Gyeongbuk and Busan-Ulsan-Gyeongnam regions in Korea, encompassing a total of 690 patients with hepatocellular carcinoma (HCC). The study aimed to investigate the incidence of variceal bleeding (VB) and its associated risk factors in patients receiving Atezolizumab-Bevacizumab (Atezo-Bev) combination therapy.

Results: Of the 690 patients studied, the mean age was 66.2 years, with 609 (88.3%) being male. The predominant cause of hepatocellular carcinoma (HCC) was chronic hepatitis B virus infection, accounting for 59.1% of cases, and 595 (86.9%) were classified at BCLC stage C. Portal vein invasion (PVI) was noted

in 283 patients (41.0%). Over a median follow-up period of 8.0 months, variceal bleeding (VB) developed in 62 patients (79.0%). The cumulative incidence of VB was 6.7% at 6 months and 12.4% at 12 months. Of the total cohort, 8 patients (1.6%) succumbed to variceal bleeding. Multivariable analysis indicated that main PVI (hazard ratio [HR]: 2.718, 95% confidence interval [CI]: 1.51–4.89), a prior history of variceal bleeding (HR: 23.41, 95% CI: 12.64–43.35), and the presence of varices (HR: 3.59, 95% CI: 1.64–7.83) significantly increased the risk of VB.

Conclusions: Portal vein invasion (PVI), a history of variceal bleeding, and the presence of varices were identified as significant risk factors for variceal bleeding (VB) in patients treated with Atezolizumab-Bevacizumab (Atezo-Bev) for hepatocellular carcinoma (HCC). Recognizing these factors is crucial for clinicians to effectively assess and manage the risk of VB in a clinical environment.

Keywords: Hepatocellular Carcinoma, Atezolizumab-Bevacizumab Therapy, Variceal Bleeding

Saturday, May 31, 2025, 09:30-10:30

14. HBV and LC, Basic

OP-78

Liver on the Mend: CRISPR-Based Gene Therapy as a Game-Changer for Genetic Hepatic Diseases

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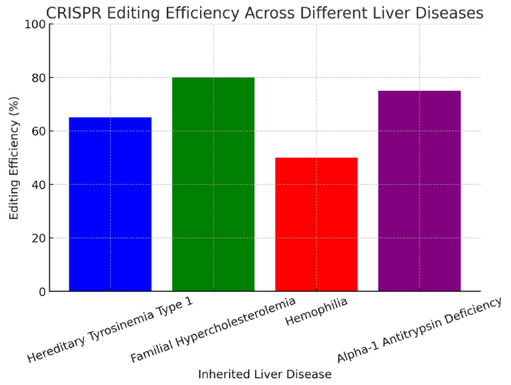
Aims: Inherited liver diseases, often resulting from specific genetic mutations, present significant clinical challenges. Traditional treatments, such as liver transplantation, are limited by donor availability and the need for lifelong immunosuppression. The emergence of CRISPR/Cas9 gene editing technology offers a promising alternative by enabling precise correction of disease-causing mutations. This systematic review evaluates the efficacy and safety of CRISPR-based gene editing in treating inherited liver diseases, synthesizing findings from recent preclinical and clinical studies.

Methods: A systematic literature search was conducted across databases including PubMed and Scopus, focusing on studies published between January 2015 and December 2024. Keywords used included "CRISPR," "gene editing," "inherited liver disease," and "gene therapy." The inclusion criteria encompassed preclinical and clinical studies employing CRISPR/Cas9 technology to target monogenic liver disorders. Data extracted included study design, target disease, delivery methods, editing efficiency, therapeutic outcomes, and reported adverse effects. Study quality was assessed using standardized risk of bias tools.

Results: A total of 15 studies met the inclusion criteria, targeting various inherited liver diseases such as hereditary tyrosinemia type 1, familial hypercholesterolemia, hemophilia, and alpha-1 antitrypsin deficiency. Delivery methods varied, with adeno-associated virus (AAV) vectors and lipid nanoparticles (LNPs) being the most common. Editing efficiencies ranged from 20% to 80%, with higher rates generally correlating with improved therapeutic outcomes. Notably, studies utilizing LNPs reported fewer immune responses compared to those using viral vectors. Off-target effects were minimal across studies, with no significant adverse events reported. However, variability in delivery efficiency and long-term outcomes highlighted the need for further optimization.

Conclusions: CRISPR/Cas9 gene editing demonstrates significant potential as a therapeutic strategy for inherited liver diseases, offering advantages over traditional treatments. While preclinical results are promising, further research is necessary to optimize delivery methods, enhance editing efficiency, and ensure long-term safety. Rigorous clinical trials and standardized protocols will be essential to transition this technology from experimental models to widespread clinical application.

Keywords: CRISPR/CAS9 Gene, Inherited Liver Disease, Adeno-Associated Virus, Alpha-1 Antitrypsin



OP-79

In Silico Design and Evaluation of siRNA Targeting HBV S and C Genes for Hepatitis B Treatment

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Aims: Hepatitis B virus (HBV) remains a significant global health challenge, with chronic infections leading to liver fibrosis, cirrhosis, and hepatocellular carcinoma. RNA interference (RNAi) using small interfering RNA (siRNA) is a promising therapeutic strategy for HBV suppression. This study aims to design and evaluate siRNA candidates targeting the Surface (S) and Core (C) genes of HBV as potential antiviral agents.

Methods: siRNA candidates were designed using siPRED, an advanced siRNA prediction tool. Further computational analysis, including MaxExpect and DuplexFold, was performed to evaluate RNA secondary structure stability and target accessibility. Candidate siRNAs were ranked based on predicted efficacy, thermodynamic stability, and target site conservation.

Results: The designed siRNA sequences targeting the S and C genes demonstrated high inhibition efficiency, with top candidates showing inhibition rates above 94%. For the S gene, the most effective siRNA had an inhibition rate of 94.78%, while the best siRNA targeting the C gene showed an inhibition rate of 94.73%. Network analysis of the siRNA-target interactions confirmed optimal binding affinities and minimal off-target effects. The selected siRNAs target highly conserved regions of HBV, ensuring broad genotype coverage.

Conclusions: This study successfully designed and evaluated siRNA candidates targeting the S and C genes of HBV, showing strong potential for RNAi-based antiviral therapy. Future in vitro and in vivo studies are needed to validate these findings and develop an effective siRNA-based treatment for chronic HBV infections.

Keywords: Hepatitis B Virus, Sirna Design, S and C Genes, RNA Silencing

Rank	Antisense strand 5'-3'	Sense strand 5'-3'	Position	Inhibition (%)
1	UUGAGAUCUUCUGCGACGC	GCGUCGCAGAAGAUCUCAA	600 - 618	94.78
2	UUUCUCUUCCAAAAGUAAG	CUUACUUUUGGAAGAGAAA	409 - 427	94.03
3	UAGCUGACUACUAAUUCCC	GGGAAUUAGUAGUCAGCUA	332 - 350	93.98
4	UUUAUAUGGGUCAAUGUCC	GGACAUUGACCCAUAUAAA	90 - 108	93.88
5	UCUAACAACAGUAGUUUCC	GGAAACUACUGUUGUUAGA	519 - 537	93.64
6	UUCUUCUAGGGGACCUGCC	GGCAGGUCCCCUAGAAGAA	544 - 562	93.32
7	UAUGGGUCAAUGUCCAUGC	GCAUGGACAUUGACCCAUA	86 - 104	93.25
8	UUGUCUGAUUUUUAGGCCC	GGGCCUAAAAAUCAGACAA	366 - 384	92.39
9	AUAGCUGACUACUAAUUCC	GGAAUUAGUAGUCAGCUAU	333 - 351	92.32
10	AAAAAGAGAGUAACUCCAC	GUGGAGUUACUCUCUUUUU	124 - 142	91.17

gene C siRNA of HBV

Rank	Antisense strand 5'-3'	Sense strand 5'-3'	Position	Inhibition (%)
1	UUGUCAACAAGAAAAACCC	GGGUUUUUCUUGUUGACAA	574 - 592	94.73
2	UUUACUGUUCCGGAACUGG	CCAGUUCCGGAACAGUAAA	437 - 455	94.61
3	UUGUACAGCAACAAGAGGG	CCCUCUUGUUGCUGUACAA	925 - 943	94.59
4	UAGAGGUUCCUUGAGCAGG	CCUGCUCAAGGAACCUCUA	901 - 919	94
5	UACAAGUGCAGUUUCCGUC	GACGGAAACUGCACUUGUA	952 - 970	93.94
6	UAGGAAUCUUGCGAAAGCC	GGCUUUCGCAAGAUUCCUA	990 - 1008	93.67
7	AAAUUGAGAGAAGUCCACC	GGUGGACUUCUCUCAAUUU	626 - 644	93.63
8	UUUGAGUUGGCUCCGAACG	CGUUCGGAGCCAACUCAAA	98 - 116	93.21
9	UUUUGUACAGCAACAAGAG	CUCUUGUUGCUGUACAAAA	927 - 945	93.2
10	UUGAUGUUCCUGGAAGUAG	CUACUUCCAGGAACAUCAA	847 - 865	93.14

gene S siRNA of HBV

OP-80

cccDNA as a Therapeutic Target in Hepatitis B Virus Infection: Mechanisms and Drug Development - A Systematic Review

Lok Ranjan Rajmohan

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Aims: Covalently closed circular DNA (cccDNA) plays a pivotal role in the persistence of Hepatitis B Virus (HBV) infection, acting as the template for viral replication and transcription. Despite advances in antiviral therapy, current treatments rarely achieve a functional or sterilizing cure due to the stability and resilience of cccDNA in infected hepatocytes. This systematic review aims to evaluate current understanding of cccDNA biology, mechanisms regulating its formation and maintenance, and to comprehensively assess emerging therapeutic strategies targeting cccDNA to achieve an HBV cure.

Methods: A comprehensive literature search was conducted across PubMed, Web of Science, and Scopus from database inception to January 2025, following PRISMA guidelines. Inclusion criteria encompassed preclinical studies, clinical trials, and reviews focused on cccDNA-targeted therapies, including gene editing technologies, epigenetic modulators, and antiviral agents aiming to degrade or silence cccDNA. Data extraction included information on therapeutic mechanisms, efficacy in cccDNA reduction, and safety outcomes. Quality assessment was performed using the Cochrane risk-of-bias tool for randomized studies and ROBINS-I for non-randomized studies.

Results: Fifty-eight studies met the inclusion criteria, including 27 preclinical investigations and 31 clinical trials or translational studies. CRISPR/Cas9 and other gene editing technologies demonstrated potential for direct cccDNA cleavage in vitro, with significant reductions in cccDNA levels (up to 70%) but posed concerns regarding off-target effects. Epigenetic modulators, including histone deacetylase inhibitors and DNA methyltransferase inhibitors, were shown to suppress cccDNA transcription activity, leading to decreased HBV replication and antigen production. Small molecule inhibitors targeting viral or host factors involved in cccDNA formation and maintenance, such as CCC_R08 and RG7834, have shown promising antiviral activity in animal models and early-phase clinical trials.

Conclusions: Targeting HBV cccDNA represents a critical frontier in the quest for a functional or sterilizing cure of chronic hepatitis B. While several therapeutic strategies have demonstrated efficacy in preclinical models, clinical translation remains in its infancy. Combination approaches integrating gene editing, epigenetic modulation, and antiviral therapies may offer the most effective route to eliminate or silence cccDNA. Further research is needed to optimize delivery methods, enhance

specificity, and address safety concerns to make these strategies viable in clinical practice.

Keywords: Hepatitis B Virus, Cccdna, Gene Editing, Antiviral Therapy

OP-81

In Patients with Hepatocellular Carcinoma, Autologous NK Cell Immunotherapy after Transarterial-Chemoembolization (TACE) Increased Disease-Free Survival and Improved Liver Fibrosis: Proof of Concept Study

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Aims: Natural killer (NK) cells are one of the key members of innate immunity. Liver-specific NK cells are lymphocytes with antiviral and antitumor properties. Also, it is known that the crosstalk between NK cells and hepatic stellate cells (HSCs) plays an important role in liver fibrosis. NK cells have antifibrotic activity by inhibiting activated HSCs. In our previous study, we reported that autologous NK cell therapy can improve recurrence-free survival after conventional TACE in intermediate stage hepatocellular carcinoma (HCC) patients. In this study, we assessed whether post-TACE autologous NK cell immunotherapy could improve liver fibrosis in clinical and experimental settings.

Methods: This prospective pilot study enrolled 10 consecutive patients with HCC of intermediate stage from CHA Bundang hospital in Korea from January 2023 to November 2023. Patients were successively assigned to either autologous NK cell therapy (immunotherapy group) adjunct after TACE or TACE alone without NK cell therapy (control group). The patients who assigned to immunotherapy group underwent conventional TACE followed by activated autologous NK cell therapy (1 weeks after TACE, up to 3 cycles). We analyzed the progression-free survival (PFS) and objective tumor response rate (ORR). In addition, the proportion of patients with improved liver fibrosis was identified through the FibroScan test 3 months after the treatment. We also conducted an in-vitro study to confirm the antifibrotic effect of NK cell therapy. LX2 (HSC cell line) was used to confirm the antifibrotic cytotoxicity of NK cells to HSC. In order to induce liver fibrosis, LX2 cells were treated with 5 or 10 ng of TGF-β and NK cells were co-cultured for 4 hours, and then analyzed using flow cytometry.

Results: In our study, the 6-month and 1-year ORR were higher in the NK cell therapy group compared with the controls, but it was not statistically significant. However, NK cell therapy group showed significantly longer PFS (9.3 vs 3.2 months, P<0.05) than the control group. The proportion of patients with improving liver fibrosis, whose liver elastography scores decreased more than 1 kPa, 3 months after TACE, was higher in the immunotherapy group (80% vs 40%; P=0.18).

In our experimental in-vitro study, NK cells showed concentration-dependent cytotoxicity against LX2 cells. In addition, compared to T cells, the cytotoxicity of NK cells against LX2 was higher than that of T cells in the overall ratio. In addition, mRNA RT-PCR analysis after co-culture of NK cells and LX2 confirmed fibrosis inhibition by αSMA, Timp, and COL1A reduction (P<0.001). Also, the suppression of HSC activation was confirmed by BAX and MMP1 increase and PCNA and PDFG decrease (P<0.001).

Conclusions: In patients with intermediate stage HCC who underwent TACE, combination immunotherapy with activated NK cells increased disease-free survival and improved liver fibrosis. On these results, it is believed that augmented NK cell-mediated cytotoxicity against HSCs can effectively inhibit liver fibrosis and also improve HCC outcome with liver cirrhosis.

Keywords: Liver Fibrosis, Hepatic Stellate Cells, Natural Killer, Hepatocellular Carcinoma

✧ The proportion of patients with improving liver fibrosis, whose liver elastography stiffness decreased more than 1 kPa, 3 months after TACE, was higher in the immunotherapy group (80% vs 40%)

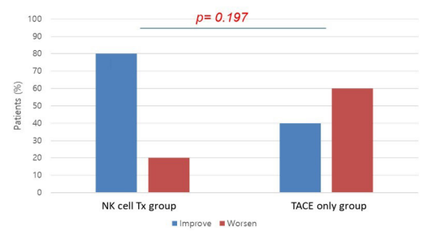

Figure 1.

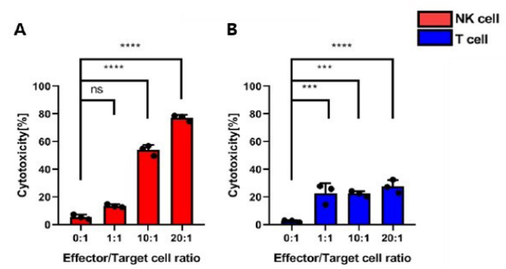

Figure 2.

OP-82

Intrahepatic B Cells Aggravate Liver Fibrosis by Producing Pro-fibrotic Mediators through CD40-mediated NKT Interaction

Jihyo Byun[1], Kyurae Kim[1], Sung Eun Choi[1], Min Jeong Kim[1], Po Sin Chung[1], Eunmi Lee[1], Kwang Woo Lee[1], Jaewoo Oh[1], Seungryong Choo[1], Won-Il Jeong[1,2]

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Aims: Liver fibrosis progression is influenced by intrahepatic immune cells. CD40 is a co-stimulatory receptor that plays an important role in B cell proliferation, differentiation, and immunoglobulin production. However, its functions in liver fibrosis remain unclear. Here, we investigate how B cells induce hepatic stellate cells (HSCs) activation through interaction with natural killer T (NKT) cells.

Methods: Wild-type (WT), global CD40 knockout (gCD40-/-), and B cell-specific CD40-depleted (bCD40-/-) mice were injected with carbon tetrachloride (CCl_4) to induce liver fibrosis. Liver tissues and isolated hepatic cells were subjected to single-cell RNA sequencing (scRNA-seq), qRT-PCR analysis, and flow cytometry. *In vitro* co-culture systems were used.

Results: In liver fibrosis, given the crucial role of CD40 in B cell activation, CD40 signaling was elevated in B cells from fibrotic liver, along with up-regulated genes related to B cell receptor activation. scRNA-seq revealed that CD40L expression was enriched in NKT cells, suggesting a potential interaction between B and NKT cells. In adaptive transfer of B cells and NKT cells, they were observed in the fibrotic septa and located near activated HSCs. *In vitro,* CD40 activation in B cells induced pro-inflammatory cytokines, including transforming growth factor-β1 (TGF-β1) and interleukin-6, promoting HSC activation. gCD40-/- mice showed a reduction in $FAS^{+}GL7^{+}$ activated B cells, B cell-derived TGF-β1, and interferon-γ secretion by NKT cells after CCl_4 injection, resulting in reduced liver fibrosis. Furthermore, we demonstrated bCD40-/- mice attenuated fibrosis, emphasizing the critical role of CD40-mediated B cell activation in HSC activation.

Conclusions: CD40 deletion ameliorates liver fibrosis by preventing B cell-NKT cell interactions and inhibiting B cell-induced HSC activation. These findings suggest that targeting CD40 could be a potential therapeutic strategy for liver fibrosis.

Keywords: Liver Fibrosis, Intrahepatic B Cell, Hepatic Stellate Cell, CD40

OP-83

Verification of Liver Sinusoid Endothelial Cell Normalization and Hepatic Progenitor Cell Activation Efficacy of Bone Marrow- Mesenchymal Stem Cell Derived Extracellular Vesicles

Mi Ra Lee[1], Jin Suk Lee[2], Seul Ki Han[1,2], Seung Chan Choi[1], Soon Koo Baik[1,2], Moon Young Kim[1,2]

[1]Department of Internal Medicine, Wonju Severance Christian Hospital; [2]Regeneration Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea

Aims: Liver sinusoidal endothelial cell (LSEC) normalization (deactivation) is important for suppressing the progression of liver fibrosis and cirrhosis by improving the liver's microenvironment and stabilizing various cells involved in liver fibrosis through cross-talk. Recent studies have revealed that the normalization (deactivation) of damaged (activated) LSECs enhances Wnt-β-catenin signaling in LSECs, which, in turn, promotes the activation of hepatic progenitor cells (HPCs) and strengthens regeneration. Therefore, LSEC normalization can serve as a critical and useful target for the treatment of liver fibrosis and liver regeneration. In this context, we aim to confirm LSEC normalization using LSEC-targeting extracellular vesicle (EVs).

Methods: The cytotoxicity of exosomes at different concentrations was assessed using the CCK-8 assay in mouse primary LSECs. The non-cytotoxic concentration of exosomes (50 μg/ml) was then treated on LSECs, and changes in the expression of factors involved in the Wnt-β-catenin signaling pathway were analyzed using qPCR and Western blot. Additionally, the expression changes of markers related to proliferation and activation in HPCs induced by exosomes were examined using molecular biological techniques.

Results: After treating LSECs with exosomes, the expression of relevant factors was analyzed 24 hours later. Gene expression of markers associated with the Wnt-β-catenin signaling pathway (eNOS, Wnt2, Wnt9b, β-catenin, caveolin1) was found to increase. Additionally, the expression of HGF and VEGF also showed an increase. Regarding protein expression changes, levels of eNOS, Wnt2, Wnt9b, and β-catenin were elevated. When HPCs were treated with exosomes, an increase in cell number was observed. Furthermore, in markers related to differentiation, the expression of Krt19, Sox9, and Epcam decreased, while the expression of CD133 and Alb increased.

Conclusions: Using BM-MSC-derived EVs, we observed an increase in factors related to normalization in LSECs. Additionally, it appears that EVs can promote both proliferation and differentiation in HPCs.

Keywords: Liver Sinusoidal Endothelial Cell, Hepatic Progenitor Cell, Extracellular Vesicle, Marrow Mesenchymal Stem Cell

Saturday, May 31, 2025, 09:30-10:30

15. Others

OP-84

ROS Mediated HMGB1-RIPK1 Upregulation Mediates Hepatocellular Injury, Inflammation Promotes Endothelial Dysfunction and Ductal Proliferation in Drug Induced Liver Injury

Himanshi Himanshi[1], Vaibhav Tiwari[1], Rajni Yadav[1], Aishwarya Bhatnagar[1], Tahseen Khan[1], Savneet Kaur[1], Dinesh Mani Tripathi[1]

Institute of Liver and Biliary Sciences

Aims: This study investigates cholangiocyte hyperplasia, hepatic stellate cell (HSC) activation, fibrosis, and endothelial dysfunction (ED) in Anti-Tubercular Therapy-Drug Induced Liver Injury (ATT-DILI), focusing on oxidative stress and inflammatory signaling pathways.

Methods: Liver biopsies from DILI patients were histologically analyzed using Hematoxylin & Eosin, Masson's Trichrome, Oil Red O, and Cytokeratin-7 (CK7) staining. Preclinical ATT-DILI animal models were developed by administering Isoniazid, Rifampicin, and Pyrazinamide for five weeks orally. Biochemical, molecular, and histological, immunohistochemistry, immunofluorescence assessments were performed to evaluate hepatic inflammation, fibrosis, oxidative stress, and endothelial function.

Results: DILI Patients liver biopsies showed increased inflammation, CK7+ cholangiocyte proliferation and periportal fibrosis. Experimentally, ATT-DILI models exhibited significant hepatic injury characterized by grade-2 inflammation, stage-2 necrosis, and grade-2/3 steatosis. Liver enzymes AST, ALT, and ALP were elevated (P<0.05). DILI markers were upregulated (P<0.05), including CYP2E1 (+14.9), Caspase-3 (+3.2), RIPK1 (+12.4), CD68 (+6.82), IL-1β (+54.5), HMGB1 (+8.21). Ductular reaction (DR) was confirmed by H&E staining, immunohistochemistry and elevated gene and protein expression of CK-19 (+1.4), EpCAM (+1.6), HNF4 (+2.1), and GGT (+3.3) (P<0.05). Peri-portal fibrosis was evident in Sirius Red and Masson's Trichrome (MT) staining and was further validated by increased hepatic collagen content in ATT-DILI (P<0.05). HSC activation was confirmed MT staining, immunohistochemistry and by increased expression of α-SMA (+13.3), Col1A1 (+1.3), Desmin (+2.2), and GFAP (+2.8) (P<0.05). Moreover, significant upregulation of fibrosis-related mediators, including TGF-β (+2.55), NOTCH1 (+2.09), ET-1 (+6.6), and MCP-1 (+40.4), was observed. Endothelial dysfunction was characterized by increased ET1 (+26), eNOS (+25), KLF2 (+22), defenestration markers, SEMA3A (+5.5), PLXND1 (+8), adhesion marker ICAM-1 and VCAM-1 (P<0.05). Additionally, CD31 expression was significantly altered, and portal perfusion pressure was increased (+7.72, P=0.05) and there was altered response in precontracted livers post-acetylcholine treatment, indicating vascular impairment. Malondialdehyde (MDA) levels and SOD levels were elevated, along with a reduction in antioxidant defense, as seen by decreased NRF2 and HO-1 expression (P<0.05). Oxidative stress markers, including 4-HNE expression and glutathione peroxidase (GPX) levels, were increased. Markers of mitochondrial dysfunction MT-CYB (+5), ATP5F (+6), PINK1 (+60) were also increased.

Conclusions: HMGB1-RIPK1 mediated oxidative stress contributes to hepatocellular damage, loss of endothelial functionality, leading to cholangiocyte proliferation, periportal fibrosis in ATT-DILI which exacerbates hepatic injury, highlighting potential targets for therapeutic intervention.

Keywords: Drug Induced Liver Injury, Endothelial Dysfunction, Oxidative Stress, Ductular Reaction

GRAPHICAL ABSTRACT

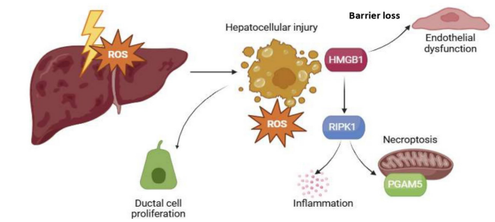

Figure 1

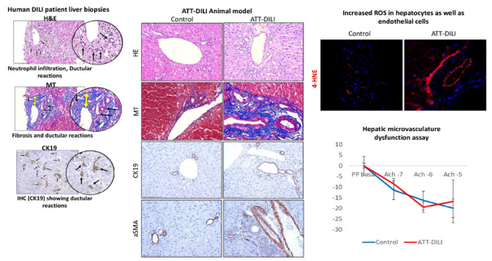

Figure 2.

OP-85

STRAP Promotes Drug-Induced Acute Liver Injury via mTOR-Mediated Autophagy

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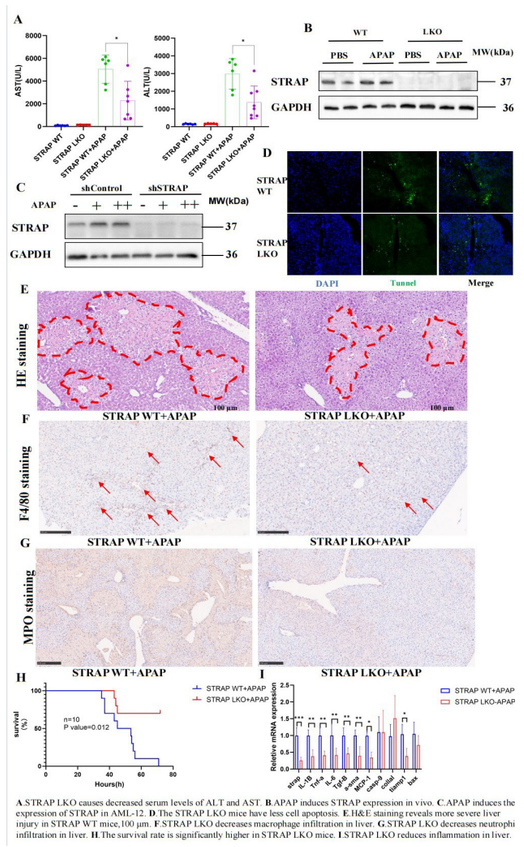
Aims: Acetaminophen (APAP), a widely used antipyretic and analgesic drug, is the leading cause of drug-induced liver injury (DILI) and subsequent acute liver failure (ALF). Hepatic inflammatory stimulation is a critical hallmark of DILI. STRAP (Serine/Threonine Kinase Regulatory Adaptor Protein), a multifunctional regulator, plays essential roles in apoptosis, tumorigenesis, and metabolic homeostasis. Previous studies suggest that autophagy is involved in the pathological progression of acetaminophen-induced liver injury (AILI); however, the biological function and molecular mechanisms of STRAP in DILI remain unclear. This study aims to systematically investigate the role of STRAP in AILI and its underlying regulatory mechanisms.

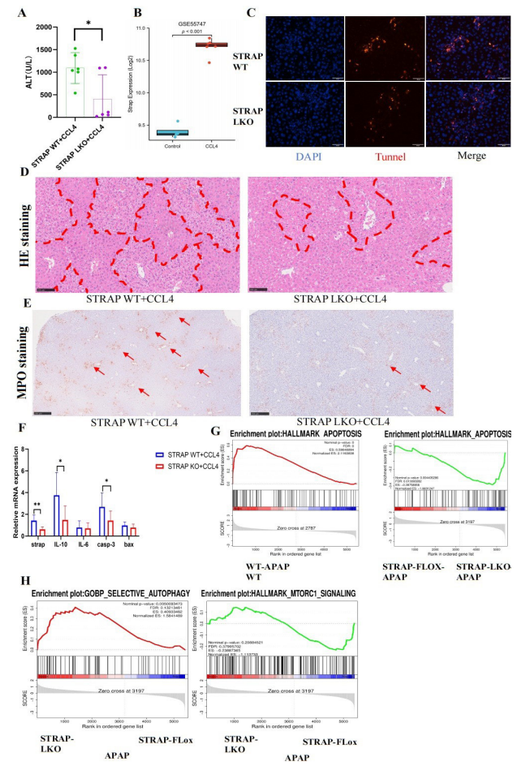


A.STRAP LKO causes decreased serum levels of ALT and AST. **B**.APAP induces STRAP expression in vivo. **C**.APAP induces the expression of STRAP in AML-12. **D**.The STRAP LKO mice have less cell apoptosis. **E**.H&E staining reveals more severe liver injury in STRAP WT mice,100 μm. **F**.STRAP LKO decreases macrophage infiltration in liver. **G**.STRAP LKO decreases neutrophi infiltration in liver. **H**.The survival rate is significantly higher in STRAP LKO mice. **I**.STRAP LKO reduces inflammation in liver.

Figure 1

Methods: This study established APAP- and carbon tetrachloride (CCl_4)-induced DILI animal models. Age-matched hepatocyte-specific STRAP knockout (STRAP$^{\Delta hep}$) mice and their wild-type (WT) littermates were subjected to systematic phenotypic analyses to compare their susceptibility to hepatotoxic injury. Additionally, an in vitro DILI model was generated by treating STRAP-knockout AML-12 hepatocytes with APAP. Proteomic analysis, combined with quantitative real-time PCR (qRT-PCR), Western blot (WB), immunohistochemistry (IHC), and TUNEL apoptosis assays, was employed to evaluate the transcriptional and translational expression profiles of key regulatory genes.

Results: This study first observed significant upregulation of STRAP during DILI progression. Phenotypic analyses revealed that STRAP$^{\Delta hep}$ mice exhibited attenuated histopathological liver damage, reduced serum transaminase levels, and suppressed inflammatory cytokine expression compared to WT controls across multiple DILI models. Proteomic analysis further demonstrated that STRAP regulates AILI through the mTOR signaling pathway and mediates autophagy network, suggesting the STRAP/mTOR/autophagy axis as a potential therapeutic target for DILI intervention, which have been confirmed by qRT-PCR and WB.



A.STRAP LKO causes decrease serum levels of ALT. **B**.The expression level of STRAP was elevated after CCL4 treatment. **C**.The STRAP LKO mice have less cell apoptosis in CCL4 induced liver injury. **D**.H&E staining reveals more severe liver injury in STRAP WT mice. **E**.STRAP LKO decreases neutrophil infiltration in liver. **F**.STRAP LKO decreases inflammation in liver. **G**.STRAP LKO inhibits apoptosis pathway. **H**.STRAP LKO activates mTOR mediated autophagy.

Figure 2.

Conclusions: STRAP exacerbates drug-induced liver injury via mTOR-mediated autophagy. This study unveils the previously

unrecognized role of STRAP in AILI pathogenesis and provides novel insights into its underlying mechanisms.

Keywords: Acetaminophen (APAP), Drug-Induced Liver Injury (DILI), Carbon Tetrachloride (CCL4), Autophagy

OP-86

3D Bioprinted Tubular Hepatobiliary Model Enabling Bile Acid Transport and Drainage

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Aims: Bile acid drainage (BAD) is essential for lipid digestion, metabolism, and bile acid homeostasis. Its failure leads to severe pediatric hepatobiliary disorders, such as biliary atresia and Alagille syndrome. While organoid technology replicates bile acid production and transport, it lacks a macroscale bile duct with a lumen for BAD. In this study, we developed a 3D bioprinted tubular bile duct integrating hepatocytes and cholangiocytes to enable BAD via hierarchical bile acid transportation, mimicking physiological function. Our BAD-capable model holds potential for drug testing platforms and advances in liver transplantation research.

Methods: To fabricate the hepatobiliary model, we utilized a tissue-specific bioink and 3D bioprinting technology. HepG2 (hepatocytes) and HuCC-T1 (cholangiocytes) were embedded in a liver-derived decellularized extracellular matrix (LdECM) and printed into a sheet with a tubular duct traversing it. Tissue maturation and functionality were evaluated through immunofluorescence staining and a qPCR assay. Furthermore, cholyl-lysine fluorescein (CLF), a fluorescent bile acid analog, was used to assess bile acid transport dynamics in real-time within the hepatobiliary model.

Results: Bile canaliculi between hepatocytes was confirmed by tight junction marker E-Cadherin and bile acid transporters BSEP and MRP2. Cholangiocyte polarity was validated through the expression of ASBT, OSTβ, AE2, and CFTR, demonstrating their role in bile acid absorption and modification. CLF staining confirmed hierarchical bile acid transport, showing bile acid secretion from hepatocytes, transportation through bile canaliculi, and drainage by cholangiocytes, leading to accumulation in the bile duct lumen.

Conclusions: The incorporation of LdECM provided biochemical cues, enhancing the expression of hepatobiliary-specific markers involved in BAD. Moreover, the tubular geometry imposed by bioprinting facilitated functional maturation compared to models relying solely on cellular self-assembly. Furthermore, the presence of functional transporters, hierarchical bile acid transportation and drainage establishes its potential as a physiologically relevant platform for studying pediatric hepatobiliary disorders, bile acid metabolism, and drug testing applications, providing a useful tool for liver disease research.

Keywords: 3D Bioprinting, DECM, Hepatobiliary, Bile ACID Transportation and Drainage

OP-87

Targeting Hepatic Stem Cell Niche with Epigenetic Modulators for Accelerated Liver Regeneration in Advanced Hepatic Fibrosis

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Aims: This study investigates the therapeutic potential of targeting the hepatic stem cell niche using epigenetic modulators to enhance liver regeneration in advanced stages of hepatic fibrosis. While hepatic stem cells (HSCs) have shown promise in liver repair, their regenerative potential is often impaired by fibrosis. We hypothesize that manipulating the epigenetic landscape of HSCs within the fibrotic liver microenvironment can restore their regenerative capacity, leading to improved outcomes in liver diseases such as cirrhosis and advanced non-alcoholic steatohepatitis (NASH).

Methods: A cohort of 100 patients with varying degrees of liver fibrosis (F2 to F4 based on the METAVIR scoring system) was recruited. Liver biopsies and serum samples were collected at baseline. In vitro, primary hepatocytes and HSCs were isolated from liver biopsies and subjected to epigenetic modifications using selective inhibitors of histone deacetylases (HDACs) and DNA methyltransferases (DNMTs). These modifications aimed to reverse the fibrotic phenotype of the cells. In vivo, we used a murine model of liver fibrosis (CCl_4-induced) to assess the effect of combined epigenetic therapy and stem cell transplantation. Outcome measures included liver regeneration rates (assessed by Ki-67 and α-SMA staining), fibrosis resolution (via Masson's Trichrome and Sirius Red staining), and functional liver biomarkers (ALT, AST, albumin).

Results: In vitro, epigenetic modulation resulted in the reactivation of key stem cell markers (e.g., Sox9, EpCAM) and enhanced hepatocyte proliferation in the presence of fibrosis-related cytokines. In vivo, the combination of epigenetic modulators and HSC transplantation resulted in significant improvement in liver regeneration and fibrosis resolution compared to controls (P<0.01). Histological analysis revealed a 40% reduction in liver fibrosis and a threefold increase in hepatocyte proliferation in the treated group. Furthermore, serum levels of ALT, AST, and bilirubin were significantly normalized in the treatment group, indicating improved liver function.

Conclusions: This study demonstrates that targeting the hepatic stem cell niche through epigenetic modulation can restore liver regenerative capacity in the context of advanced fibrosis. These findings suggest that epigenetic therapies, in combination with stem cell-based approaches, could represent a powerful strategy to promote liver regeneration and reverse fibrosis in patients with advanced liver disease. Further clinical trials are warranted to explore the safety and efficacy of these therapies in human populations.

Keywords: Stem Cell, Fibrotic, Regenration

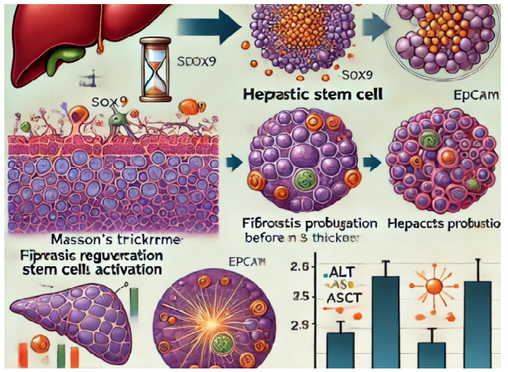

Figure 1. A scientific illustration showing liver regeneration in a fibrotic liver after epigenetic therapy. The image includes three panels

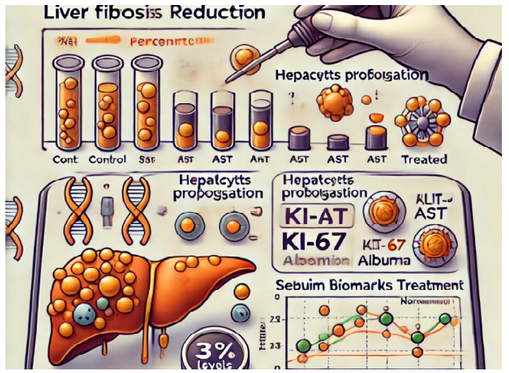

Figure 2. A detailed scientific statistical image illustrating the effects of epigenetic therapy on liver regeneration.

OP-88

A Prospective Cohort Study of Hepatic and Biliary Complications in Pediatric Patients with Sickle Cell Disease in India

Ashishkumar Chaudhari

GMERS Medical College, India

Aims: To identify hepatic and biliary complications in pediatric patients with sickle cell disease through a prospective cohort study.

Methods: This prospective cohort study commenced in March 2019, enrolling paediatric patients with sickle cell disease who were followed up for a period of five years. A purposive sampling technique was used to select participants. A total of 163 children with sickle cell disease were included in the study, all of whom were under the age of 13 at the time of enrolment. The patients were followed up for the five-year period.

Results: The yearly attrition rate was found to be 8.1%, with 112 patients remaining in the study after five years. Data were collected through a review of the patients' medical records. Among the participants, 26.8% experienced at least one hepatic or biliary complication. The most prevalent complication was cholelithiasis, affecting 20.5% of patients, followed by acute hepatic crisis 5.3% and transfusion-related iron overload 3.6%. Acute hepatic sequestration and autoimmune hepatitis were each observed in 2.67% patients. The mean total bilirubin level in patients with cholelithiasis was found to be 1.81 mg/dl, with a mean conjugated bilirubin of 0.4 mg/dl. In patients experiencing acute hepatic crisis, the mean total bilirubin was 2.1 mg/dl, while the mean conjugated bilirubin was 0.87 mg/dl.

Conclusions: In summary, liver and biliary disorders were commonly observed in children with sickle cell disease within our extensive cohort. Cholelithiasis was the most prevalent condition, affecting 21% of patients, and in some cases, led to significant complications that could be avoided through elective cholecystectomy. Although rare, hepatic crises can be extremely severe, and should be investigated in suspected cases.

Keywords: Sickle Cell Disease, Cholelithiasis, Acute Hepatic Crisis, Acute Hepatic Sequestration

OP-89

The Effectiveness of Abdominal Doppler Ultrasound, Measurement of Abdominal Fat, and the Value of Swm/Att in the Assessment of Liver Disease

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Seoul, Korea

Aims: Abdominal doppler ultrasound (US), measurement of abdominal fat, and Shear Wave Measurement (SWM)/Attenuation measurement (ATT) cab be readily applied to the liver disease using abdominal US. The aim of this study is to identify the effectiveness of these tools in various liver disease.

Methods: During August 2024 - March 2025, total 234 patients with liver diseases were prospectively enrolled in Soonchunhyang University Seoul Hospital. Among these, the results of 209 cases were finally analyzed. Portal vein velocity (PPV), portal venous pulsatility index (VPI), hepatic vein wave form (HVWF), and hepatic artery resistive index (HARI) were measured in doppler US. The abdominal fat was measured with subcutaneous fat (SF) and visceral fat (VF) ranging from the skin to the anterior wall of the abdominal aorta. Liver stiffness was measured using SWM, and fatty liver estimations was made with the ATT on the ARIETTA 850 (FUJIFILM ultrasound). The value of SWM and ATT was compared with that of liver stiffness and controlled attenuation parameter (CAP) of the FibroScan. Spearman's rank correlation analysis, independent samples t-test, and Chi-Squared test were used for statistical analysis.

Results: The number of included diseases were as follows; metabolic dysfunction-associated steatotic liver disease (MASLD) 65, hepatitis B virus infection 63, MASLD combined with other liver disease 36, alcoholic liver disease 14, hepatitis C virus infection 7, primary biliary cholangitis 2, cryptogenic liver cirrhosis 2, autoimmune hepatitis 1, others 3. In PPSV, SF, and PF, there was significant difference between patients with MASLD and without MASLD [PPSV; 16.34±3.11 vs 17.96±3.86, (*P*=0.001), SF; 2.39±0.91 vs 1.83±0.74, (*P*<0.001), PF; 5.67±1.93 vs 3.40 ±1.85 (*P*<0.001)]. HVWF shows statistical tendency between patients with cirrhosis and without cirrhosis (monophasic or biphasic HVWF; 28% in cirrhosis vs 13.5% without cirrhosis, *P*=0.061). The correlation coefficient between ATT and CAP values was 0.423, and that of SWM and liverstiffness was 0.633, repectively (*P*<0.001).

Conclusions: The values of PSV, SF, and PF was significant to identify MASLD in US and SWM/ATT showed good correlation with liver stiffness and CAP of FibroScan.

Keywords: Ultrasound, Doppler, Fibroscan, Visceral Fat

Saturday, May 31, 2025, 09:30-10:30

16. Liver Cancer, Clinical 4

OP-90

Comparative Effectiveness of Entecavir, Tenofovir Disoproxil Fumarate, and Tenofovir Alafenamide in HCC Recurrence and Mortality after Curative Treatment

Ji Eun Han[1], Gi Hyeon Seo[2], Yoon Je Cho[1], Hyo Jung Cho[1], Jae Youn Cheong[1], Soon Sun Kim[1]

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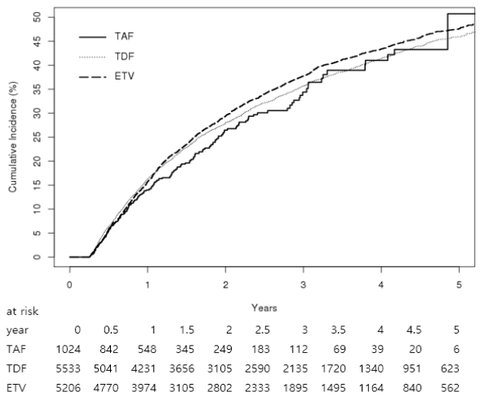
Aims: Chronic hepatitis B (CHB) can lead to hepatocellular carcinoma (HCC) due to persistent covalently closed circular DNA and integrated HBV DNA, even after curative HCC treatment. Hepatitis B viral load is a key prognostic factor for HCC recurrence, necessitating optimal antiviral therapy. Entecavir (ETV), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) are first-line nucleot(s)ide analogs for CHB. However, real-world long-term data on TAF's impact on HCC recurrence or death remain limited. This study aimed to compare the effects of ETV, TDF, and TAF on HCC recurrence or death after curative treatment.

Methods: This retrospective cohort study used data from the Korean Health Insurance Review and Assessment Service and included 11,763 CHB patients (aged 19–99) who received ETV, TDF, or TAF for ≥3months and underwent curative HCC treatment (surgical resection or local ablation) between 2017 and 2023. Patients who switched to TAF for ≥90 days were classified into the TAF group. HCC recurrence or death was the primary outcome. Inverse probability of treatment weighting (IPTW), Kaplan-Meier analysis, and Cox proportional hazards models were used to assess risk differences.

Results: A total of 11,763 patients (TAF:1,024, TDF:5,533, ETV:5,206) were analyzed, with a median follow-up of 29.4 months. The incidence rates of HCC recurrence or death per 100 person-years were 16.66 (TAF), 15.20 (TDF), and 16.57 (ETV). IPTW-adjusted analysis showed no significant difference between TAF and ETV (HR:0.88, 95% CI:0.76–1.02, *P*=0.098) or TAF and TDF (HR:0.93, 95% CI:0.80–1.07, *P*=0.307). Multivariate Cox analysis identified male sex, older age, diabetes, liver cirrhosis, and local ablation therapy as independent risk factors for overall adverse outcomes (all *P*<0.05). Kaplan-Meier analysis showed no significant difference between groups.

Conclusions: TAF showed no statistically significant difference in HCC recurrence or death compared to ETV and TDF in patients with HCC after curative treatment.

Keywords: Hepatocellular Carcinoma, Chronic Hepatitis B, Antiviral Therapy



at risk											
year	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
TAF	1024	842	548	345	249	183	112	69	39	20	6
TDF	5533	5041	4231	3656	3105	2590	2135	1720	1340	951	623
ETV	5206	4770	3974	3105	2802	2333	1895	1495	1164	840	562

Figure 1.

		Total	TAF	TDF	ETV
No.		11,763	1,024	5,533	5,206
Outcomes		4,113	202	1,960	1,951
	Recurrence	3,895	193	1,854	1,848
	Death	218	9	106	103
Total		25,882	1,212	12,892	11,777
	person-year	4,113	202	1,960	1,951
	No. of outcomes	15.89(15.41-16.38)	16.66(14.44-19.13)	15.20(14.54-15.89)	16.57(15.84-17.32)
	incidence (per 100py)				
Age 19-59		13,328	649	7,243	5,436
	person-year	1,934	112	1,017	805
	No. of outcomes	14.51(13.87-15.17)	17.26(14.21-20.77)	14.04(13.19-14.93)	14.81(13.80-15.87)
	incidence (per 100py)				
Age 60-99		12,553	564	5,649	6,341
	person-year	2,179	90	943	1,146
	No. of outcomes	17.36(16.64-18.10)	15.97(13.84-19.43)	16.69(15.64-17.79)	18.07(17.04-19.15)
	incidence (per 100py)				
Male		19,366	875	9,816	8,675
	person-year	3,311	165	1,605	1,541
	No. of outcomes	17.10(16.52-17.69)	18.85(16.08-21.96)	16.35(15.56-17.17)	17.76(16.89-18.67)
	incidence (per 100py)				
Female		6,516	337	3,076	3,103
	person-year	802	37	355	410
	No. of outcomes	12.31(11.47-13.19)	10.98(7.73-15.13)	11.54(10.37-12.81)	13.21(11.97-14.56)
	incidence (per 100py)				
Hepatectomy		17,112	815	8,735	7,562
	person-year	2,343	154	1,158	1,051
	No. of outcomes	13.69(13.14-14.26)	16.44(13.77-19.47)	13.26(12.50-14.04)	13.90(13.07-14.77)
	incidence (per 100py)				
Local Treatment		8,770	397	4,157	4,216
	person-year	1,770	68	802	900
	No. of outcomes	20.18(19.25-21.15)	17.12(13.30-21.71)	19.29(17.98-20.67)	21.35(19.98-22.79)
	incidence (per 100py)				

Figure 2.

Crude HR (95% CI)						
	TAF	0.85(0.74-0.99)	0.034	0.92(0.80-1.07)	0.281	ref
	TDF	0.93(0.87-0.99)	0.016	ref		1.08(0.94-1.25) 0.281
	ETV	ref		1.08(1.01-1.15)	0.016	1.17(1.01-1.35) 0.034
Adjusted HR (95% CI)						
	TAF	0.88(0.76-1.01)	0.073	0.92(0.80-1.07)	0.274	ref
	TDF	0.95(0.89-1.01)	0.108	ref		1.08(0.94-1.25) 0.274
	ETV	ref		1.05(0.99-1.12)	0.108	1.14(0.99-1.32) 0.073
IPTW HR (95% CI)						
	TAF	0.88(0.76-1.02)	0.098	0.93(0.80-1.07)	0.307	ref
	TDF	0.95(0.90-1.02)	0.143	ref		1.08(0.93-1.25) 0.307
	ETV	ref		1.05(0.98-1.12)	0.143	1.13(0.98-1.31) 0.098

Figure 3.

OP-91

The Role of TARE for Bridging and Downstaging of HCC before Resection or Liver Transplant: A Retrospective Analysis

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Aims: Background/Aim: Hepatocellular carcinoma (HCC) often presents at advanced stages, rendering many patients ineligible for curative surgery. This study investigates whether transarterial radioembolization (TARE) can effectively bridge or downstage HCC to enable conversion surgery, hypothesizing that TARE enhances resectability and improves surgical and oncological outcomes.

Methods: Methods: A retrospective observational study was conducted on 25 HCC patients initially deemed unresectable due to tumor size, multifocality, or vascular invasion. Patients underwent TARE with Y-90 microspheres, followed by reassessment for surgical eligibility based on tumor response and liver function. Seventeen underwent surgical resection, and eight received living donor liver transplantation (LDLT). Tumor response (size, necrosis), resectability rates, postoperative complications, and survival outcomes were analyzed using statistical tools, including Chi-square tests and Kaplan-Meier survival curves.

Results: Results: TARE achieved tumor downstaging in most cases, with 68% of patients proceeding to surgery (17 resections, 8 LDLTs). Tumor necrosis ranged from 0-100%, with 56% showing >50% necrosis. Resection had higher complication rates (35.3%, e.g., nausea, liver function elevation) than LDLT (0% reported). LDLT patients exhibited more advanced disease (75% microvascular invasion vs. 23.5% in resection, *P*=0.028). Median disease-free survival (DFS) was 11.2 months overall (3.65 months with recurrence vs. 27.1 months without), and overall survival (OS) was 33.4 months. LDLT showed superior OS (near 100%) and DFS compared to resection (declining to ~60%, *P*<0.05). Adverse effects (e.g., renal dysfunction, radiation pneumonia) occurred in 32% of cases, often linked to advanced fibrosis.

Conclusions: Conclusion: TARE effectively downstages HCC, facilitating conversion surgery with favorable outcomes, particularly in LDLT, which offers lower complications and better survival than resection. These findings highlight TARE's role in expanding surgical candidacy, though patient selection and multimodal strategies are critical for optimizing results. Larger studies are needed to refine protocols.

Keywords: Hepatocellular Carcinoma (HCC), Living Donor Liver Transplant (LDLT), Surgical Resection, Transarterial Radioembolization (TARE).

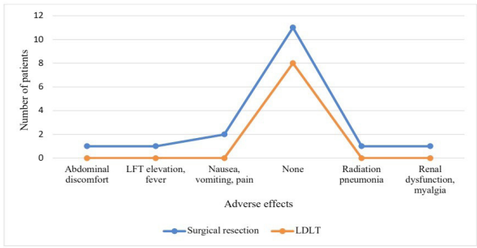

Figure 1: Adverse effect between surgical resection and LDLT (living donor liver transplantation)

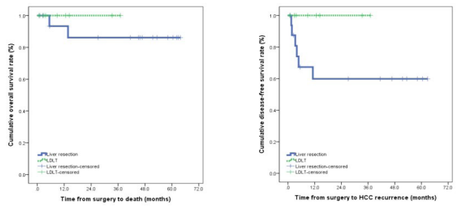

Figure 2: Kaplan-Meier survival curves comparing liver resection and living donor liver transplantation (LDLT). (A) Cumulative overall survival rates (%) from surgery to death, showing superior long-term survival in the LDLT group, which maintained nearly 100% survival, whereas the liver resection group experienced a decline, particularly within the first two years. (B) Cumulative disease-free survival rates (%) from surgery to hepatocellular carcinoma (HCC) recurrence, demonstrating a significant early decline in the liver resection group, stabilizing around 60%, while the LDLT group maintained nearly 100% disease-free survival. LDLT provides superior long-term survival and lower HCC recurrence compared to liver resection.

Surgery Date	TARE Date	Recur date	Death date	DFS	OS	TARE_Op
29-08-2018	25-01-2018	06-12-2018	08-02-2019	3.3	5.4	7.1
03-12-2018	09-01-2018	18-01-2019	26-03-2024	1.5	63.8	10.8
04-01-2019	03-07-2018	26-03-2024	26-03-2024	62.8	62.8	6.1
23-01-2019	24-05-2018	24-05-2019	26-03-2024	4	62.1	8
13-03-2019	04-09-2018	26-03-2024	26-03-2024	60.5	60.5	6.3
24-05-2019	24-07-2018	26-03-2024	26-03-2024	58.2	58.2	10
16-10-2019	30-04-2019	26-03-2024	26-03-2024	53.4	53.4	5.6
13-11-2019	23-04-2019	08-01-2020	02-01-2021	1.8	13.7	6.7
13-12-2019	27-12-2018	26-03-2024	26-03-2024	51.5	51.5	11.5
04-05-2020	01-10-2019	26-03-2024	26-03-2024	46.8	46.8	7.1
03-06-2020	03-08-2017	26-10-2020	26-03-2024	4.8	45.8	34
24-06-2020	12-11-2019	31-05-2021	26-03-2024	11.2	45.1	7.4
12-10-2020	14-01-2020	26-03-2024	26-03-2024	41.5	41.5	8.9
24-12-2021	16-06-2020	26-03-2024	26-03-2024	27.1	27.1	18.3
07-03-2023	12-04-2022	26-03-2024	26-03-2024	12.7	12.7	10.8
23-02-2021	18-09-2018	26-03-2024	26-03-2024	37.1	37.1	29.2
15-06-2021	08-05-2019	26-03-2024	26-03-2024	33.4	33.4	25.3
17-01-2023	19-07-2022	26-03-2024	26-03-2024	14.3	14.3	6
28-12-2023	20-09-2022	26-03-2024	26-03-2024	2.9	2.9	15.3
10-01-2024	01-11-2022	26-03-2024	26-03-2024	2.5	2.5	14.3
21-02-2024	08-11-2022	26-03-2024	26-03-2024	1.1	1.1	15.5
29-06-2023	03-01-2023	26-03-2024	26-03-2024	8.9	8.9	5.8
10-10-2023	10-01-2023	26-03-2024	26-03-2024	5.5	5.5	9
05-12-2023	17-01-2023	26-03-2024	26-03-2024	3.7	3.7	10.6
03-03-2024	30-05-2023	26-03-2024	26-03-2024	0.8	0.8	9.1

Supplementary Table 2: Details of the surgery date, TARE date, Recurrence Date, and death date, along with disease-free survival and Overall survival.

OP-92

Proteinuria and Its Clinical Implications in HCC Patients Treated with Atezolizumab/Bevacizumab: A Multicenter Real-World Study

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Aims: Atezolizumab/bevacizumab (atezo/bev) has been demonstrated as an effective first-line treatment for hepatocellular carcinoma (HCC). Proteinuria is one of the common adverse events of atezo/bev therapy. Therefore, we evaluated the Prevalance and risk factors for proteinuria in patients treated with atezo/bev for unresectable HCC in a large, multicenter real-world population.

Methods: From July 2020 to October 2024, this retrospective cohort study included 869 patients with HCC from 9 tertiary hospitals who were treated with atezo/bev. The level of proteinuria was evaluated based on the Common Terminology Criteria for Adverse Events version 5.0.

Results: During a median follow-up of 8.4 months, 200 (23.0%) patients developed proteinuria at a median of 3.3 months. Three patients permanently discontinued atezo/bev due to proteinuria, and 12 patients temporarily discontinued or reduced the dose of atezo/bev. Treatment duration of atezo/bev was not significantly different between the proteinuria and non- proteinuria groups. However, both overall survival and progression-free survival were significantly higher in patients with proteinuria compared with patients without proteinuria (log-rank test: P=0.002, P<0.001, respectively). In the multivariate analysis, proteinuria was significantly associated with the presence of hypertension and serum creatinine level (all P<0.05).

Conclusions: The occurrence of proteinuria during atezo/bev treatment in patients with advanced HCC is not associated with a poor prognosis if treated appropriately.

Keywords: Hepatocellular Carcinoma, Immunotherapy, Proteinuria

OP-93

Role of ALBI Score as a Predictive Factor for Mortality in Patients with Hepatocellular Carcinoma Undergoing Transarterial Chemoembolization

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[1]Division of Gastroenterology, Department of Internal Medicine, and [2]Department of Radiology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: This study was to investigate the role of Albumin-Bilirubin (ALBI) grade as a predictive factor for mortality in patients with hepatocellular carcinoma (HCC) undergoing transarterial chemoembolization (TACE). In particular, we investigated the effect of high ALBI grade on overall survival in Child-Pugh class A and low MELD score (<10) receiving TACE.

Methods: A total of 267 HCC patients with Child-Pugh class A and low MELD score (<10) undergoing TACE as an initial treatment were analyzed. Predictive factors for overall survival in patients receiving TACE were investigated. High ALBI grade is defined as ALBI grade ≥2 (ALBI score > -2.60).

Results: The mean age was 61.4 years. Of 267 patients, death was observed in 86 patients (32%). High ALBI grade was observed in 163 patients (61%). Multivariable analysis showed that the risk factors for mortality were BCLC stage C (hazard ratio [HR] 3.26 with 95% confidence interval [CI] 2.04-5.18, P<0.001), serum AFP ≥100 ng/mL (HR 1.57 with 95% CI 1.00-2.46, P=0.049), and high ALBI grade (HR 2.84 with 95% CI 1.63-4.95, P<0.001). Overall survival was significantly different according to ALBI grade (P<0.001). The 24-month, 48-month, 72-month, and 96-month survival rates of patients were 94.6%, 87.9%, 82.6%, and 75.0%, respectively, in patients with low ALBI grade; and 94.3%, 81.1%, 71.7%, and 67.3%, respectively, in patients with high ALBI grade.

Conclusions: High ALBI grade is associated with increased mortality in Child-Pugh class A and low MELD score receiving TACE for HCC. ALBI grade can be a predictive factor for overall survival in patients with relatively favorable liver function and HCC undergoing TACE.

Keywords: Hepatocellular Carcinoma, Transarterial Chemoembolization, Albi Score

OP-94

The Real Change in Cholangiocarcinoma? A Real-World Experience

Stefano Mariani[1], Valeria Pusceddu[1], Marzo Puzzoni[1], Pina Ziranu[1], Alessandra Pia D'Agata[1], Dario Spanu[2], Elisa Aresu[1], Fabiana Contu[1], Andrea Cadoni[1], Alissa Parrino[1], Mattia Cucca[1], Gianluca Pannella[1], Eleonora Lai[1], Andrea Pretta[1], Mario Scartozzi[1]

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Aims: Colangiocharcinoma (CCA) belongs to Biliary Tract Cancers (BTCs) which, despite a steadily increasing incidence, displays few therapeutic advancements and marginal improvement in the long-term survival for advanced disease. TOPAZ-1 was the first clinical trial demonstrating an overall survival (OS) benefit with immunotherapy (IT) added to standard first line standard chemotherapy (CHT). The aim of this study was to evaluate the real-world impact of adding IT to CHT, on PFS and OS, in metastatic CCA patients (pts).

Methods: This is a retrospective, monocentric, observational study which analyzes PFS and OS of first line CCA treatment for metastatic or locally advanced not resectable disease. Patients were treated with standard CHT alone or in combination with IT.

Results: Data were collected from Thirty-five (35) pts, treated since April 2019 until February 2025. 24 pts had intrahepatic CCA and 11 pts extraepatic CCA. Thirteen had locally advanced not operable disease while twenty-one had metastatic disease. Median age was 65.8 years (between 47 to 76 years), sixteen women and nineteen men. 13 pts were treated with standard CHT (Cisplatin+Gemcitabine) and 21 pts with CHT-IT (14 pts with Durvalumab and 7 pts with Pembrolizumab). The median OS in the CHT-IT group was 23 months (95% I.C. 17.48-30.296, P=0.0167) while the OS in the CHT group was 12 months (95% I.C. 13.39-22.19). The median PFS in the CHT-IT group was 16 months (95% I.C. 10.05 - 19.93, P=0.0129) and 4 months (95% I.C. 3.34 - 9.82) in the group treated with CHT. The incidence of adverse events between the two groups didn't show significant differences.

Conclusions: The result of our study confirms the survival benefit coming from the introduction of IT (Durvalumab or Pembrolizumab) to standard CHT in patients with metastatic CCA in a real world, non-selected population.

Keywords: Cholangiocarcinoma, Immunotherapy, Liver Cancer, Real World

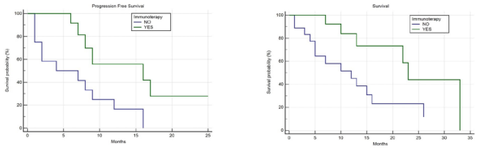

Figure 1. PFS and OS.

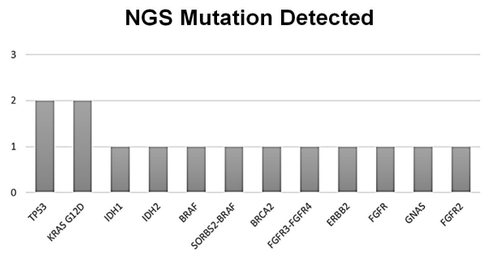

Figure 2. NGS Mutations Detected.

Adverse Events

TOXICITY	CHT-IT GROUP	CHT GROUP
Pancytopenia	4.8 %	0 %
Thrombocytopenia	9.5 %	30.7 %
Neutropenia	33.3 %	23.1 %
Asthenia	14.2 %	7.7 %
Nausea and/or vomiting	0 %	7.7 %

Figure 3. Adverse Events CHT-IT vs CHT.

OP-95

Efficacy of Lymphadenectomy in Intrahepatic Cholangiocarcinoma

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Aims: Surgical resection including lymph node dissection(LND) has been accepted worldwide as the standard treatment of Intrahepatic cholangiocarcinoma(iCCA). However, the effect of LND is still controversial. In this study, we compared the outcome of surgery for iCCA according to LND in our center.

Methods: A retrospective analysis was performed for 111 patients who underwent surgery for iCCA in our center between 2004 and 2024. The patients were categorized using the prognostic score which was composed with prognostic factors identified in our study and the outcomes of LND in each group were evaluated.

Results: Among 111 patients, 55 patients received LND and 56 patients didn't receive LND. Five-year disease-free survival(DFS) and overall survival(OS) were was 21% and 35% in LND group, and 42% and 51% in non-LND group, respectively. The baseline characteristics of patients in each group were significantly different in some variations. In this reason, the patients were categorized into 2 groups, low-risk group and high-risk group, using risk scoring which included 6 prognostic factors identified through Cox proportional hazards model. The outcome was well stratified according to the risk groups. In comparison of the effect of LND, there were no significant differences in terms of DFS and OS between LND group and non-LND group in each risk group.

Conclusions: In our study, LND didn't show the beneficial effect on outcomes of resection for iCCA. However, with limitation of our study including sample size and selection bias, further study with large scale population may needed for confirmation.

Keywords: Intrahepatic Cholangicarcinoma, Lymphadenectomy

Saturday, May 31, 2025, 09:30-10:30

17. Liver Transplantation 2

OP-96

Clinical Significance of De Novo Malignancy after Liver Transplant: Update on a Single-Center Study

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Aims: Several studies have reported that solid organ transplant recipients have a high risk for malignant tumors because the suppressed immune system fails in preventing malignant transformations. De novo malignancy after transplantation is the most common cause of death in the late period after liver transplant (LT). This study investigated the clinical significance of de novo malignancy after LT, and it is the largest study based in Korea to report long-term follow-up results associated with de novo malignancy after LT.

Methods: The study population was 2,598 adults who underwent LT from 1988 to March 2023. Data were retrospectively collected, and medical charts and data from the Ministry of Public Administration and Security were reviewed to examine the causes of death and de novo malignancy status.

Results: Of the 2598 recipients, 173 developed de novo cancer and 63 were died. Of 1296 hepatocellular carcinoma (HCC) patients, 35 died, and of 1302 non-HCC patients, 28 died with de novo cancer. De novo malignancy was the main cause of death at 5 years after LT but was not in the initial 5 years. In Korea the most common cancers that developed after LT were lymphoma 33 (%) and gastric cancer 26 (%), and De novo HCC in non-HCC cases was found in 3 patients.

Conclusions: De novo malignancy is a key factor affecting long-term survival after LT. Therefore, regular screening and education are important for improving long-term survival and quality of life in these patients after LT.

Keywords: DE NOVO MALIGNANCY, LIVER TRANSPLANTATION

OP-97

Investigating Key Factors of Fatty Liver Disease in Liver Donors

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Aims: Fatty liver disease is one of the major health issues that occur very commonly in individuals. This study looks into the main occupational, metabolic, and demographic factors that influence fatty liver in liver donors in an effort to offer practical advice on risk reduction and donor health.

Methods: Based on ultrasound results, the study classified the liver states of 101 liver donors as "normal" or "fatty liver". Diverse statistical methods, including feature analysis and chi-square testing, were used to investigate the relationships between liver status and features like follow-up information, anthropometric measurements, lifestyle choices, clinical indicators, and demographics.

Results: Fatty liver was identified in 27.7% of the liver donors and was significantly associated with a higher average BMI (27.65 kg/m^2) and older average age (32.39 years), compared to normal donors, who had an average BMI of 24.87 kg/m^2 and an average age of 29 years. Employment status was identified as the most significant contributor where 92% of fatty liver donors were employed individuals. This indicates that occupational factors like stress or sedentary behavior play a vital role. Fatty liver donors had normal creatinine and ALT levels, though slightly higher than normal donors. Gender displayed a marginal association where males are slightly more affected than females. The average follow-up frequency for donors with fatty liver was 3.54 visits, which was slightly higher than the normal donors with 3.3 visits. Interestingly, there was no observable relationship between the incidence of fatty liver and conventional risk factors including smoking, drinking, and family history.

Conclusions: The results highlight that the higher BMI, older age, and occupation-related factors, have a substantial impact on the occurrence of fatty liver in donors. It is very crucial to carry out comprehensive health examinations before donation and create focused interventions to address occupational risks and metabolic health.

Keywords: Fatty Liver Disease, Liver Donors

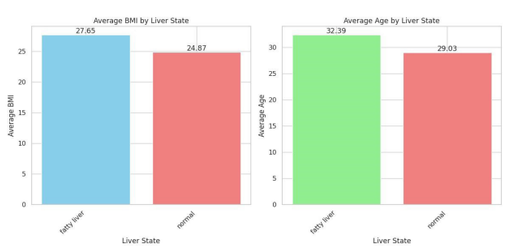

Figure 1.

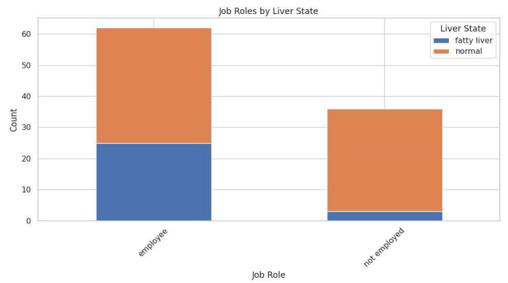

Figure 2.

OP-98

Xenotransplantation of Pancreatic Islet Cells: A Promising Approach for Type 1 Diabetes Treatment

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Aims: Type 1 diabetes mellitus (T1DM) remains a major challenge due to the lifelong need for insulin therapy and the risk of severe complications. Pancreatic islet transplantation has shown potential in improving glucose control, but the scarcity of human donor organs and the necessity of lifelong immunosuppression limit its clinical use. Xenotransplantation of pancreatic islet cells (PICs) derived from neonatal lambs and piglets represents a promising alternative, offering an abundant source of insulin-producing cells. This study evaluates the safety, efficacy, and feasibility of xenotransplantation as a therapeutic strategy for T1DM

Methods: A total of 186 patients with T1DM (aged 13–59) underwent xenotransplantation of PICs obtained from neonatal lambs (n=106) and piglets (n=80). Islets were transplanted into various sites, including the splenic capsule, round ligament of the liver, and subcutaneous tissues. Clinical outcomes were assessed based on glycemic control (fasting blood glucose, HbA1c), insulin dependence, and diabetic complications (retinopathy, nephropathy). Immunological parameters were monitored to evaluate host immune response.

Results: At 9 months post-transplantation, most patients demonstrated improved glycemic control, with 50% achieving a >40% reduction in exogenous insulin requirements. The incidence of diabetic complications decreased significantly compared to the control group. Immunological evaluation revealed transient increases in autoantibody levels, but no severe graft rejection was observed. The procedure was well tolerated, with minimal adverse effects

Conclusions: Xenotransplantation of PICs appears to be a feasible and effective approach for improving metabolic control in T1DM. It offers a potential solution to the limited availability of donor pancreases while reducing long-term insulin dependence. Further research is needed to optimize immunosuppressive strategies and evaluate long-term graft survival

Keywords: Xenotransplantation, Pancreatic Islet Cells, Type 1 Diabetes, Cell Transplantation

OP-99

Ameliorating Effect of Curcumin Loaded Silver Nanoparticles against Liver Transplantation Associated Ischemia-Reperfusion Injury by Downregulating Inflammation and TLR-4/NF-κB/NLRP3 Signalling Pathway

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Aims: Curcumin is a natural polyphenol having significant potential against oxidative stress, inflammation, cancer and hepatic toxicity. But due to its poor solubility and bioavailability, its clinical use is limited. Therefore, in present study, we focused on the biofabrication and evaluation of protective effect of curcumin loaded silver nanoparticles (CuAgNP) on hepatic ischemia-reperfusion injury in vitro and in vivo, along with evaluation of underlying mechanism.

Methods: Male Sprague–Dawley rats were utilized for in vivo study, divided into five groups and administered with CuAgNP by intraperitoneal route at three dose levels, i.e., 5, 10 and 20 mg/kg/IP for 14 days and subjected to liver transplant. Regarding in vitro assay, RAW 264.7 cells under hypoxia/reoxygenation model was used and treated at 1, 10, and 20 μM concentration. CuAgNP potential against hepatic ischemia-reperfusion injury was estimated by determining liver enzymes (aminotransferase and aspartate aminotransferase), cytokine status estimation, hepatocyte apoptosis level estimation. Neutrophil and pro-inflammatory cytokines protein and mRNA expression were detected by western blot technique and qRT-PCR, respectively.

Results: Results exhibited formation of spherical nanoparticles in size range of 80-100 nm, while in vivo study revealed pathological liver alterations. Level of serum aminotransferase as well as proinflammatory cytokines (IL-1, IL-18 and TNF-α) were significantly decreased by CuAgNP. Moreover, reduced protein expression level of TLR-4, p-IκBα, p-IKKα, p-IKKβ, p-IKK, NLRP3, p-P65MyD88, TNF-α, Cleaved caspase-1, IL-1β, IL-6 and IL-18, associated with TLR-4/NF-κB/NLRP3 inflammatory signalling pathways, were observed in rats with liver transplantation. In vitro study results showed dose-dependent inhibition of protein expression associated with TLR-4/NF-κB/NLRP3 inflammatory pathway in RAW264.7 cells in CuAgNP group.

Conclusions: CuAgNP exerts an anti-inflammatory effect in hepatic ischemia-reperfusion injury in liver transplantation by regulating the TLR-4/NF-κB/NLRP3 inflammatory signalling pathway.

Keywords: Reperfusion

OP-100

Machine Perfusion in Marginal Liver Grafts: A Systematic Review of Clinical Impact on Liver Transplantation

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Aims: The shortage of suitable liver grafts has led to increased reliance on marginal grafts, including those from donation after circulatory death (DCD) donors and extended criteria donors (ECD). These grafts carry a higher risk of primary non-function and ischemia-reperfusion injury. Machine perfusion (MP), including hypothermic oxygenated perfusion (HOPE) and normothermic machine perfusion (NMP), has emerged as an innovative strategy to enhance organ preservation and improve outcomes. This systematic review aims to evaluate the clinical impact of machine perfusion on the viability and outcomes of marginal liver grafts in transplantation.

Methods: Following PRISMA guidelines, a systematic literature search was conducted across PubMed, Web of Science, and Scopus databases up to January 2025. Included studies were randomized controlled trials (RCTs), cohort studies, and meta-analyses assessing MP in marginal liver grafts. Primary outcomes included graft survival, incidence of early allograft dysfunction (EAD), primary non-function (PNF), and ischemic cholangiopathy. Secondary outcomes were postoperative complications, length of ICU/hospital stay, and biliary complications. Study quality was evaluated using the Newcastle-Ottawa Scale and the Cochrane Risk of Bias tool.

Results: A total of 22 studies comprising 3,274 liver transplants using marginal grafts were included. MP significantly reduced the incidence of EAD (OR: 0.52; 95% CI: 0.38–0.70) and ischemic cholangiopathy (OR: 0.46; 95% CI: 0.33–0.65) compared to static cold storage (SCS). Graft survival at one year was improved in MP groups (MP: 85.7%, SCS: 78.2%). Hypothermic oxygenated perfusion (HOPE) showed particular benefit in reducing biliary complications in DCD grafts, while normothermic perfusion allowed better graft viability assessment. Postoperative ICU and hospital stays were shortened in MP recipients without increasing postoperative complications.

Conclusions: Machine perfusion demonstrates a significant clinical benefit in the preservation and utilization of marginal liver grafts, improving graft viability, reducing complications, and enhancing overall transplant outcomes. MP should be considered standard care in the use of marginal grafts, although further large-scale trials are needed to refine protocols and optimize outcomes.

Keywords: Machine Perfusion, Marginal Liver Grafts, Liver Transplantation, Hypothermic Oxygenated Perfusion

OP-101

Comparison of Effectiveness of Mycophenolate Mofetil Associated with Standard Dosage or Reduced-Dose Tacrolimus for Liver Transplantation Immunosuppression

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Aims: Liver transplantation necessitates lifelong immunosuppressive therapy to prevent graft rejection. This systematic review evaluates the effectiveness of mycophenolate mofetil (MMF) in combination with standard-dose (SD) versus reduced-dose (RD) tacrolimus in liver transplant recipients.

Methods: A systematic search was conducted across databases including PubMed, Cochrane, and Embase for studies published from 2000 to 2024. Inclusion criteria focused on randomized controlled trials (RCTs) and observational studies involving human subjects aged ≥18. Primary outcomes included graft survival, acute rejection rates, and patient survival, while secondary outcomes encompassed renal function, infection rates, and adverse effects.

Results: Out of 85 initially identified studies, 81 were excluded based on predetermined criteria. Ultimately, four studies involving a total of 255 patients (standard-dose: n = 131; reduced-dose: n = 124) were included for analysis. The findings indicated that mycophenolate mofetil (MMF) combined with tacrolimus, whether standard-dose or reduced-dose, allowed for a significant reduction in tacrolimus dosage, effectively minimizing nephrotoxic effects. Graft and patient survival rates were comparable between the MMF-tacrolimus regimen using standard and reduced doses. Additionally, the MMF group exhibited lower rates of acute rejection and showed improvements in renal function, with safety and efficacy profiles being similar across both dosage groups.

Conclusions: The combination of MMF with either standard-dose or reduced-dose tacrolimus is an effective immunosuppressive strategy for liver transplant recipients. Both approaches facilitate a reduction in tacrolimus dosage while maintaining similar safety and efficacy. The MMF-tacrolimus regimen contributes to lower rates of acute rejection, with comparable graft and patient survival rates. Further research is warranted to optimize immunosuppressive protocols and enhance patient outcomes.

Keywords: Liver Transplantation, Immunosuppression, Tacrolimus, Mycophenolate Mofetil

Saturday, May 31, 2025, 09:30-10:30

18. Liver Cancer, Basic 3

OP-102

Characterization of Diverse Extracellular Nanoparticles and Tumorigenic Relevance in Hepatocellular Carcinoma

Charlotte Jiaqi Lai[1], Cherlie Lot Sum Yeung[1], Le Cui[1], Lavisha Korani[1], Tung Him Ng[1], Xiaoxin Zhang[1], Zhixian Chen[1], Ricky Ruiqi Ma[1], Chi-Ming Che[2], Judy Wai Ping Yam[1]

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Aims: Tumor-derived extracellular nanoparticles termed exomere (EM), distinct to small extracellular vesicles (sEV), act as critical mediators of the tumour microenvironment (TME) formation. This study aims to characterize these novel subpopulations and investigate their role in tumor progression and therapy resistance in hepatocellular carcinoma (HCC).

Methods: sEV and EM were all isolated from numerous normal and cancer cell lines by using serial ultracentrifugation. The physical and biomedical characterization of EM versus sEV was conducted through transmission electron microscopy (TEM) and mass spectrometry (MS) analysis. Potential molecular EM markers were identified based on distinct proteomic profiles between sEV and EM. The tumorigenic potentials of HCC-EM were evaluated using *in vitro* assays and *in vivo* mice models. Relevant oncogenic mechanisms were studied according to the cargo content differences between HCC- and normal-EM, as well as differential gene expression inside recipient cells by RNA sequencing. The effects of cell cycle promotion and metabolic dysregulation were investigated by flow cytometry and analytical metabolomic/lipidomic approaches.

Results: TEM and MS analysis demonstrated a relatively large difference in morphology and protein identities between sEV and EM. GALNS and MAN2B1 were identified as potential EM markers, showing exclusive or significantly higher expression. Functionally, EM released from HCC cells, instead of normal hepatocytes, stimulated cell growth, motility and tumor development. The human-originally oncogenic EM exhibited increased WNT5A, LRP5, and LRP6 levels, activating PI3K/AKT/mTOR pathway in recipient cells. In addition, murine HCC cells-derived EM accelerated cell cycle progression by shifting cells through the checkpoint into the G1 phase, and reconstitute the lipid pattern to be enriched with a very-long chained saturated fatty acid, which triggers the metabolic reprogramming.

Conclusions: Collectively, our findings underscore the unique characteristics of EM as a nanoparticle subpopulation that dif-

fers from sEV, and that EM derived from HCC can play a significant role in tumorigenesis and metastasis.

Keywords: Hepatocellular Carcinoma, Tumor Microenvironment, Extracellular Vesicles And Nanoparticles, Tumorigenesis and Pathogenesis

OP-103

Spatial Transcriptomics Uncovers Intratumoral Molecular Heterogeneity in Hepatoblastoma

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Aims: Hepatoblastoma, the most common pediatric liver malignancy, is well known for significant intratumoral histological heterogeneity. Our previous work suggested that certain histological patterns correlate with poor patient prognosis, leading to the proposal of a novel histological grading system of hepatoblastoma. In this follow-up study, we analyzed molecular differences between histologic patterns of hepatoblastoma using spatial transcriptomics.

Methods: Twenty resected hepatoblastoma samples were microscopically examined to determine histologic patterns. Five cylindrical cores representing different histologic patterns were obtained from each tumor to create tissue microarrays. Their transcriptomic profiles were analyzed using Nanostring GeoMx DSP.

Results: Different histologic components were distinctively clustered by multidimensional scaling visualization. Especially, embryonal, cholangioblastic, and small cell undifferentiated (SCUD) patterns were separated from fetal and pleomorphic patterns. Epithelial components showed upregulation of MYC targets variant 1 and 2, E2F targets, G2/M checkpoint, fatty acid metabolism, peroxisomes, bile acid biosynthesis, and mTORC1 signaling pathways, but downregulation of epithelial-mesenchymal transition and muscle differentiation pathways compared to mesenchymal and teratoid components. Embryonal, cholangioblastic, and SCUD patterns showed upregulation of E2F targets, MYC targets variant 1 and 2, G2/M checkpoint, mitotic spindle assembly, and canonical beta-catenin pathways, but downregulation of coagulation cascade, bile acid biosynthesis, interferon alpha and gamma responses, TNF α signaling via NF-κB, IL6/JAK/STAT3 signaling, and inflammation pathways compared to fetal and pleomorphic patterns. The pleomorphic pattern showed upregulation of interferon alpha and gamma responses, TNF α signaling via NF-κB, and epithelial-mesenchymal transition, but downregulation of MYC targets variant 1 and 2, E2F targets, and G2/M checkpoint pathways compared to the fetal pattern.

Conclusions: Histological patterns of hepatoblastoma are associated with distinct transcriptomic profiles, which may explain their prognostic significance and provide novel therapeutic approaches.

Keywords: Liver Neoplasms, Pediatrics, Hepatoblastoma, Gene Expression Profiling, Histology

OP-104

Differential Infiltration of T-Cell Populations in Tumor and Liver Tissue Predicts Recurrence-Free Survival in Surgically Resected Hepatocellular Carcinoma

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Aims: Liver and tumor-infiltrating T cells in hepatocellular carcinoma (HCC) are heterogeneous, comprising the $CD69^+$ tissue-resident T cell and the $CD69^-$ circulating T-cell populations. However, the impact of these distinct T-cell populations on patient prognosis is unclear; hence further studies are needed.

Methods: Tumor and distant liver tissues from 57 HCC patients with various chronic liver disease etiologies were analyzed. Single-cell dissociation and flow cytometry were used to assess $CD69^+$ and $CD69^-$ T-cell populations and their correlation with recurrence-free survival (RFS).

Results: $CD69^+/CD69^-$ subpopulations within $CD4^+$ and $CD8^+$ T cells varied by patient and alcohol etiology. $CD69^-$ populations among $CD4^+$ T cells were less frequent in both tumor and non-tumor tissues of alcohol-related HCC patients ($P<0.05$). Higher frequencies of $CD69^-CD4^+$ and $CD8^+$ T cells in tumors and $CD69^+CD103^+CD8^+$ T cells in liver tissues were associated with better RFS. $CD69^-$ T cells expressed lower PD-1 levels, indicating less exhaustion, with PD-1 expression inversely correlated with $CD69^-$ frequency. PD-1 expression was higher on $CD69^-CD4^+$ T cells in alcohol-related HCC.

Conclusions: We provided a detailed analysis of the heterogeneous characteristics of tumor- and liver-infiltrating T cells in HCC, emphasizing the distinct roles of $CD69^+$ and $CD69^-$ cell populations and their impact on RFS. $CD69^+$ T cells were associated with immune exhaustion and tumor aggressiveness, whereas $CD69^-$ T cells appeared to significantly contribute to the influence of alcohol intake on the immune landscape of HCC in the tumor microenvironment. However, further research should validate these findings in larger cohorts to enhance our understanding.

Keywords: Hepatocellular Carcinoma, Liver-Infiltrating T Cells, Tumor-Infiltrating T Cells, Recurrence-Free Survival

OP-105

Visceral Adipose Tissue from Morbid Obesity Patients Promotes the Proliferation of Hepatocellular Carcinoma Cells

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Aims: Obesity is a major risk factor for metabolic dysfunction-associated steatotic liver disease (MASLD) and hepatocellular carcinoma (HCC). Recent studies suggest that visceral adipose tissue (VAT) plays a more significant role than subcutaneous adipose tissue (SAT) in cancer progression. However, although VAT is involved in cancer progression, its specific role and underlying molecular mechanisms in HCC remain poorly understood

Methods: To investigate the role of VAT in HCC, RNA sequencing (RNA-seq) was performed on VAT and SAT samples obtained from male and female obese patients. KEGG pathway analysis was conducted to identify differentially activated signaling pathways. In addition, conditioned media (CM) from VAT (VAT-CM) and SAT (SAT-CM) from male obese patients were applied to Hep3B (hepatocellular carcinoma cell line), and cell proliferation was assessed using the CCK-8 assay.

Results: KEGG pathway analysis revealed that multiple oncogenic pathways, including WNT signaling, IGF signaling, and inflammatory response pathways, were significantly upregulated in VAT compared to SAT. These pathways are known to be strongly associated with HCC development and progression. Furthermore, Hep3B cells treated with VAT-CM exhibited significantly enhanced proliferation compared to those treated with SAT-CM, suggesting that VAT-derived factors may contribute to HCC growth.

Conclusions: These findings suggest that VAT, particularly from male obese patients, contributes to HCC progression by activating oncogenic pathways and enhancing cancer cell proliferation. This study highlights the importance of VAT-derived factors in obesity-associated HCC and suggests that targeting VAT-related inflammatory and metabolic pathways may provide potential therapeutic strategies.

Keywords: Visceral Adipose Tissue (VAT), Subcutaneous Adipose TissuE (SAT), Obesity, Hepatocellular CarcinomA (HCC)

OP-106

CTC-537E7.3 as a Liver-Specific Biomarker for Hepatocellular Carcinoma: Diagnostic and Prognostic Implications

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Aims: Hepatocellular carcinoma (HCC) is a prevalent and deadly malignancy worldwide, yet reliable biomarkers for early diagnosis and prognosis are limited. This study aims to identify CTC-537E7.3, a long non-coding RNA (lncRNA), as a potential diagnostic and prognostic biomarker for HCC.Hepatocellular carcinoma (HCC) is a prevalent and deadly malignancy worldwide, yet reliable biomarkers for early diagnosis and prognosis are limited. This study aims to identify CTC-537E7.3, a long non-coding RNA (lncRNA), as a potential diagnostic and prognostic biomarker for HCC.

Methods: Transcriptomic analyses were conducted using TCGA_LIHC, GSE77314, and GSE124535 datasets to identify lncRNAs specifically downregulated in HCC. CTC-537E7.3 expression was validated across multiple datasets and further assessed via qRT-PCR in 97 paired tumor and non-tumor liver tissues. Kaplan–Meier survival analysis determined its prognostic significance, and correlation analysis evaluated its relationship with clinical parameters, including serum alpha-fetoprotein (AFP) levels.

Results: CTC-537E7.3 was significantly downregulated in HCC tissues compared to normal liver tissues ($P<0.0001$). ROC analysis confirmed its diagnostic potential, with an AUC of 0.95 (95% CI: 0.91–0.99, $P<0.0001$). Notably, CTC-537E7.3 demonstrated strong diagnostic accuracy in early-stage HCC (pUICC stage I/II, AUC = 0.95, $P<0.0001$). Low CTC-537E7.3 expression correlated with poor overall survival (hazard ratio [HR] = 1.88, $P=0.0004$) and reduced disease-free survival (HR = 1.50, $P=0.015$). Additionally, a significant negative association was observed between CTC-537E7.3 and AFP levels (r = -0.24, $P=0.018$).

Conclusions: These findings establish CTC-537E7.3 as a novel liver-specific lncRNA biomarker with significant diagnostic and prognostic value in HCC. Its potential role as a complementary biomarker to AFP suggests clinical applicability in enhancing HCC detection and patient stratification.

Keywords: Prognostic Biomarker, Hepatocellular Carcinoma, Long Non-Coding RNA (LNCRNA), Diagnostic Biomarker

OP-107

RBBP7 Promotes Hepatocellular Carcinoma Progression via Enhancing Small Extracellular Vesicle Secretions

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Aims: Hepatocellular carcinoma (HCC) poses a significant global health challenge, especially in Asia. Recent studies emphasize the critical role of small extracellular vesicles (sEV) in coordinating communication within the HCC microenvironment by facilitating the exchange of molecular cargo among cancer cells and various cell types. This study explores the interplay between sEV secretion and HCC progression.

Methods: A chemical library was screened to identify chemical that inhibits sEV secretion by metastatic HCC cells using Amplified Luminescent Proximity Homogeneous Assay. Conditioned medium of chemical-treated cells was incubated with donor beads and acceptor beads conjugated with antibodies targeting sEV markers, CD63 or CD9. The close proximity of beads resulted in emission of fluorescence for sEV quantification. Mass spectrometry was conducted to identify protein targets of the identified chemical that inhibits sEV biogenesis. The number of multivesicular bodies per cell profile was quantified via transmission electron microscopy. The fusion events of lysosome and endocytic cargo were assessed by calculating the overlapping events of Dextran-AF488 and Magic Red cathepsin B dye.

Results: A promising compound named 1G2 was identified that attenuated sEV release in HCC cells. 1G2 was shown to reduce multivesicular body (MVB) count and promote endolysosomal fusion, leading to a compromised sEV secretion. Subsequent analyses identified RBBP7 as a key mediator in regulating sEV biogenesis and secretion. Silencing RBBP7 significantly decreased sEV production, highlighting its role in modulating tumor-derived sEV dynamics. Furthermore, the decreased MVB count and enhanced endolysosomal fusion upon RBBP7 knockdown reveal a link between intracellular trafficking pathways and sEV secretion. Clinical data show the overexpression of RBBP7 in HCC and its positive correlation with proteins associated with sEV biogenesis.

Conclusions: These findings not only highlight RBBP7 as a potential therapeutic target in HCC management but also illustrate the intricate interplay between cellular trafficking mechanisms and intercellular communication in cancer progression.

Keywords: Small Extracellular Vesicles, Hepatocellular Carcinoma

Saturday, May 31, 2025, 09:30-10:30

19. Liver Cancer, Clinical 5

OP-108

Clinical Outcomes of Atezolizumab plus Bevacizumab in Viral and Non-viral Advanced HCC Patients : A Real-World, Multicenter Study

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Aims: Atezolizumab plus bevacizumab is the preferred first-line therapy for advanced hepatocellular carcinoma (HCC). Given the heterogeneity of HCC etiologies and their potential role in shaping the tumor microenvironment, it is essential to assess how different liver disease etiologies affect therapeutic efficacy. This study aimed to examine the impact of HCC etiology on clinical outcomes and immune-related adverse events (irAEs) following atezolizumab-bevacizumab treatment.

Methods: This retrospective, real-world study included 839 patients treated at seven South Korean medical centers from January 2021 to January 2025. Patients were categorized into viral and non-viral HCC groups. The viral group included hepatitis B virus and hepatitis C virus infections, while the non-viral group included alcohol-related liver disease, metabolic dysfunction-associated liver disease, and cryptogenic liver disease. Baseline clinical and laboratory characteristics were analyzed, and uni- and multivariate analyses were conducted to evaluate overall survival (OS) and time-to-progression (TTP). irAEs were recorded throughout the treatment period.

Results: A total of 839 patients were enrolled, including 557 with viral HCC and 282 with non-viral HCC. The disease control rate was 41.3% in the viral and 56.7% in the non-viral HCC group. The median overall survival (mOS) for the entire cohort was 22.0 months (95% CI: 19.87–24.21 months). There was no significant difference in mOS between the viral and non-viral HCC groups (21.3 vs. 21.8 months, *P*=0.14). Similarly, TTP did not differ significantly (11.89 vs. 13.3 months, *P*=0.308). irAEs were observed in 11.3% (n = 61) of patients with viral and 10.1% (n = 30) of non-viral HCC cases, with no statistically significant difference ($\chi^2 = 0.28$, P=0.60).

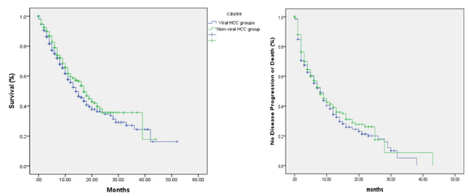
Conclusions: This study suggests that the impact of etiology on treatment strategies remains inconclusive. Further studies on immunotherapy-based combination treatments and their interaction with the tumor immune microenvironment are needed.

Keywords: Hepatocellular Carcinoma, Immunotherapy, Tumor Immune Microenvironment

Table 1. Baseline characteristics

Variable		Total (n=839)		*P* value
		Viral (n=557)	Non-viral (n=282)	
Clinical				
Sex, n (%)	Male	470 (84.4)	262 (92.9)	*0.0007*
	Female	87 (15.6)	20 (7.1)	
Age, years (median)		71	64	*<0.0001*
1st Treatment, n(%)		261 (31.3)	145 (51.4)	
Previous RFA, n(%)		129 (15.4)	57 (20.2)	
Previous TACE, n(%)		301 (35.9)	129 (45.7)	
Previous TARE, n(%)		10 (1.2)	10 (3.5)	
Liver cirrhosis, n(%)		216 (25.7)	112 (39.7)	
Child-Pugh, n	A	181	109	
	B	32	2	
	C	3	1	
BCLC, n(%)	B	67 (12.0)	35 (12.4)	
	C	489 (87.8)	245 (86.9)	
	D	1 (0.2)	2 (0.7)	
Laboratory				
Platelet, /nL		165 (156 – 174)	186 (176 – 197)	*0.0025*
Albumin, g/dL		3.85 (3.80 - 3.89)	3.9 (3.8 – 4.0)	*0.2803*
Bilirubin, mg/dL		1.18 (1.1 – 1.3)	1.05 (0.8 – 1.3)	*0.0908*
AST, U/L		71.2 (64.9 – 77.3)	69.4 (60.2 – 78.6)	*0.5139*
ALT, U/L		37.7 (34.7 – 40.7)	41.7 (33.8 – 49.7)	*0.5776*
AFP, ng/mL		9975.3 (5856.3 – 14095.3)	5904 (3102 - 8706)	*0.7485*
PIVKA II,		10997.1	14581.6	*0.0162*
mAU/mL		(8296.6 – 13697.6)	(9807.8 – 19355.2)	
Etiology				
HBV, n(%)		447 (80.2)		
HCV, n(%)		94 (16.9)		
HBV+HCV, n(%)		16 (2.9)		
MASH/MASLD, n(%)			53 (18.8)	
Alcohol, n(%)			160 (56.7)	
Cryptogenic			69 (24.5)	

Figure 1. Kaplan-Meier Analysis of Overall and Time-to-Progression



A. Overall Survival B. Survival without Disease Progression

OP-109

Hepatic Perivascular Epithelioid Cell Tumor (PEComa) Mimicking Hepatocellular Carcinoma

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Aims: Hepatic perivascular epithelioid cell tumors (PEComas) are very rare over the world. Decisions regarding patient diagnosis and management are currently based on a few small case series. The aim of this study was to report the clinicopathological features of PEComa in order to provide guidance for management.

Methods: We report a case of primary hepatic PEComa in a 48-year-old woman.

Results: A 48-year-old woman presented with asymptomatic hepatic mass that unexpectedly detected during the abdominal sonography. The patient underwent a total thyroidectomy for papillary thyroid cancer 11 years ago and was treated with asunaprevir plus daclatasvir for genotype 1b chronic hepatitis 10 years ago. After the treatment of chronic hepatitis C, there was no regular liver test. In an ultrasound performed at a private clinic, a low echogenic mass measuring 2.4 × 1.3 cm was observed in segment 4 (S4) of the liver. On liver CT performed at our hospital, the mass showed enhancement during the arterial phase and slight low attenuation in the delayed phase. On liver MRI, the mass exhibited enhancement in the arterial phase and washout in the delayed phase, making hepatocellular carcinoma (HCC) the most suspected diagnosis. AFP and PIVKA-II levels were within the normal range. The patient wished to proceed with surgical removal without undergoing a biopsy, so surgery was performed. The tumor measured 2.1 × 1.4 cm and was composed of epithelioid cells arranged in a trabecular growth pattern. The mitotic count was less than 1 per 10 high-power fields (HPF). Immunohistochemical staining revealed positivity for SMA, HMB-45, MART-19 (Melan A), and caldesmon, leading to a diagnosis of perivascular epithelioid cell tumor (PEComa). The patient was discharged without complications after surgery and is currently under follow-up observation.

Conclusions: PEComa is a very rare liver tumor, and differentiation is necessary because its radiological findings can resemble those of HCC, especially in cases with specific underlying liver diseases. When surgically removed, most cases show a favorable prognosis, and additional drug therapy is not required.

Keywords: PEComa, HCC, Chronic Hepatitis C

OP-110

Machine Learning-Based Risk Stratification to Optimize Treatment Selection between Surgical Resection and Liver Transplantation

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Aims: Among curative treatments, Liver transplantation (LT) generally offers better long-term outcomes for patients with early-stage hepatocellular carcinoma (HCC) compared to surgical resection (SR), but donor availability is limited, and lifelong immunosuppression is required. This study aims to develop and validate machine learning (ML)-based risk stratification models to enable individualized treatment selection between two treatments and ultimately improve outcomes.

Methods: A total of 4,530 HCC patients were analyzed, including 3,916 from the Korea Central Cancer Registry as the development/internal cohort and 614 from an independent dataset for external validation. Separate ML models were developed to predict three-year overall survival (OS) for each treatment, stratifying patients into low- and high-risk groups. Combinatorial risk stratification was applied to identify LT-favorable and non-favorable groups. Finally, OS was compared between ML-guided and non-ML-guided treatment groups.

Results: The Support Vector Machine demonstrated the highest AUC (0.82) for the LT cohort, while the CatBoost yielded the best AUC (0.79) for the SR cohort. Patients at high LT but low SR risk had better OS with SR (P=0.027), whereas those at low LT but high SR risk benefited more from LT (P=0.0031). No OS difference was observed in patients at low- or high-risk for both treatments. The LT-favorable group, defined as low-risk for LT but high-risk for SR, was characterized by younger age, higher albumin, lower bilirubin/creatinine, higher platelet counts, lower PIVKA-II, better ECOG performance status, and a lower prevalence of diabetes mellitus. ML-guided treatment was associated with improved OS, with 5-year and 10-year survival probabilities of 0.83 and 0.78, compared to 0.63 and 0.56 in discordant cases (P<0.001). These findings were consistent in the independent cohort.

Conclusions: ML-based risk stratification identified patient subgroups with differential survival outcomes following SR or LT, with ML-guided treatment guidance associated with improved OS. These findings suggest that ML-assisted decision-making may enhance personalized treatment selection for early-stage HCC patients.

Keywords: Machine Learning, Hepatocellular Carcinoma, Personalized Treatment Selection

OP-111

Clinical Outcomes of 2,000 Hepatocellular Carcinoma Patients Treated with Proton Beam Therapy at Single Center: Toward Further Optimized Treatment Strategies

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Aims: Hepatocellular carcinoma (HCC) staging and management are guided by the Barcelona Clinic Liver Cancer (BCLC) system; yet its clinical implementation remains challenging. Proton beam therapy (PBT) is increasingly recognized for effective local tumor control in HCC. Since initiating PBT in December 2015, our center has treated over 2,000 patients with HCC. This study aims to evaluate its clinical outcomes as a potential alternative within the BCLC system.

Methods: We reviewed the medical records of HCC patients who underwent PBT from December 2015 to September 2024. For intrahepatic lesions (IH), the treatment techniques, including breath-hold (BH), gating, or encompassing whole amplitudes, were, with the modality administered either passive scattering (PS) or pencil beam scanning (PBS). The primary end points were overall survival (OS) and progression free survival (PFS).

Results: Overall, 1,861 patients (93.0%) underwent treatment for IH, whereas 139 (7.0%) received extrahepatic lesions (EH). Among IH, 1,434 patients (77.1%) received with curative intent, while 427 (22.9%) with palliative intent. The annual treated patients increased from 83 in 2016 to 321 in 2023, showing an upward trend. It aligned with PBT advancements, with gating and PBS emerging as the dominant techniques in recent practice.

The median follow-up duration was 19.7 months (interquartile range, 8.6–39.7). The 3-year OS rates for IH-curative, IH-palliative, and EH were 77.6%, 48.8% and 39.9%, while the 3-year PFS rates were 29.0%, 5.4% and 5.0%, respectively. By BCLC staging (0, A, B, C, D) in IH patients, the 3-year OS rates were 88.5%, 75.4%, 56.2%, 50.0% and not reached (NR), respectively. Similarly, the 3-year PFS rates were 33.1%, 27.7%, 7.7%, 10.9% and NR, respectively.

Conclusions: We demonstrate the efficacy of PBT as a viable alternative in various HCC treatment scenarios, highlighting its potential to address the unmet needs of the BCLC system and serve as a promising therapeutic option.

Keywords: HCC, BCLC, Proton Beam Therapy, Radiotherapy

OP-112

Liver Resection in Stage 0-A HCC in Segments 7/8: A Propensity-Matched Analysis Comparing Open, Laparoscopic, and Robotic Approach

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Aims: Both laparoscopic hepatectomy (LH) and robotic hepatectomy (RH) have been performed for tumors in nearly all liver segments. However, Few studies have compared the outcomes of patients who underwent open hepatectomy (OH), LH and RH for the treatment of Barcelona Clinic Liver Cancer (BCLC) stage 0-A HCC in S7/8.

Methods: The clinical data of patients who underwent S7/8 resection for the treatment of BCLC stage 0-A HCC in the First Affiliated Hospital of Guangxi Medical University from July 2017 to July 2023 were retrospectively collected. To minimize selection bias, propensity score matching (PSM) analysis was performed using demographic and oncology characteristics.

Results: A total of 401 patients met the study criteria, of whom 209 (52.1%) underwent OH, 110 (27.4%) underwent LH, and 82 (20.5%) underwent RH. After PSM, 61 OH (28.6), 74 LH (34.8), and 78 RH (36.6) were included. RH group had the least blood loss among the three groups (OH, 300 vs. LH, 215 vs. RH, 100 mL, P<0.001). Conversion rate was significantly lower in RH group compared to LH group [LH, 10 (13.5%) vs. RH, 1 (1.3%), P=0.003]. Although minimally invasive group (RH+LH) took slightly longer operative time (OH, 233 vs. LH, 255.5 vs. RH, 257 minutes, P=0.068), there was no statistical difference. The minimally invasive group had fewer postoperative hospital stay (OH, 8 vs. LH, 6 vs. RH, 6 days, P<0.001). The minimally invasive group had lower rates of surgical complications (OH, 37.7% vs. LH, 20.3% vs. RH, 11.5%) and reported lower scores on the numeric rating scale (OH, 2 vs. LH, 1 vs. RH, 1, P<0.001). However, there were no statistically significant variations observed in the disease-free survival or overall survival rates among the three groups.

Conclusions: The safety and efficacy of RH for the treatment of BCLC stage 0-A HCC patients in S7/8 was comparable to LH and OH. RH showed advantage over the OH and LH in short-term outcomes, and non-inferiority in survival outcomes.

Keywords: Hepatocellular Carcinoma, Bclc Stage 0-A, Open Hepatectomy, Laparoscopic Hepatectomy, Robotic Hepatectomy

Saturday, May 31, 2025, 09:30-10:30

20. Biliary and Pancreatic Surgery

OP-113

Robotic-Assisted Surgery for Complex Biliary Strictures: A Prospective Study

Nandha Kumar

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Aims: Robotic-assisted surgery offers enhanced precision for managing complex biliary strictures, but its long-term outcomes remain underexplored.

Methods: A prospective study of 75 patients undergoing robotic-assisted biliary reconstruction assessed outcomes, including bile duct patency and complication rates, over two years.

Results: Robotic surgery improved bile duct patency by 90% and reduced complication rates by 25% compared to open surgery.

Conclusions: Robotic-assisted surgery provides superior outcomes for complex biliary strictures, underscoring its value in modern surgical practice.

Keywords: Biliary Strictures, Robotic-Assisted Surgery, Minimally Invasive Surgery

OP-114

Effect of Head Coring with Lateral Pancreaticojejunostomy on Pancreatic Exocrine Function in Patients with Idiopathic Chronic Pancreatitis – A Prospective Observational Study

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Aims: Chronic pancreatitis (CP) is a progressive fibroinflammatory disorder leading to chronic pain, pancreatic insufficiency, and reduced quality of life. Exocrine pancreatic insufficiency (EPI) is a common consequence but remains underdiagnosed. In recent literature, early surgery has been shown to be effective for pain relief, but its impact on pancreatic exocrine function is unclear. This study aimed to evaluate the effect of Frey's procedure on pancreatic exocrine function in CP patients.

Methods: A prospective observational study was conducted from July 2021 to June 2024 in the Department of Surgical Gastroenterology, AIIMS, Patna, India. 70 CP patients who underwent Frey's procedure (head coring and longitudinal pancreaticojejunostomy) were included. Preoperative assess-

ment included fecal elastase-1 (FE-1), Glycated Haemoglobin (HbA1c), Visual Analogue Score (VAS) for pain, and weight. Postoperative follow-ups were conducted at 3 months, with a final evaluation at 6 months. Statistical analyses were performed using SPSS v22, with p-values <0.05 considered significant.

Results: The study included 70 patients, with a mean age of 30.4 years. Frey's procedure resulted in significant pain reduction (median VAS: 8 to 1, P<0.001) and weight gain (48.3 kg to 51.8 kg, P<0.001), suggesting improved nutritional intake. However, pancreatic exocrine function remained unchanged, with median FE-1 levels of 15 µg/g (IQR: 3.17–77.3) preoperatively and 15 µg/g (IQR: 0.44–156) postoperatively (P=0.078). Similarly, HbA1c levels showed no significant difference, with a median of 5.75 (IQR: 4.90–14.4) preoperatively and 5.60 (IQR: 5.20–13.5) postoperatively (P=0.178). Postoperative complications included pancreatic fistula (2.8%) and post-pancreatectomy haemorrhage (2.8%), both managed conservatively. No 30-day mortality was observed.

Conclusions: Frey's procedure effectively relieved pain and improved nutritional status but did not restore pancreatic exocrine or endocrine function. Patients with CP often present late with advanced disease. Earlier surgical intervention may help preserve pancreatic function, warranting further studies with larger populations.

Keywords: Chronic Pancreatitis, Idiopathic Chronic Pancreatitis, Lateral Pancreaticojejunostomy, Exocrine Pancreatic Insufficiency

OP-115

Terminal Complement Cascade Contributes to the Pathogenesis of Severe Acute Pancreatitis by Intracellular Calcium Overload Induced Pyroptosis

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Aims: Acute pancreatitis (AP) is a prevalent acute abdominal emergencies in the gastrointestinal system, with severe acute pancreatitis (SAP) carrying a mortality rate approximating 30%. Complement activation has been identified as a critical mediator of the systemic inflammatory response and multiorgan dysfunction characteristic of SAP. Nevertheless, the pathophysiological mechanisms underlying terminal complement cascade (TCC)-mediated injury, along with its precise contribution to disease progression, remain incompletely characterized.

Methods: Pancreatic tissues obtained from patients with AP and a sodium taurocholate (NaTC)-induced SAP mouse model were employed to assess the activation status of the complement system. Complement component 6 knockout ($C6^{-/-}$) mice, which block the TCC and the formation of the membrane attack complex (MAC), along with their wild-type littermates, were subjected to the NaTC-induced SAP model. The islet β-cell line MIN6, the complement regulatory protein CD59, and the calcium antagonist ethylenediaminetetraacetic acid (EDTA) was utilized to elucidate the potential mechanisms underlying MAC-mediated pyroptosis.

Results: During the progression of SAP progression, activation of the TCC was observed. In the NaTC group, MAC levels exhibited a progressive increase over time, demonstrating a positive correlation with pancreatic necrotic areas. Genetic ablation of C6 in the NaTC-induced SAP model demonstrated that C6 deficiency mitigated multiorgan histopathological injury and improved 72-hour postoperative survival. Compared with wild-type mice, $C6^{-/-}$ mice demonstrated markedly downregulated expression levels of pyroptosis-related genes (NLRP3, IL-1β, Pro-IL-18, IL-18) and proteins (NLRP3, ASC, c-GSDMD, c-Caspase 1) in pancreatic tissues. Mechanistically, NaTC triggered MAC deposition in a concentration- and time- dependent manner, with more MAC deposition linked to lower cell viability. MAC deposition rapidly induced intracellular calcium influx, peaking within 5 minutes, which orchestrated pyroptotic cell death—a cascade abrogated by CD59-mediated complement inhibition or EDTA-mediated calcium chelation.

Conclusions: These findings collectively demonstrate that the TCC mediates the pathophysiological progression of severe acute pancreatitis by orchestrating calcium flux-driven pyroptotic cell death. Pharmacological modulation of the TCC, through targeted inhibition of MAC assembly or calcium dysregulation, emerges as a novel therapeutic paradigm with translational relevance for SAP.

Keywords: Severe Acute Pancreatitis, Complement, Complement Terminal Cascade, Complement Regulation, Pyroptosis

OP-116

Immediate Results of Laparoscopic Spleen-Preserving Distal Pancreatectomy: Kimura vs. Warshaw Operation

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Aims: Laparoscopic distal spleen-preserving pancreatectomy is the standard of care for benign tumors of the body and tail of the pancreas. There are currently two methods: the Kimura-type, when the splenic vessels are preserved, and the Warshaw-type, when the splenic artery and veins are resected with preservation of short gastric vessels. There is no consensus on which method of preserving the spleen is optimal; most often, the choice of method is made empirically, based on the experience of the operating surgeon and the anatomy of the patient's splenic vessels, their relationship with the tumor.

Methods: The retrospective analysis included 60 patients who underwent distal pancreatectomy from February 2020 to February 2024. All patients were divided into 2 groups: 1 - Kimura-type (n = 34); 2 - Warshaw-type (n = 26).

Results: There were no statistically significant differences in the baseline clinical characteristics of patients between the groups. A statistically significant difference in tumor size was found: larger tumors were more common in the WT group than in the KT group (2.85 cm vs. 4.7 cm, P=0.026). There were no statistically significant differences in the histological structure of the tumor between the groups. The average duration of surgery in the WT group was 197.27 ± 42.09 min (95% CI 184.36 – 240.64) compared to the KT group (269.06 ± 70.95 (95% CI 227.74 – 319.95)), P=0.006. No statistically significant differences were found between the groups in the analysis of blood loss, length of hospital stay, frequency of laparotomy, splenectomy, and reoperation. When assessing the incidence of POPF depending on the type of surgery, it was not possible to establish statistically significant differences (P=0.474). In the CT group, 1 (5.9%) bleeding from the splenic artery was observed on the 7th day of the postoperative period (splenectomy). No statistically significant differences in the incidence of postoperative complications Clavien-Dindo> III, mortality between the groups were found.

Conclusions: Both the Warshaw and Kimura techniques are safe and effective surgical approaches that provide similar results. The Warshaw method may be more advantageous in terms of the use of limited surgical resources without compromising the immediate surgical results of treatment.

Keywords: Distal Pancreatectomy, Benign Pancreatic Neoplasia, Laparoscopic Surgery,

OP-117

Preoperative UGI Scopy: Reducing Post-Cholecystectomy Syndrome and Pain Severity

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Aims: Post-cholecystectomy syndrome (PCS) is a frequent complication following gallbladder removal, often due to unrecognized pre-existing gastrointestinal conditions. Differentiating between symptoms caused by gallstone disease and other upper GI disorders is essential for reducing PCS incidence. This study evaluates the role of preoperative upper gastrointestinal (UGI) endoscopy (UGI scopy) in minimizing PCS occurrence, incorporating pain severity assessment using a Likert Scale.

Methods: A prospective study was conducted on 40 patients diagnosed with symptomatic cholelithiasis. Participants were divided into:

Group A (Test Group, n=20): Underwent UGI scopy before surgery.

Group B (Control Group, n=20): Direct surgery without UGI scopy.

Patients were followed postoperatively for three weeks, and symptoms were evaluated using Likert Scale scores and symptom prevalence.

Results: Endoscopic Findings (Group A): Gastritis (50%), gastric erosions (40%), lax LES & esophagitis (30%), and H. pylori (20%).

Group A (Test Group): Lower incidence of PCS symptoms.

Group B (Control Group): Higher prevalence of regurgitation, biliary colic, and persistent pain.

Likert Scale Pain Scores:

Group A (UGI Scopy): 70% of patients reported pain scores ≤1 (mild), with only 10% experiencing scores ≥3 (severe).

Group B (No UGI Scopy): 55% had scores ≥3 (severe/very severe), indicating higher PCS symptom burden.

Conclusions: Preoperative UGI scopy significantly reduces PCS incidence by detecting and treating coexisting upper GI conditions before cholecystectomy. Pain severity was lower in patients undergoing UGI scopy, reinforcing its role in improving post-surgical outcomes. A Likert Scale-based symptom assessment enhances the accuracy of PCS evaluation. Routine preoperative UGI scopy is recommended to minimize postoperative complications and optimize patient recovery.

Keywords: UGI Scopy, Post-Cholecystectomy Syndrome

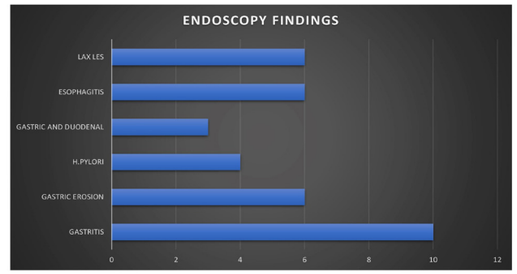

Figure 1.

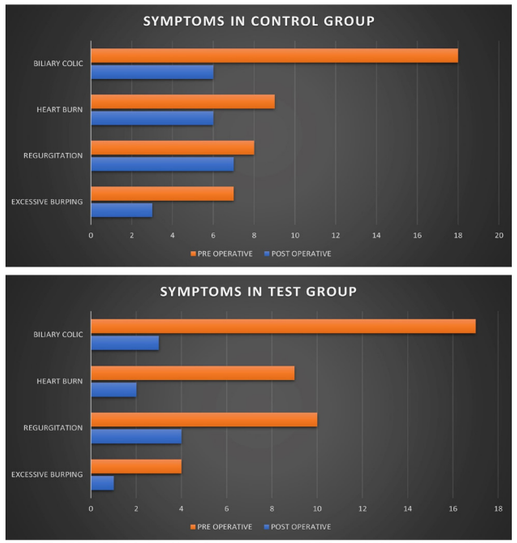

Figure 2.

study group and 44 in the placebo group. SIRS scores declined in both groups over time, but the difference between groups remained statistically insignificant (p-values: 0.42 at admission, 0.64 at 24 hours, 0.59 at 48 hours, 0.31 at 72 hours). CRP levels decreased in the intervention group (56.8% to 40.9%), but the difference between groups was not significant (*P*=0.285). No significant differences were observed in hospital stay, ICU stay, organ failure, or mortality between groups.

Conclusions: Although rectal indomethacin reduced the SIRS score in patients with acute pancreatitis, the difference compared to placebo was not statistically significant in preventing the progression of mild and moderate acute pancreatitis to severe acute pancreatitis.

Keywords: Rectal Indomethacin, Acute Pancreatitis, Severity of Pancreatitis

OP-118

Comparison of Rectal Indomethacin with Placebo in Reducing the Clinical Progression of Mild and Moderate Acute Pancreatitis to Severe Acute Pancreatitis- A Double Blinded Randomized Controlled Trial

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Aims: Nonsteroidal anti-inflammatory drugs (NSAIDs) have been tested for acute pancreatitis treatment. Rectal NSAIDs manage pain and inflammation while avoiding gastrointestinal side effects. Despite promising results, their use remains limited. Currently, rectal NSAIDs are mainly used prophylactically for post-ERCP pancreatitis (PEP). This study evaluates the efficacy of rectal indomethacin in reducing acute pancreatitis severity.

Methods: This single-center, double-blinded, randomized controlled trial involved two groups: Rectal Indomethacin and Placebo. The Indomethacin group received a loading dose of two 50mg suppositories, followed by 50mg every 8 hours for 48 hours (up to 6 doses). The Placebo group received glycerin suppositories at the same intervals. Outcomes measured included changes in SIRS score, CRP levels, BUN levels, organ failure, pancreatitis severity, ICU and hospital length of stay, and 30-day mortality for both groups.

Results: A total of 88 patients were included, with 44 in the

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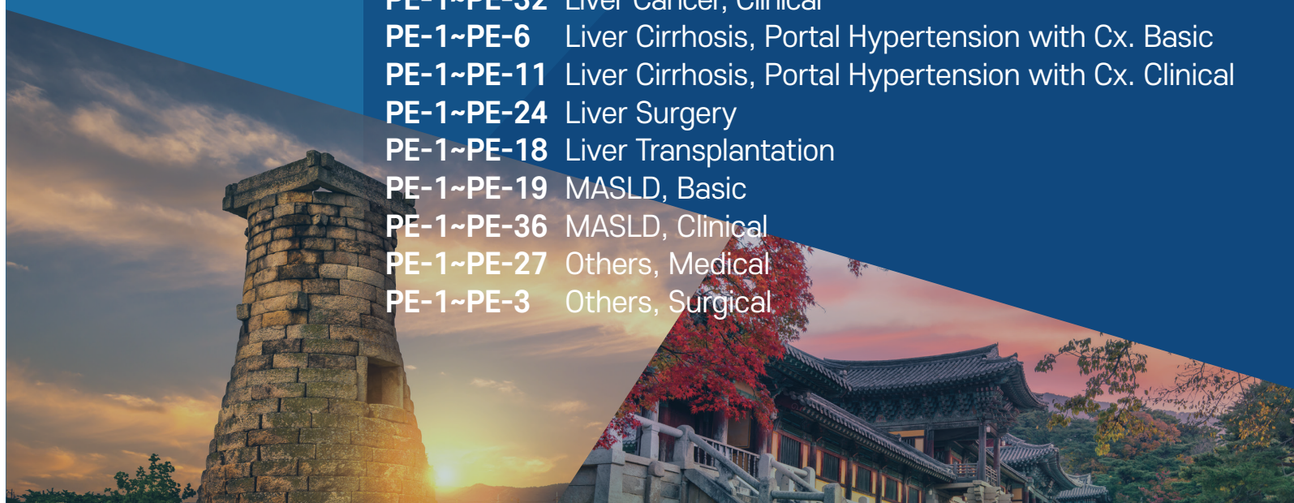
PE-1~PE-11 Acute Liver Failure and Drug-Induced Liver Injury
PE-1~PE-8 Alcohol-Related Liver Disease, Basic
PE-1~PE-3 Alcohol-Related Liver Disease, Clinical
PE-1~PE-4 Autoimmune Liver Disease
PE-1~PE-32 Biliary and Pancreatic Surgery
PE-1~PE-5 HBV, Basic
PE-1~PE-13 HBV, Clinical
PE-1~PE-6 HCV, Basic
PE-1~PE-8 HCV, Clinical
PE-1~PE-10 Liver Cancer, Basic
PE-1~PE-32 Liver Cancer, Clinical
PE-1~PE-6 Liver Cirrhosis, Portal Hypertension with Cx. Basic
PE-1~PE-11 Liver Cirrhosis, Portal Hypertension with Cx. Clinical
PE-1~PE-24 Liver Surgery
PE-1~PE-18 Liver Transplantation
PE-1~PE-19 MASLD, Basic
PE-1~PE-36 MASLD, Clinical
PE-1~PE-27 Others, Medical
PE-1~PE-3 Others, Surgical



1. Acute Liver Failure and Drug-Induced Liver Injury

PE-1

Risk Factors Leading to Acute Liver Failure in Cirrhosis Patients Treated at Thai Nguyen Central Hospital and Control Results

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Aims: Acute liver failure (ALF) in patients with underlying cirrhosis, also known as acute-on-chronic liver failure (ACLF), is a severe condition associated with high morbidity and mortality. Various risk factors, including infections, gastrointestinal bleeding, and drug-induced liver injury, contribute to disease progression. Early identification of these risk factors and appropriate interventions are crucial for improving patient outcomes.

Aim: To identify risk factors leading to acute liver failure in cirrhotic patients treated at Thai Nguyen Central Hospital and to evaluate treatment outcomes.

Methods: A descriptive, prospective study was conducted on cirrhotic patients who developed acute liver failure and were treated at Thai Nguyen Central Hospital from January 2023 to October 2024. Clinical features, laboratory parameters, and potential risk factors were analyzed. Treatment effectiveness was assessed based on clinical improvement, liver function recovery, and survival outcomes.

Results: The mean age of the study subjects was 49 ± 18.5. The youngest patient was 47, the oldest was 68, and there were more males than females.

The main cause of acute liver failure is acute poisoning, accounting for 83.36%, of which mainly poisoning with traditional medicine. Jaundice was a clinical symptom present in most patients (92.8%).

The rate of death/return accounted for 47.56%. Hepatic brain level, SOFA, NH3 have a strong positive correlation with the risk of death of patients with acute liver failure. Some factors have a role in the prognosis of overall mortality in patients with acute liver failure including SOFA > 8 points, mechanical ventilation, NH3 >70 U/l, lactate > 3 mmol/l, INR > 2. There was clinical improvement and some liver function tests after treatment.

Conclusions: Research results have certain contributions in clinical practice, contributing to the prognosis and treatment of patients with acute liver failure.

Keywords: Acute Liver Failure, Treatment, Cirrhosis, Risk Factors

PE-2

Hepatotoxicity of Statins: A Real-World Study Based on the US Food and Drug Administration Adverse Event Reporting System Database

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Aims: Statins, as an important class of lipid-lowering drugs, play a key role in the prevention and treatment of cardiovascular diseases. However, with their widespread use in clinical practice, some adverse events have gradually emerged. In particular, the hepatotoxicity associated with statins use has become one of the clinical concerns that require sufficient attention.

Methods: In this study, we conducted a comprehensive and detailed analysis of the hepatotoxicity of statins based on the data of the US Food and Drug Administration Adverse Event Reporting System database from the first quarter (Q1) of 2004 to the Q1 of 2024 and used Reporting Odds Ratios and Empirical Bayes Geometric Mean to mine the signal of adverse events.

Results: In this study, hepatic disorder related seven statins all exhibited positive signals. Through signal mining, we identified a total of 14511 cases of adverse events associated with hepatic disorder caused by these statin drugs, with atorvastatin, simvastatin, and rosuvastatin occurring at a higher rate. A total of 148 positive signals related to adverse events of hepatic disorder were captured. Autoimmune hepatitis and drug-induced liver injury both presented positive signals across multiple statin drugs. Notably, atorvastatin had the most significant signal strength in cholestatic pruritus and bilirubin conjugation abnormal. Fluvastatin also showed notable signal strength in autoimmune hepatitis, while simvastatin had a relatively weaker signal strength for hepatic enzyme increased.

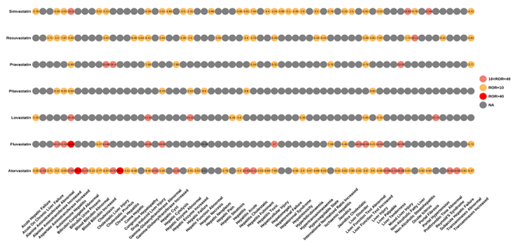

Figure 1. Signal heatmap of seven statins-related hepatic disorder adverse events calculated by ROR.

Conclusions: This study discovered specific adverse event signal values, revealing potential hepatotoxic risks associated with the use of statin drugs. The results provide an important reference for the safe clinical use of drugs, help to improve the understanding of the safety of statins, and also provide a scientific basis for clinicians to make more accurate and safe decisions when making treatment plans.

Keywords: Statins, Faers, Hepatotoxicity, Adverse Event

PE-3

Prevalence and Prognostic Significance of Cachexia Diagnosed by Novel Definition for Asian Population among Chinese Cirrhotic Patients

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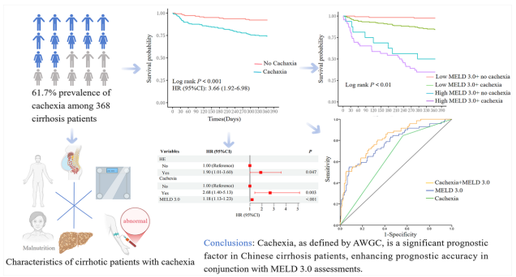
Aims: Cachexia is a multifaceted metabolic disorder often linked to chronic illnesses, characterized by substantial weight reduction, inflammatory states, and loss of appetite. The novel diagnostic criteria concerning cachexia established by the Asian Working Group for Cachexia (AWGC) have not been fully validated in Chinese populations with cirrhosis. To assess the prognostic impact of AWGC-defined cachexia among hospitalized cirrhotic patients and explore the synergistic impact of Model for End-Stage Liver Disease 3.0 (MELD 3.0) scores with cachexia status on prognosis.

Methods: We retrospectively analyzed clinical data from patients with decompensated cirrhosis admitted to our tertiary hospital between January 2021 and December 2023. Cachexia was identified according to AWGC criteria, and disease severity was assessed using MELD 3.0 scores. The study's primary outcome was all-cause mortality within one year.

Results: A total of 368 patients were included in the analyses. The prevalence of cachexia was 61.7%, and patients with cachexia had a significantly higher one-year all-cause mortality rate (26.4% vs. 7.8%, $P<0.001$). Multivariate Cox regression analysis showed that cachexia (HR 2.68, 95%CI 1.40-5.13, $P=0.003$), along with MELD 3.0 (HR 1.18, 95%CI 1.13-1.23, $P<0.001$), were independent predictors of one-year mortality. The combined assessment of cachexia and MELD 3.0 scores yielded a higher discriminative ability for predicting one-year mortality compared to either metric alone.



Conclusions: AWGC-defined cachexia is a significant prognostic factor in hospitalized patients with cirrhosis. The integration of cachexia with MELD 3.0 scoring enhances prognostic prediction, underscoring the importance to introduce cachexia evaluation during clinical practice for this vulnerable setting.

Keywords: Cachexia, Asian Working Group for Cachexia, MELD 3.0, Cirrhosis

PE-4

Characteristics of the Patient with Drug-Induced Liver Injury at the Gastroenterology and Hepatology Center, Bach Mai Hospital, Vietnam

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Aims: To describe the clinical and paraclinical characteristics and causes of drug-induced liver injury at the Gastroenterology and Hepatology Center, Bach Mai Hospital.

Methods: A cross-sectional description of 54 patients with drug-induced liver injury treated from August 2022 to July 2023. Patients were diagnosed with drug-induced hepatitis according to the updated RUCAM scale.

Results: The mean age was 56.74 ± 12.74 years old, 56% of patients were female. The average time of onset was 22.19 ± 17.12 days. Common clinical symptoms included fatigue (85.2%) and jaundice (75.9%), subcutaneous hemorrhage (14.8%), and only 7.4% of cases had hepatic encephalopathy. Regarding laboratory tests, the AST, ALT, and total bilirubin indexes were 652 ± 746 U/L, 845 ± 891 U/L, and 197.5 ± 140.7 µmol/l, respectively. Regarding coagulation function, PT time below 70% was found in 31.5%, and INR index ≥ 1.5 was found in 18.5%. Regarding lesion morphology, the necrosis/ biliary obstruction/ mixed lesions rates were 66.6/ 16.7/ 16.7 (%), respectively. In terms of severity, the rates of mild/moderate/severe/acute liver failure/critical disease were 16.7/5.5/61.1/14.8/1.9 (%). The most common cause of liver damage was herbal medicine at 50.0%, followed by Western medicine at 44.4%, and only 5.6% was due to functional foods. The leading Western medicines included slow-acting anti-inflammatory drugs or immunosuppressants (Azathioprine, Cyclosporine, Methotrexate, Hydroxychloroquine), Paracetamol, anti-tuberculosis drugs (4-drug combination regimen), and treatment of lipid disorders (Atorvastatin, Benzafibrate, Fenofibrate).

Conclusions: Drug-induced liver injury has a similar clinical picture to other causes of hepatitis but is often severe, acute liver failure. The leading cause is herbs, followed by long-acting anti-inflammatory drugs, immunosuppressants, and paracetamol.

Keywords: DILI

PE-5

Oxidative Catastrophe: The Ferroptotic Paradigm in Hepatic Necroinflammation

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Aims: Acute liver failure (ALF) is a critical condition characterized by the rapid decline of liver function, often associated with oxidative stress, glutathione depletion, and mitochondrial dysfunction. Recent studies suggest that ferroptosis—an iron-dependent, regulated form of cell death driven by lipid peroxidation—plays a pivotal role in ALF pathogenesis. This research aims to synthesize data from experimental studies to evaluate the role of ferroptosis in ALF, identify key mechanisms, and explore potential therapeutic targets.

Methods: A systematic review and meta-analysis were conducted following PRISMA guidelines. Studies published between 2010 and 2024 were sourced from databases such as PubMed, Scopus, and Web of Science. Inclusion criteria encompassed experimental models of ALF induced by acetaminophen (APAP), lipopolysaccharide (LPS), and D-galactosamine (D-GalN). Studies employing genetic modifications (e.g., knockout models), pharmacological interventions (e.g., ferroptosis inhibitors), and assays assessing oxidative stress, mitochondrial function, and cell death pathways were included. Data on reactive oxygen species (ROS) production, glutathione (GSH) levels, glutathione peroxidase 4 (GPX4) activity, and mitochondrial dysfunction were extracted and analyzed.

Results: Analysis of 20 studies revealed a significant association between ferroptosis and hepatocyte death in ALF models. Key findings include:

Oxidative Stress and Lipid Peroxidation: All included studies reported elevated ROS production and lipid peroxidation in ALF models, correlating with increased markers of ferroptotic cell death.

Glutathione Depletion and GPX4 Inhibition: Meta-analysis showed a consistent decrease in GSH levels and GPX4 activity across ALF models, impairing lipid peroxide detoxification and facilitating ferroptosis ($P<0.001$).

Mitochondrial Dysfunction: Significant mitochondrial abnormalities were identified, including voltage-dependent anion channel 1 (VDAC1) oligomerization and disruptions in lipid metabolism. These mitochondrial changes were linked to enhanced susceptibility to ferroptosis.

Regulatory Pathways: Alterations in the nuclear factor erythroid 2-related factor 2 (Nrf2), heme oxygenase-1 (HO-1), and high mobility group box 1 (HMGB1) pathways were frequently observed, suggesting their role in modulating ferroptosis during ALF.

Therapeutic Interventions: The use of ferroptosis inhibitors, such as ferrostatin-1 and deferoxamine, significantly mitigated liver damage and reduced markers of ferroptosis in experimental ALF models ($P<0.01$).

Conclusions: This systematic review confirms that ferroptosis is a central mechanism driving acute liver failure, primarily through oxidative stress, lipid peroxidation, and mitochondrial dysfunction. Therapeutic strategies targeting ferroptosis, including antioxidant modulation, lipid peroxidation inhibition, and mitochondrial stabilization, hold promise for ALF treatment. Further clinical research is necessary to validate these findings and translate them into effective therapies for ALF management.

Keywords: Reactive Oxygen Species, Acetaminophen, Ferroptosis, Glutathione Depletion

PE-6

Adeno Associated Virus Vector Gene Therapy Related Acute Liver Failure-Challenges Faced by Pediatric Hepatologist

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Aims: Adeno associated virus vector therapy (zolgensma) is associated with Acute Liver Failure. We describe post zolgensma associated acute liver failure mortality. This is the third such reported case.

Methods: Descriptive case report

Results: A male diagnosed with spinal muscular atrophy (SMA) type 1 received zolgesma at 21 months of age, weight 10 kg. He was started on prednisolone at 1 mg/kg from day 1 of receiving the therapy. AST/ALT were serially monitored and 35 days post therapy AST/ALT increased to 1127/966 (IU/L). Other causes of hepatitis were ruled out and prednisolone dose was hiked to 2 mg/kg. Increasing trend of AST/ALT (2287/1398) continued with increase in INR to 1.96, thus, inj methyl prednisolone was started at 10 mg/kg. Following this AST/ALT showed improvement, however INR and ammonia continued to worsen (Table 1). Bilirubin remained static and liver span was reducing. In view of increasing INR and development of HE I, he was started on Tacrolimus and MPS dose was hiked to 30 mg/kg. His INR continued to worsen and subsequently became unrecordably high with PT > 320 seconds along with development of ascites and pleural effusion. Sirolimus was then initiated, following which INR improved to 4.18. However, post day 3 of sirolimus, he developed hypertensive encephalopathy and had to be intubated. Doppler showed left renal artery thrombosis and right renal artery partial thrombosis. Cause of arterial thrombosis was attributed to sirolimus, levels of which were found to be 23 ug/l. His CYP3A4/3A5 polymorphism showed that he was a slow metabolizer of sirolimus. Following stoppage of sirolimus and reduction of steroid, INR and bilirubin again showed a increasing trend, for which 3 sessions of standard volume plasma exchange was done. His liver functions gradually stabilized; however he developed ventilator associated pneumonia, lower limb arterial thrombosis with gangrene requiring thrombectomy and ultimately expired due to sepsis with shock, 59 days after receiving zolgensma. Post mortem liver biopsy showed regenerative changes with ductular proliferation and pseudoglandular rosettes, with absence of massive hepatic necrosis, suggestive that the liver had recovered.

Conclusions: The challenges in managing hepotoxicity due to adeno associated viral vector gene therapy stem from lack of good quality evidence on the appropriate protocols for immunosuppression. High dose immnuosuppression in acute liver failure is fraught with complications. There is an urgent need for further research.

Keywords: Adeno Associated Virus Vector, Liver Failure, Mortality, Immunosuppression

Table 1- serial trends of lab values post zolgesma therapy

Date	T/Dbil (mg/dl)	AST	ALT	TPrt/Alb	INR	Hb (g/dl)	TLC (/mm3)	Ammonia (umol/L)	Prednisolone	Tac	comments
2 April 2024		32	19						10 mg		Zolgesma given
16/4/2024		142	106						10 mg		
30/4/2024		692	664		1.27				10mg		
7/5/2024		**1127**	**966**						**20mg**		
11/5/2024	4.6/3.1	2287	1398	6.1/3.3	1.96	8.6	20.17		MPS-100mg		
14/5/2024	**4.5/3.6**	**1229**	**1050**	**4.9/2.48 (IV albumin)**	**2.68**				**MPS-300mg**	**0.5 mg BD**	
16/5/2024 (Morning)	5.05/4.2	459	718	4.9/2.86 (IV albumin)	3.11	7.8	10.9	110	MPS-300mg	0.5 mg BD	
17/5/2024	5.53/4.82	333	591	4.9/2.9 (IV albumin)	3.81			86	MPS-300mg	0.5 mg BD (Tac level-10.30 ng/ml)	
19/5/2024					**PT>320 sec**				MPS 200 mg	0.5 mg	Sirolimus 1 mg OD
22/5/2024					**3.68**				MPS 200 mg	0.5 mg	Developed Hypertensive encephalopathy requiring intubation
22/5/2024-25/5/2024									Stress dose hydrocortisone	0.5 mg,	Underwent 3 sessions of standard volume plasmaexchange, sirolimus stopped
1/06/2024	2.64/1.69	70	54	3.25	**1.98**	6.1	5.9	48	Steroids stopped	0.5 mg	Underwent left femoral artery thrombectomy due to left lower limb ischemia
14/6/2024	2.37/1.49	33	32	2.87	**2.56**	8.1	19.00	20			Sepsis with shock with DIC

PE-7

Toxic Hepatitis and Dilated Cardiomyopathy Induced by Creosote Oil Toxicity: A Rare Case Report

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Aims: We aim to highlight the severe systemic effects of prolonged creosote oil exposure, particularly its impact on the liver and cardiovascular system, by documenting a rare case of toxic hepatitis and dilated cardiomyopathy. Additionally, it emphasizes the importance of early detection, occupational safety measures, and preventive strategies for individuals at risk.

Methods: A 28-year-old male patient was admitted with severe systemic symptoms after prolonged exposure to creosote-treated wood while constructing a house. Clinical evaluation included liver function tests, echocardiography, computed tomography (CT) imaging, and hemodynamic assessment. The patient's biochemical parameters, cardiac function, and disease progression were monitored throughout hospitalization.

Results: The patient exhibited significantly elevated liver enzymes (AST: 1,116 IU/L, ALT: 7,995 IU/L), gamma-glutamyl transpeptidase (234 IU/L), lactate dehydrogenase (3,684 IU/L), and total bilirubin (2.41 mg/dL). CT imaging confirmed acute hepatitis with mild hepatomegaly. Echocardiography revealed dilated cardiomyopathy, with an ejection fraction of 18.8%, left atrial dilation (4 cm), and left ventricular dilation (5.8 cm). All four cardiac chambers were enlarged, with severe left ventricular systolic dysfunction, hypertension, and akinesia in the interventricular septum, anterior, and lateral walls. The patient required intensive medical care, and despite treatment, his condition deteriorated before stabilizing over a prolonged recovery period.

Conclusions: Prolonged creosote oil exposure can result in severe systemic toxicity, including toxic hepatitis and dilated cardiomyopathy. This case underscores the need for strict occupational safety regulations, early detection strategies, and preventive measures for individuals at environmental or occupational risk. Increased awareness and medical surveillance are crucial in mitigating the toxic effects of creosote exposure.

Keywords: Creosote Oil, Toxic Hepatitis, Dilated Cardiomyopathy, Environmental Toxicity

PE-8

Liver Injury Induced by Stannous Oxide Nanoparticles (SnO 2 NPs) by COX-2 and αSMA Modulation in the Liver of Wistar Rats

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Aims: Tin oxide has a wide usage for disparate purposes due to which it has been brought into contact with the environment as well as to the population to an increasing extent.Studies on nano-particles specially research on metal nano-particles, particularly SnO_2NPs, has garnered significant attention due to their unique physicochemical properties, such as a large surface area to volume ratio. However, alongside their benefits; concerns have arisen regarding their potential health hazards, particularly their tendency to accumulate and persist in biological tissues like the brain and testes. However there is a dearth of studies on its pathological effects on liver in Wistar rats. The main objective of this study is to explore the effectof stannous oxide nano-particles in the induction of liver injury in male rats.

Methods: The authors have devised SnO_2NPs induced injury in rats and explored it's restitution by pomegranate juice application. Hepatic damage in rats was induced by SnO_2NPs at a dose of 1ml/kgb.wt after exposure of 21days. The activities of liver function indices, LPO, SOD, CAT etc were analyzed. Histopathological evaluation and ultrastructural assessment was also performed.

Results: Results obtained from immunohistochemical staining of α-SMA and COX-2 and histopathological stainings by Picrosirius red, Masson's trichrome, Hematoxylin and eosin gave a clear demonstration of the refurbishment of induced injury by pomegranate juice.

Conclusions: Stannous oxide nano-particles induced acute liver injury at a dose of COX-2 and α-SMA were the key players in the underlying mechanism

Keywords: Liver Injury, Tin Oxide Nanoparticles, Induced Liver Injury

PE-9

Exploration of Hepatoprotective Plants in Indonesia as Green Future Drug Candidates: A Network Pharmacology Approach

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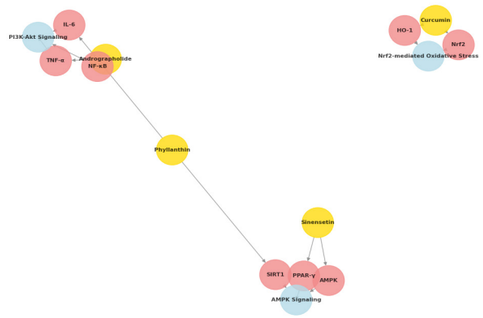
Aims: Liver diseases, including non-alcoholic fatty liver disease (NAFLD), hepatitis, cirrhosis, and hepatocellular carcinoma, remain a major global health problem. Conventional hepatoprotective drugs often have limitations such as side effects, high cost, and reduced efficacy in multifactorial liver disorders. Indonesia, as one of the most biodiverse regions in the world, has many medicinal plants with potential as hepatoprotectors. However, the multi-component and multi-target properties of these herbal compounds remain largely unexplored. Network pharmacology, an integrative approach in drug discovery, facilitates systematic analysis of compound-target interactions and biological pathways. This study aimed to identify promising Indonesian plant-derived hepatoprotective agents that are aligned with green pharmaceutical principles, which emphasize sustainability and minimal environmental impact.

Methods: Bioactive compounds were retrieved from TCMSP, PubChem, and SwissADME, selecting compounds that had similarities to drugs based on Lipinski's Rule of Five. Potential target proteins were predicted using SwissTargetPrediction, STITCH, and STRING databases, and compound target pathway (C-T-P) networks were constructed using Cytoscape. KEGG pathway enrichment analysis was performed to identify the major molecular pathways involved in hepatoprotection.

Results: Four hepatoprotective plants; Curcuma longa (turmeric), Andrographis paniculata (sambiloto), Phyllanthus niruri (meniran), and Orthosiphon aristatus (cat whisker) were identified as promising plants as hepatoprotectors. Tissue pharmacology analysis revealed 32 bioactive compounds interacting with 48 potential target proteins, with curcumin, andrographolid, phyllanthin, and sinensetin emerging as the major hepatoprotective agents. STRING analysis showed strong interactions between these compounds and proteins involved in the regulation of oxidative stress (Nrf2, HO-1), inflammation (NF-κB, TNF-α, IL-6), and lipid metabolism (PPAR-γ, AMPK, SIRT1). KEGG enrichment analysis identified significant involvement in Nrf2-mediated oxidative stress response (P<0.001), PI3K-Akt signaling (P<0.005), and AMPK signaling (P<0.01), confirming its role in hepatoprotection. Molecular docking results showed strong binding interactions, with curcumin showing a binding affinity of -8.5 kcal/mol with Nrf2, and andrografolid showing a binding affinity of -9.2 kcal/mol with NF-κB, indicating their potential for direct modulation of these pathways.



Conclusions: There are 4 plant species that can be used as medicinal drug candidates. The identified bioactive compounds showed significant interactions with key liver-related proteins, supporting their use as multi-target hepatoprotective agents.

Keywords: Hepatoprotective, Green Future Drug, Pharmacology

PE-10

Artificial Liver Support Systems in Acute Liver Failure: A Systematic Review of Efficacy and Limitations

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Aims: Acute liver failure (ALF) is a life-threatening condition characterized by rapid deterioration of liver function, often resulting in multi-organ failure and high mortality rates. Artificial liver support systems (ALSS), including molecular adsorbent recirculating systems (MARS), fractionated plasma separation and adsorption (Prometheus), and single-pass albumin dialysis (SPAD), have been developed as bridging therapies to liver transplantation or recovery. This systematic review aims to evaluate the efficacy and limitations of current ALSS in improving survival and clinical outcomes in ALF patients.

Methods: A systematic search of PubMed, Web of Science, and Scopus databases was conducted according to PRISMA guidelines, covering studies published until January 2025. Inclusion criteria were randomized controlled trials, prospective cohort studies, and meta-analyses evaluating the use of ALSS in ALF patients. Primary outcomes assessed included overall survival, transplant-free survival, and biochemical improvements (bilirubin, ammonia, and INR levels). Secondary outcomes included complications and adverse events. The Cochrane Risk of Bias tool and Newcastle-Ottawa Scale were used for quality assessment.

Results: Twenty-seven studies involving 2,148 patients were included in the analysis. ALSS demonstrated significant reductions in serum bilirubin (mean difference -5.2 mg/dL), ammonia levels, and improvement in hepatic encephalopathy grades in most studies. MARS was the most commonly used system and was associated with improved biochemical parameters and hepatic encephalopathy, but no consistent benefit on overall or transplant-free survival. Prometheus showed similar biochemical improvements but higher rates of hypotension. Common limitations of ALSS included cost, resource intensity, limited accessibility, and variable survival benefit. The need for liver transplantation remained unchanged in the majority of studies, emphasizing that ALSS should be considered a bridging therapy rather than a definitive treatment.

Conclusions: Artificial liver support systems offer significant short-term clinical benefits in patients with acute liver failure, particularly in improving biochemical markers and hepatic encephalopathy. However, their impact on long-term survival remains limited. Further large-scale, randomized trials are required to define the optimal patient selection, timing, and combination strategies to maximize outcomes.

Keywords: Acute Liver Failure, Artificial Liver Support, MARS, Liver Transplantation

PE-11

Biomarkers for Early Diagnosis and Prognosis of Drug-Induced Liver Injury: A Systematic Review

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Aims: Drug-induced liver injury (DILI) remains a significant clinical challenge due to its unpredictable nature, delayed diagnosis, and potential for acute liver failure. Conventional liver function tests lack sensitivity and specificity for early detection and prognosis. Emerging biomarkers offer promise in improving DILI diagnosis, risk stratification, and predicting outcomes. This systematic review aims to critically evaluate the current landscape of biomarkers for the early diagnosis and prognosis of DILI, focusing on their clinical applicability and limitations.

Methods: Following PRISMA guidelines, a systematic literature search was conducted in PubMed, Web of Science, and Scopus databases up to January 2025. Eligible studies included randomized controlled trials, cohort studies, and case-control studies assessing serum, genetic, proteomic, and metabolomic biomarkers for DILI in human populations. Outcomes included diagnostic accuracy (sensitivity, specificity), prognostic value, and utility in clinical decision-making. The quality of the studies was assessed using the Newcastle-Ottawa Scale and the QUADAS-2 tool for diagnostic studies.

Results: From 823 articles screened, 47 studies met the inclusion criteria. Prominent biomarkers identified included microRNA-122 (miR-122), high mobility group box-1 (HMGB1), glutamate dehydrogenase (GLDH), and keratin-18 (K18). miR-122 and GLDH consistently demonstrated superior sensitivity (82–94%) and specificity (80–90%) for early DILI detection compared to traditional aminotransferase tests. HMGB1 and K18 provided valuable prognostic information, particularly in differentiating necrosis from apoptosis and predicting progression to acute liver failure. Genetic markers such as HLA alleles (e.g., HLA-B*57:01) were strongly associated with idiosyncratic DILI risk. Despite these promising findings, heterogeneity in study design and biomarker cut-off thresholds limits generalizability and clinical integration.

Conclusions: Emerging biomarkers enhance the early diagnosis and prognostication of drug-induced liver injury. miR-122, HMGB1, and GLDH are among the most promising candidates for clinical use. Future multicenter validation studies and standardized protocols are necessary to confirm their utility and facilitate widespread adoption in clinical practice.

Keywords: Drug-Induced Liver Injury, Biomarkers, Early Diagnosis, Prognosis

2. Alcohol-Related Liver Disease, Basic

PE-1

Complement Deficiency and Inflammatory Markers in Acute Pancreatitis: A Comparative Analysis of Alcoholic vs. Non-Alcoholic Types

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Aims: Study changes in the humoral branch of the innate immune response in acute pancreatitis (AP) and evaluate their association with disease severity.

Methods: Methods: Retrospective study of patients hospitalized with AP from 2020 to 2024. Patients classified by etiology (alcoholic and non-alcoholic pancreatitis) and disease course (abortive). Serum levels of complement components (C3, C5), C-reactive protein (CRP), and lactoferrin determined using ELISA. Disease severity assessed with the APACHE II scale. Descriptive statistics and significance tests, including t-tests, employed for analysis.

Results: Results: Significant changes in humoral immune response markers were observed in patients with abortive AP. In the non-alcoholic AP group, C3 decreased to 7.02±0.29 pg/ml ($p < 0.01$) and C5 to 10.53±0.25 pg/ml ($p < 0.01$). In the alcoholic AP group, C3 was 7.12±0.42 pg/ml ($p < 0.05$) and C5 was 9.69±0.55 pg/ml ($p < 0.01$). CRP levels were significantly elevated: 18.94±0.43 mg/l ($p < 0.001$) in non-alcoholic AP and 16.83±0.84 mg/l ($p < 0.001$) in alcoholic AP. Lactoferrin levels were also increased: 1612.54±61.39 ng/ml ($p < 0.001$) in non-alcoholic AP and 1808.35±39.99 ng/ml ($p < 0.001$) in alcoholic AP, indicating enhanced inflammation.

Conclusions: Conclusion: Acute pancreatitis involves a significant reduction in complement components (C3, C5) and an increase in CRP and lactoferrin levels, indicating pronounced inflammation. Complement depletion may signal immune system dysfunction, while elevated CRP and lactoferrin confirm ongoing inflammation. These findings underscore the importance of inflammatory markers for assessing disease severity and developing personalized treatment strategies. The study provides valuable insights into the immunological aspects of acute pancreatitis, especially in the context of biliary and pancreatic surgery, aiding in optimizing diagnosis and treatment.

Keywords: Acute Pancreatitis, Complement Deficiency, Inflammatory Markers, Immune Dysfunction

PE-2

The MTHFR C677T Polymorphism: A Double-Trouble in Metabolic Health and Alcohol Use Disorder

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Aims: Chronic alcohol intake is associated with liver dysfunction, increased homocysteine levels, and neurotransmitter imbalances, all of which exacerbate in individuals harboring the methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism. Notably, emerging evidence suggests a potential genetic predisposition to alcohol use disorder influenced by variations in methylation-related genes, including MTHFR C677T. Despite growing interest in the interplay between MTHFR polymorphism, metabolic health, and alcohol consumption, the precise mechanisms underlying their combined effects remain incompletely understood. This study aims to explore the dual impact of the MTHFR C677T polymorphism and alcohol intake on metabolic health, with a particular focus on homocysteine metabolism, and susceptibility to alcohol use disorder.

MTHFR C677T is not only favoring alcohol use disorder but also increasing serum Homocysteine level and adding cardiovascular disease risk. Understanding this interaction could provide valuable insights into personalized risk assessment and potential therapeutic strategies for individuals genetically predisposed to alcohol-related metabolic dysfunctions.

Methods: A cross-sectional study was conducted and sociodemographic data was obtained with semi structured questionnaire. The polymorphism in MTHFR C677T gene of 120 current alcoholic participants from a suburban community of central Nepal was analyzed by real time polymerase chain reaction (PCR) and serum homocysteine was measured by immunoassay method. Descriptive analysis was performed using STATA version 14.

Results: Out of all 120 participants, 50% had no mutation on MTHFR C677T gene, 35.8% had homozygous (TT) mutation and 14.2% heterozygous (CT) mutation. Out of both homozygous and heterozygous mutation, 63.3% had alcohol use disorder and 41.7% had hyperhomocysteinemia.

Conclusions: Polymorphism of MTHFR C677T gene not only influencing alcohol use disorder but also creating another trouble of cardiovascular disease risk and fatty liver.

Keywords: MTHFR C677T, Alcohol Use Disorder, Homocysteine

PE-3

Comprehensive Profiling of Infiltrated Circulating Immune Cell Types and Their Subset Responsible for Alcoholic Steatohepatitis by Scrnaseq Analysis

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Aims: Alcoholic steatohepatitis (ASH) is primarily caused by inflammatory processes that occur after repeated exposure to alcoholic byproducts released into the bloodstream, causing circulating immune cells to infiltrate the liver and generate additional acute or chronic inflammatory reactions. Despite several investigations, little focus has been made to identifying immune cell type response on ASH at the single cell level. Therefore, in this study, we explored the heterogenous immune leukocytes from ALD induced and healthy control mouse groups that are responsible for ASH at a single cell level by high-dimensional single cell RNA sequencing (scRNAseq) analysis.

Methods: In our study, t-distributed stochastic neighbor embedding (t-SNE) dimensionality reduction and 2D-visualization plot were used to visualize heterogenous immune cell types. Moreover, singleR was used for automated cell annotation to identify the cell types and differentially expressed genes (DEGs) from each cell type and their subsets were identified respectively.

Results: In particular, we observed population decline in B cells and their subsets with up and downregulated genes denoted innate pro-inflammatory response as an important sign of alcoholic induced liver fibrosis. Similarly, neutrophils deficient in alcoholic-induced mouse group was another key finding of ASH, and an increase in eosinophils diverts further complications of liver fibrosis suggesting functional heterogeneity of granulocyte subsets. Overall, all these circulating immune cells were significantly reduced by frequent alcohol exposure, which may fail to protect the liver from pathogenic microbe or antigen infection.

Conclusions: Our findings may assist in discovering potential ALD biomarker cell types and enhance our understanding of the circulating immune leukocytes that lead to alcoholic-induced liver fibrosis.

Keywords: Alcoholic Steatohepatitis, Scrnaseq, Liver Fibrosis, Biomarker

PE-4

Bile Acid Signaling Induces Retinol Metabolism in Hepatic Stellate Cells to Protect against Alcohol-induced Liver Injury

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Aims: Alcohol and its metabolites (e.g. acetaldehyde) are known to be carcinogenic and linked to advanced liver diseases. However, majority of individuals with alcohol-related liver disease (ALD) remain in the early stages of steatosis, suggesting potential protective mechanisms. This research investigates how interactions between hepatocytes and hepatic stellate cells (HSCs) influence early-stage ALD. Specifically, it explores how bile acids act as signaling molecules, activating HSCs to enhance retinol metabolism for protection against alcohol-induced injury.

Methods: Wild-type and HSC-specific knockout of alcohol dehydrogenase class 3 (*Adh5*) ($Lrat^{\Delta Adh5}$) mice were fed an isocaloric maltose-dextrin (Pair) or 4.5% liquid ethanol (EtOH) diet for 8 weeks. Sera were subjected to bile acid (BA) measurement, and liver tissues were analyzed using spatial and RNA-sequencing. *In vitro*, isolated HSCs and hepatocytes were co-cultured and analyzed for the production and transport of BA and retinoic acids (RA).

Results: As in patients, the serum level of BAs was increased in EtOH-fed mice compared to Pair-fed controls. Particularly, the expression of multidrug resistance-associated protein 3 (MRP3), encoded by *Abcc3*, was expanded around the pericentral region. Treatment of taurocholic acid (TCA) to HSCs revealed physiological changes similar to those freshly isolated from EtOH-fed mice were observed, including loss of retinol-storing lipid droplets and increased expression of retinol metabolism-related genes. In fact, FXR stimulation in HSCs increased *Adh5* expression and RA production, while RA treatment elevated GSH synthesis and suppressed MYC and γ-H2AX in EtOH-exposed hepatocytes. Additionally, we confirmed the bidirectional transfer of BA and RA between EtOH-fed hepatocytes and HSCs through co-culture system. Furthermore, EtOH-fed $Lrat^{\Delta Adh5}$ mice showed aggravated liver injury aggravated with reduced RA delivered to hepatocytes, implicating the protective effect of HSC-derived retinoids.

Conclusions: This study uncovers a novel metabolic synapse between hepatocytes and HSCs through BA and RA, offering new insights into the protective mechanism in ALD.

Keywords: Bile Acid, Retinoic Acid, Hepatic Stellate Cell, Alcohol Dehydrogenase Class 3

PE-5

Identification and Validation of Severe Alcoholic Hepatitis Therapeutic Targets Based on Meta-Analysis through Animal Model

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Aims: Alcoholic liver disease is recognized as a complex condition caused by alcohol abuse, encompassing a wide range of liver disorders. Severe alcoholic hepatitis (SAH) is a major disease that causes liver damage and inflammation, highlighting the need for effective treatment development. Therefore, to identify therapeutic targets and validate selected genes through meta-analysis, genes that play a critical role in the onset and progression of SAH were selected, and their therapeutic potential was evaluated in an SAH animal model.

Methods: Using bioinformatics data, we collected gene expression information related to SAH and analyzed genetic data and biological pathways from multiple databases. Changes in gene expression, selected through meta-analysis, were confirmed in liver tissues of SAH animal models using molecular biological techniques, including qPCR and western blot.

Results: Meta-analysis results showed that specific genes cause significant changes in SAH and are promising candidates as therapeutic targets. First, it was confirmed that the expression of TNF-α and iNOS, genes related to inflammation, increased in the liver tissue of the animal model, creating an animal model that reflects SAH well. In addition, among the 10 genes that showed an increase in the AH genes selected by the meta-analysis, TGF-b1, LYN, TLR2, HDAC9, MAPK3, and AFP showed a significant increase in expression, and among the 18 genes that showed a decrease, GSTP1, SREBF2, CBS, PCBP2, PPARA, AGT, MAPK8, MET, LPIN1, DNAJB1, NR3C1, and LIPC showed a significant decrease in expression.

Conclusions: These results not only provide important basic data for the development of diagnostic and therapeutic strategies for SAH, but also show the possibility of suggesting new therapeutic approaches in future studies. This study provides an important step toward discovering new targets for SAH treatment and demonstrates the usefulness of bioinformatic analysis.

Keywords: Severe Alcoholic Hepatitis, Meta-Analysis

PE-6

Deep Multi-Omics Fusion Predicts Alcohol-Induced Hepatic Ferroptosis and Identifies Targetable Lipid Peroxidation Regulators in Alcohol-Related Liver Disease

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Aims: Alcohol-Related Liver Disease (ALD) is a leading cause of liver failure, yet predicting patient-specific susceptibility to ferroptosis—an iron-dependent form of cell death driving ALD progression—remains unresolved. Oxidative stress and lipid peroxidation contribute to hepatocellular injury, but no existing framework integrates multi-omics data to stratify ALD patients based on ferroptosis risk and therapeutic reversibility. This study develops an AI-driven model to predict ALD progression, identify ferroptotic regulators, and define precision-targeted therapeutic windows for ferroptosis inhibitors.

Methods: Multi-omics data from established cohorts, including Alcoholic Hepatitis Network (AlcHepNet), Liver Cirrhosis Cohort (NIAAA-LCC), UK Biobank, and the Mass Spectrometry Lipidomics Atlas (MSLA), were integrated to analyze ferroptosis-related pathways in ALD. Single-cell metabolic flux profiling was utilized to characterize lipid peroxidation dynamics across fibrosis stages, while genomic and clinical data were incorporated for disease progression modeling. MRI-based hepatic iron mapping was used to assess iron deposition, and LC-MS lipidomics data quantified polyunsaturated fatty acid oxidation. A Multi-Modal Deep Graph Neural Network (DGNN) integrated these datasets to predict ferroptotic pathways, while a multi-task Transformer model simulated ferroptosis progression using longitudinal electronic health records (EHR). Model interpretability was assessed through SHAP analysis and ferroptosis network topology analysis.

Results: The model achieved an AUROC of 0.85 (95% CI: 0.81–0.86) for predicting ferroptosis-driven ALD progression, outperforming FIB-4 (AUROC 0.71) and MELD (AUROC 0.74, P<0.0001). Three ferroptosis subtypes were identified: Lipid-Resistant ALD, characterized by low lipid peroxidation and reduced cirrhosis risk (HR 3.2, P<0.0001); Iron-Driven ALD, defined by high hepatic iron deposition (HR 2.61, P<0.0001); and Lipid-Peroxidation ALD, showing high lipid peroxidation and iron overload (HR 5.9, P<0.00001), with accelerated cirrhosis progression. Ferroptosis inhibitors (RSL3, Liproxstatin-1) demonstrated a 61% fibrosis reversal probability (P<0.00001), validated in external ALD cohorts (AUROC = 0.82, 95% CI: 0.80–0.84).

Conclusions: This study presents an AI-driven model integrating single-cell lipidomics, iron mapping, and deep graph networks to predict ferroptosis-mediated fibrosis progression in ALD, define ferroptosis subtypes, and identify precision-targeted therapies, advancing AI-driven hepatology.

Keywords: Ferroptosis, LIPID Peroxidation, Multi-Omics Integration, Alcohol-Related Liver Disease

PE-7

SCL1 Protein of Streptococcus Pyogenes Induces Fibrosis by Activating TGFbR1 Kinase in Alcohol-Related Liver Disease

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Aims: Background and Aims: ALD is worsened by gut dysbiosis, affecting inflammation, fibrosis, and metabolism. While gut microbiota influence fibrosis, their role in ALD is unexplored. This study investigates how alcohol-associated gut microbiota (AGM) induces liver kinome alterations, driving inflammation and fibrosis.

Methods: Method: ALD rats were developed using a 40% Lieber-DeCarli ethanol diet. AGM-linked kinome changes were studied in humanized rats colonized with stool from SAH patients (SAHs→HR) and compared to ALD rats transplanted with healthy donor stool (HD→ALDR). Stool and liver samples (n=6/group) underwent metaproteome and phosphoproteome analyses. AGM-associated kinome changes were identified and correlated with each other to identify the bacteria which correlated with bacteria. Ability of Streptococcal collagen like protein (Scl1) to bind to TGFBR1 kinase was investigated by molecular docking.

Results: Results: Stool metaproteome identified significant increase in 10 bacterial genera including *Streptococcus, Staphylococcus, Clostridium*, & others in SAHs→HR similar to ALD (P<0.05). COG functional analysis showed increased post-transcriptional protein modifications (PTM) & reduced lipid transport & metabolism, indicating that AGM contributes to PTM changes & steatosis as seen in ALD (P<0.05). Liver kinome analysis in SAHàHR rats showed 85 significantly upregulated kinases, with 34 overlapping with ALD rats (P<0.05) associated with inflammation (12: Mapk14, Map3k10, & others), fibrosis (4-Igf1r, Tgfbr1, Col4a1), lipid metabolism (11-Cdk14, Cdk18, Cdk13, & others), & regeneration (3-Bmpr1a, Met, Igf1r). Interestingly, HD□ALDR significantly reversed the levels of Streptococcus 10 folds, Staphylococcus 3 folds, and Clostridium 5 folds & 18 kinases associated to inflammation (Btk, Camk4, Mapk, Met, Nuak1 & others) & fibrosis (Col4a1, Tgfbr1, Fgfr2 & others, P<0.05). Metaproteome & kinome correlation analysis showed that Streptococcus genus directly correlated with inflammation & fibrosis (Btk, Mapk, Tgfbr1) linked kinases (r2>0.9, P<0.05), suggesting that AGM may promote fibrosis in ALD via modulation of these kinome. SAH patients showed significant increase in Scl1 protein from *Streptococcus pyogenes*. Molecular dockinf showed significant association of Scl1 protein with TGFBR1 kinase receptor suggesting that bacterial load populated with *Streptococcus pyogenes* induces fibrosis in ALD.

Conclusions: •Gut microbiota influence TGFBR1 kinase expression ans downstream signaling in Alcohol-related liver disease.

• Streptococcus-derived Scl1 protein is elevated in SAH stool samples.

• Molecular docking confirms strong Scl1-TGFBR1 interaction.

• FMT from healthy donors restores microbial and kinase balance.

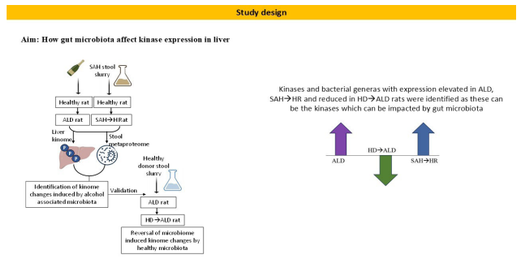

Figure 1.

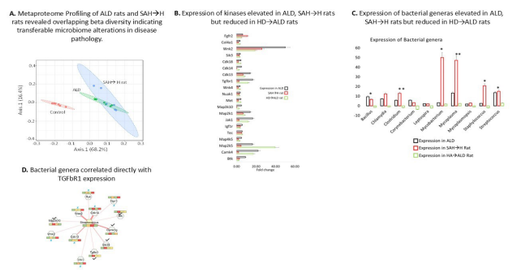

Figure 2.

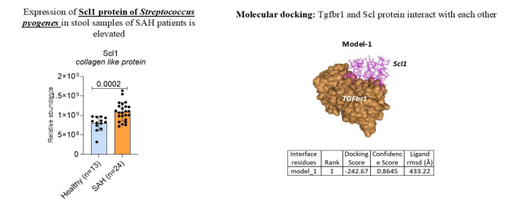

Figure 3.

Keywords: Fibrosis, Metaproteome, Streptococcus Collagen Like ProteiN, TGFBR1

PE-8

Elucidation of Leptosidin Loaded Mesoporous Silica Nanoparticles on Acute Alcoholic Liver Injury (Ali) in a Mouse Model via Alteration of Apoptosis, Autophagy, and Ferroptosis (GPX4/SLC7A11/Beclin-1/ATG5/LC3II/I/FTL/P62) Cascade

Manvendra Singh, Deepika Singh

HMFA-MIET, SIHAS, SHUATS, India

Aims: Acute alcoholic liver injury (ALI) is a critical liver disorder caused by excessive alcohol intake, leading to oxidative stress, inflammation, and hepatocellular damage. Targeting autophagy and ferroptosis pathways presents a promising therapeutic approach for ALI management. In this study, we investigated the hepatoprotective effects of leptosidin-loaded mesoporous silica nanoparticles (Lep@MSNs) in a mouse model of ALI and scrutinize its underlying mechanism

Methods: Lep@MSNs were fabricated by Stober method, and the size, zeta potentials, and drug encapsulation efficiency were characterized using analytical methods. All the rats were randomly divided into six groups and Lep@MSNs were orally administered to all ethanol-induced groups. Blood samples were collected to estimate the hepatic, non-hepatic, oxidative stress parameters, cytokines, inflammatory and apoptosis parameters. hematoxylin-eosin (H&E) staining, immunohistochemical analysis, and tissue iron were measured using liver tissue. Autophagy and ferroptosis-related proteins were determined by Western blotting analysis and along with histopathological investigation.

Results: The result indicated that Lep@MSNs have small particle size with higher entrapment efficieny and excellent zeta potential with smooth morphology. It significantly improves the hepatic and non-hepatic profile (AFP, AST, ALT, ALP, TBL, GGT), antioxidant profile (LPO, SOD, CAT, GSH, GPx), inflammatory cytokines (TNF-α, IL-1β, Il-6, IL-10, IL-18, IL33), inflammatory parameters (COX-2, iNOS, VEGF, PGE2, NFκB). Lep@MSNs showed improved alcohol-caused liver cell damage, with increased levels of heme oxygenase 1 (HO-1) and nuclear factor erythroid 2–related factor 2 (Nrf2). It also mitigates liver, spleen, and kidney index and tissue iron and altered the expression of Bax, Bcl-2 and caspase-3.. Our results indicate that Lep@MSNs effectively modulate autophagy and ferroptosis by regulating key molecular markers, including GPX4, SLC7A11, Beclin-1, ATG5, LC3II/I, FTL, and P62 which was confirmed by western blotting. By restoring cellular homeostasis and mitigating oxidative damage, Lep@MSNs significantly reduce liver injury and inflammation

Conclusions: These findings highlight the potential of Lep@MSNs as a novel nanotherapeutic strategy for ALI by targeting apoptosis, autophagy and ferroptosis-related pathways.

Keywords: Leptosidin, Mesoporous Silica Nanoparticles, Acute Alcoholic Liver Injury, Autophagy, Ferroptosis, Apoptosis

3. Alcohol-Related Liver Disease, Clinical

PE-1

Early Hepatic Changes and Biomarkers in Alcohol-Related Liver Disease: A Cross-Sectional Study of Short-Term Consumption

Nandha Kumar

ACS Medical College and Hospital, India

Aims: Alcohol-related liver disease (ARLD) is a leading cause of liver morbidity and mortality. Alcohol intake influences the evolution of fatty liver to cirrhosis and hepatocellular carcinoma (HCC). The current study seeks to analyze the clinical presentation of ARLD in short-term drinkers based on liver function tests, imaging, and the earliest biomarkers. We suspect that clinical factors can be used to predict ARLD severity even in new drinkers.

Methods: This cross-sectional investigation included 50 individuals with previous ARLD in the previous six months, grouped according to self-reported drinking: low (1-2 drinks/day), moderate (3-4 drinks/day), and heavy (≥5 drinks/day). Liver biomarkers (ALT, AST, GGT) and imaging (ultrasound or elastography) and demographic variables were measured. Hepatic steatosis, fibrosis, and cirrhosis were identified, and comparisons were made to assess trends for alcohol use against liver markers.

Results: Early findings demonstrate a significant association between heavy drinking and high liver enzymes (AST, ALT, GGT) in 65% of subjects. Fatty liver occurred in 45% of heavy drinkers and 78% of moderate drinkers. Although cirrhosis and HCC were not identified, mild to moderate fibrosis was observed in 20% of heavy drinkers. Biomarkers like the AST/ALT ratio and GGT levels were significantly associated with acute liver injury. There was a linear correlation between the period of alcohol consumption and liver damage.

Conclusions: The results indicate that short-term drinking can lead to liver damage with early presentation of raised liver enzymes and fatty liver in moderate and heavy drinkers. Early liver damage can be picked up by non-invasive modalities such as LFTs and imaging possibly before advanced ARLD ensues. Long-term follow-up is needed to validate these findings and determine the prognosis.

Keywords: Alcohol Related Liver Disease, Liver Fibrosis, Liver Markers, Fatty Liver

PE-2

The Impact of Alcohol Consumption on the Risk of Liver-Related Mortality in People with Metabolic Risk Factors

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Aims: The impacts of alcohol consumption amount in people with metabolic risk factors on the risk of liver-related outcomes are not fully studied. In this study, we investigated the effects of alcohol consumption amount on the risk of liver-related mortality in participants with metabolic risk factors of the United Kingdom Biobank study (UKB) study, a prospective cohort.

Methods: We included UKB participants without prior diagnosis of cirrhosis at the time of enrollment. Metabolic traits (hypertension, type 2 diabetes mellitus, dyslipidemia, and obesity) were defined based on self-reported history, medication use, previous hospital diagnosis, or laboratory/anthropometric values. Alcohol consumption amount was reported from a self-reported alcohol use questionnaire. The alcohol consumption was categorized into 0-10g, 10-20g, 20-30g, 30-40g, 40-50g, 50-60g, >60g per day. Cox proportional hazards models was used to evaluate the effects of alcohol intake amount on time to liver-related mortality. In addition, we investigated whether the effect of alcohol intake can alter by the status of *PNPLA3* genotype.

Results: In 263,052 participants with at least one metabolic trait (mean age 57.39 years, male 51.7%), 92,481 (35%), 73,758 (28%), 43,606 (17%), 22,499 (8.5%), 13,358 (5.1%), 6,832 (2.6%), 10,518 (3.9%) participants consumed 0-10g, 10-20, 20-30, 30-40, 40-50, 50-60, >60g per day, respectively. During a median follow-up of 12 years, 654 (0.2%) participants developed liver-related mortality. We observed a statistically significantly higher risk of liver-related mortality from those who drank between 20-30 g per day (aHR 1.45 [95% CI: 1.10-1.92]) compared to those who drank <10g per day, after adjusting for age, sex, race/ethnicity, BMI, diabetes, hypertension, hyperlipidemia, household income. Furthermore, we observed synergistic interaction in those who drank >60g per day and PNPLA3 homozygote carriers for liver-related mortality (p-interaction <0.01, aHR 5.28 [95% CI: 3.68-7.57] in alcohol intake >60g per day, aHR1.62 [95% CI: 0.783-3.39] in PNAPL3 homozygous carriers, aHR 25.6 [95% CI: 3.58-182.5] in both alcohol intake >60g per day and PNPLA3 homozygous carriers).

Conclusions: In the UK Biobank, there was an incremental risk of liver-related mortality by the amount of alcohol consumption. The increased liver-related mortality was observed from those with > 20g/day of alcohol use. We need to counsel the risk of alcohol consumption on the progression to liver-related outcomes in people with metabolic risk factors.

Keywords: Alcohol, Liver-Related Mortality, Metabolic Syndrome, Mortality

PE-3

Early Liver Transplantation for Severe Alcoholic Hepatitis: A Systematic Review of Outcomes and Ethical Considerations

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Aims: Severe alcoholic hepatitis (SAH) is associated with high short-term mortality, particularly in patients who are nonresponsive to medical therapy. Early liver transplantation (ELT) has emerged as a potential life-saving intervention for carefully selected patients. However, ELT raises significant ethical debates concerning the traditional six-month abstinence rule, organ allocation fairness, and risk of post-transplant alcohol relapse. This systematic review aims to evaluate clinical outcomes and explore ethical considerations surrounding ELT for SAH.

Methods: A systematic literature search was conducted in accordance with PRISMA guidelines across PubMed, Web of Science, and Scopus databases, covering studies published up to January 2025. Inclusion criteria encompassed randomized controlled trials, observational cohort studies, and ethical analyses addressing ELT in SAH. Data extracted included patient selection criteria, survival rates, rates of alcohol relapse, graft utilization, and ethical discussions. Study quality was assessed using the Newcastle-Ottawa Scale for observational studies and the CASP checklist for qualitative studies.

Results: Fourteen studies, encompassing 1,245 patients, met the inclusion criteria. ELT demonstrated a significant survival benefit compared to non-transplantation approaches, with one-year survival rates ranging from 77% to 89% versus 25% to 30% in non-transplanted controls. The median time from listing to transplantation was 10 to 15 days post non-response to corticosteroid therapy. Alcohol relapse rates varied from 10% to 25% over a two-year follow-up, with most relapses occurring beyond the first post-transplant year. Ethical analyses emphasized the need for multidisciplinary selection committees, psychosocial evaluation, and family support as critical components in candidate selection. Concerns regarding equitable organ allocation persist but are counterbalanced by evidence of favorable outcomes and low graft consumption (less than 3% of available organs in reviewed cohorts).

Conclusions: Early liver transplantation offers a substantial

survival advantage for highly selected patients with severe alcoholic hepatitis unresponsive to medical treatment. Ethical concerns necessitate rigorous candidate selection and post-transplant support protocols. Future research should focus on standardized selection criteria and long-term outcomes to inform ethical and clinical guidelines.

Keywords: Severe Alcoholic Hepatitis, Early Liver Transplantation, Survival Outcomes, Ethical Considerations

4. Autoimmune Liver Disease

PE-1

Azomethine-Clubbed Thiazoles as Dual-Target Therapeutics for Autoimmune Liver Disease: Anti-Ferroptotic and Bile Acid Regulatory Potential via Nrf2-Keap1 and FXR Modulation

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Aims: Autoimmune liver disease (AILD), including autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC), involves chronic immune-mediated liver injury with bile acid dysregulation, oxidative stress, and inflammation. Ferroptosis, a lipid peroxidation-driven cell death, exacerbates liver damage in AILD, necessitating novel multi-target therapeutics. Azomethine-clubbed thiazoles, integrating the antioxidant and immunomodulatory properties of the thiazole core and azomethine linkage, were explored for their ability to activate Nrf2-Keap1 to combat oxidative injury and modulate FXR to restore bile acid homeostasis and suppress inflammatory signaling in AILD.

Methods: Seven azomethine-clubbed thiazole derivatives were screened against Nrf2-Keap1 (PDB: 5CGJ) and FXR (PDB: 3DCT) using AutoDock Vina, with bardoxolone methyl and obeticholic acid as reference ligands. ADMET profiling assessed pharmacokinetics and safety, while in silico modeling predicted antioxidant and anti-inflammatory activities. β-Cyclodextrin complexation was evaluated to enhance solubility and hepatic distribution.

Results: Azomethine-clubbed thiazoles exhibited high binding affinity for Nrf2-Keap1 (-9.10 to -8.20 kcal/mol) and FXR (-9.00 to -7.80 kcal/mol), with compound 3a demonstrating comparable efficacy to reference drugs. Nrf2 activation upregulated antioxidant defenses, mitigating ferroptotic damage via enhanced glutathione biosynthesis and lipid peroxide detoxification. FXR modulation regulated bile acid metabolism and dampened inflammatory responses, crucial for AILD management. ADMET analysis predicted favorable oral bioavailability (90.26–92.80%), low clearance (0.19–0.285 log ml/min/kg), and moderate toxicity (LD50: 2.22–2.64 mol/kg). β-Cyclodextrin inclusion complexes improved solubility and hepatic retention.

Conclusions: Azomethine-clubbed thiazoles present a promising dual-target approach for AILD by mitigating oxidative stress, ferroptotic injury, and bile acid dysregulation. Their Nrf2-Keap1 activation and FXR modulation provide a novel therapeutic strategy with enhanced pharmacokinetics via β-cyclodextrin complexation, supporting their potential in immune-mediated liver diseases.

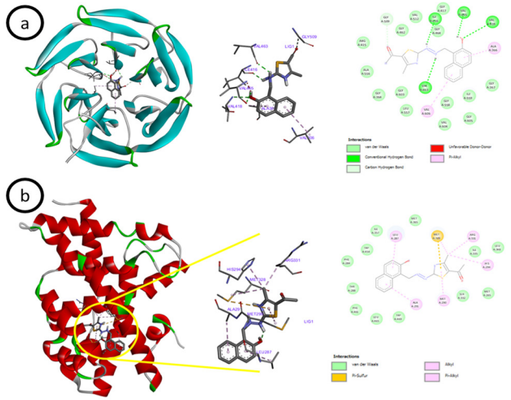

Figure 1. *3D and 2D Interaction between 3a (Azomethine-clubbed thiazole derivative) toward protein receptor a) Nrf2-Keap1 (PDB: 5CGJ) and b) FXR (PDB: 3DCT)*

Figure 1. 3D and 2D Interaction.

Table 1. General properties

GENERAL PROFILES			
Molecules/Pubchem ID	**3a**	**3d**	**3h**
MW	325.38	275.33	312.39
Binding Affinity			
farnesoid X receptor (FXR) (kcal/mol)	-9.00	-7.80	-7.80
Nrf2-Keap1 (kcal/mol)	-9.10	-8.20	-8.30
LIPOPHILICITY			
Log P (octanol-water solubility test)	3.96	2.8	3.12
Consensus Log P	3.38	2.36	3.01
PHARMACOKINETICS			
BBB Permeability (log BB)	-0.407	-0.423	0.256
CYP1A2 inhibitor	yes	yes	yes
Intestinal Absorption (Human) (% Absorbed)	90.26	90.57	92.8
Total Clearance (log ml/min/kg)	0.285	0.284	0.19
DRUGLIKENESS			
Lipinski #violations	0	0	0
Bioavailability Score	0.55	0.55	0.55
MEDICINAL CHEMISTRY			
Leadlikeness #violations	1	0	1
Synthetic Accessibility	3.25	3.04	3.24
TOXICITY			
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.22	2.34	2.64

Keywords: NRF2-KEAP1 Activation, Farnesoid X Receptor (FXR) Modulation, Ferroptosis Inhibition, Bile Acid Homeostasis

PE-2

Deep Learning-Driven Single-Cell Epigenetic Memory Mapping Identifies Regulatory T-Cell Exhaustion as a Predictor of Fulminant Autoimmune Hepatitis Progression

Prihantini Prihantini[1], Sahnaz Vivinda Putri[2], Elfiany[3], Rini Winarti[4], Andi Nursanti[5], Rifaldy Fajar[1]

[1]Mathematical and Computational BioMedicine Research Group, The Integrated Mathematical, Computational, and Data Science for BioMedicine Research Community Foundation, Indonesia; [2]Health Management Laboratory, International University Semen Indonesia, Indonesia; [3]Computational Science Research Laboratory, BLK Muhammadiyah University, Indonesia; [4]Department of Biology, Yogyakarta State University, Indonesia, [5]Department of Pharmacy, Wallacea University, Indonesia

Aims: Autoimmune hepatitis (AIH) can rapidly progress to fulminant liver failure despite immunosuppressive therapy. The underlying mechanisms driving this progression, particularly concerning epigenetic memory retention in regulatory T cells (Tregs) and intrahepatic macrophages, remain poorly understood. This study integrates single-cell epigenomic analysis and deep learning to elucidate chromatin accessibility changes associated with AIH progression and treatment resistance.

Methods: We analyzed datasets from the Gene Expression Omnibus (GEO: GSE216064, GSE136103), ENCODE, Single Cell Portal (HCA-Liver, SCP1050), and the Human Liver Cell Atlas. These datasets included 21,135 single-cell ATAC-seq and 16,842 single-cell RNA-seq profiles from AIH patients, covering treatment-naïve, steroid-responsive, and steroid-resistant subgroups. We developed a deep variational autoencoder (VAE) to model temporal chromatin accessibility, a transformer-based forecasting model to predict chromatin remodeling leading to Treg exhaustion and Kupffer cell-driven inflammation, and a graph neural network (GNN) to map enhancer-promoter interactions linked to fibrotic progression. A Bayesian survival model was trained on UK-AIH longitudinal data (n=508 AIH patients, 11-year follow-up) to predict fulminant progression risk.

Results: The model achieved AUC 0.84 (95% CI: 0.81–0.86), outperforming MELD score (AUC = 0.726). Treg exhaustion signatures (chr17q25.3, chrXq13.1) were linked to steroid resistance (P=3.2×10^{-4}). Kupffer cell enhancer remodeling at chr5q31.2 drove an IL-6/TNF-α cascade (HR = 2.89, 95% CI: 2.34–3.42, P<0.0001). The model predicted 7-year transplant-free survival with 82.5% accuracy (95% CI: 79.8–84.7), surpassing histopathological models (67.8% accuracy). High-risk AIH subgroups had a 3.2-fold increased likelihood of fulminant failure within 4 years (P=0.0003).

Conclusions: This study presents an AI-driven single-cell epigenomic analysis of AIH progression, identifying Treg exhaustion and enhancer remodeling signatures. By integrating multi-omics single-cell data with longitudinal outcomes, this approach improves risk prediction and may inform better AIH management.

Keywords: Autoimmune Hepatitis (AIH), Single-Cell Epigenomics, Machine Learning, Risk Stratification

PE-3

Epidemiological Trends of Autoimmune Hepatitis in South Korea: A Population-Based Study from 2010 to 2023

Kyung-Ah Kim[1], Hwa Youg Choi[2], Bo Hyun Kim[3], Eun Sun Jang[4], Aryoung Kim[1], Moran Ki[2], Sook-Hyang Jeong[4]

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Aims: The epidemiology of autoimmune hepatitis (AIH) has shown geographic and temporal variation. There are few longitudinal studies on the epidemiology of AIH in Korea. This study aimed to identify temporal trends in the epidemiology and outcomes of AIH in Korea from 2010 to 2023.

Methods: We obtained data from the Korean National Health Insurance Service database and the Rare Intractable Disease Registry for AIH, identified by the International Classification of Diseases, 10th Revision code K75.4, from 2010 to 2023. We calculated the prevalence and incidence of AIH adjusted by age and sex and analyzed temporal trends using Joinpoint regression. The overall survival was analyzed using the Kaplan-Meier method.

Results: During 2010-2023, 10,055 patients aged 20 years and older were newly identified with AIH (female-to-male ratio 5.3, mean age 59 years). The average age- and sex-adjusted incidence rate from 2010 to 2023 was 17.7 per million per year, and the annual incidence rate tended to increase with an average percent change of 6.5% until 2017, when it plateaued. During the COVID-19 pandemic, from 2020 to 2022, AIH incidence rates were stable. The increasing trend in AIH incidence was consistent among both sexes and in the 30+ age group and was more pronounced in the 70+ age group. Age- and sex-adjusted prevalence rates increased persistently with an average percent change of 10.8%. The increasing trend in AIH prevalence was more pronounced in the 70+ age group. Overall survival was 93.1% at five years and 86.2% at ten years, respectively. The annual case-fatality ratio was 1.95%, significantly higher in men than women. (2.72% vs 1.81%).

Conclusions: From 2010 to 2023, the average incidence of AIH in Korea was 17.7 per million per year, with an upward trend recently stalling. The prevalence of AIH has continued to increase, especially among the elderly.

Keywords: Autoimmune Hepatitis, Incidence, Prevalence, Survival

PE-4

Heterogenous MUCIN1 Positive Population of Cholangiocytes Contributes to Liver Fibrosis in Cholestatic Models

Aishwarya Bhatnagar, Rajni Yadav, Himanshi Himanshi, Vaibhav Tiwari, Tahseen Khan, Chhagan Bihari, Savneet Kaur, Dinesh Mani Tripathi

Molecular and Cellular Medicine Department, Institute of Liver and Biliary Sciences, New Delhi, India

Aims: Biliary epithelial cells (BECs), although quiescent under homeostatic conditions, exhibit significant proliferation and remodeling during injury, termed the ductular reaction (DR). DR plays a dual role in liver regeneration and disease progression. Specifically, persistent DR is associated with the severity of fibrosis. The heterogeneity of BECs and their contribution to disease progression is not known. We aim to investigate the contribution of BEC heterogeneity and its cellular crosstalk to the progression of cholestatic liver injury.

Methods: The cholestatic injury was induced in mice via bile duct ligation (mBDL), and endpoint analysis was done on day 2 (D2), and day 7 (D7). Histological, immunostaining, and gene expression analysis were done in liver tissue. Sham was taken as a control. Primary BECs and HSCs were sorted and acquired. Conditioned media of cholangiocytes were collected and analyzed the secretion of Endothelin 1 (ET-1) by cholangiocytes. 3D ductal organoids were developed and small and large cholangiocytes were acquired based on EpCAM+/MUC1+ for larger cholangiocytes (Epitehlial Cell Adhesion Molecules - EpCAM; MUCIN 1 - MUC1) and EpCAM+/MUC1- for smaller cholangiocytes. Further immune staining of MUC1 was also performed

Results: BDL induced cholestatic model is showing significantly increased DR (> 3-fold), and concentric ductular fibrosis (>2-fold) which was further validated by immune staining by CK19, α-SMA. Acquisition of CK19+ primary BECs from BDL was 89.7% (D2), and 95.6% (D7) vs.17% (sham) showing increased population along with α-SMA+ HSCs which also peaked with 52.5%(D2), and 74.8%(D7) vs. 6.96% (sham)

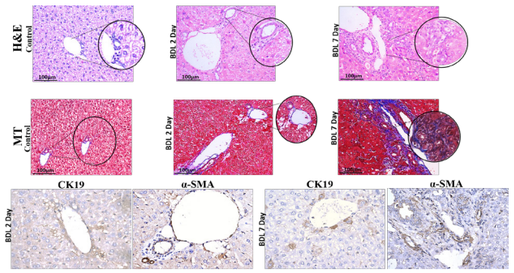
3D-Ductal organoids of D2 and D7 of BDL were developed and its secretome analysis showed increased concentration of Endothelin 1 (ET-1) levels 32.9 pg/ml (D2), 41.9 pg/ml (D4), 61.2 pg/ml (D7) showed strong cross-talk between BECs and HSCs.

Next, we checked which BEC population (small or large BECs) was increased, we further acquired epCAM+ BECs with MUC1+(large BECs) and epCAM+ with MUC1- (small BECs). MUC1+ increased by 14.3% along with MUC1- 81.5% (D2), and 24.7% MUC1+ and 62.3% MUC1- (D7).

Similar results were seen in the IHC of MUC1 for mBDL time points, which indicated an increased large cholangiocyte population with increased cholestasis.

Conclusions: This study revealed BEC dynamicity governed by MUC1+ phenotype and is responsible for pathological changes.3D organoid observation MUC1+ BECs promotes HSCs activation in ET1 dependent paracrine manner in cholestatic liver disease. Study also suggest MUC1- phenotype of BEC is closely associated with biliary homeostasis.

Keywords: Cholestatsis, Fibrosis, Biliary Epithelial Cells Heterogeneity, Organoids



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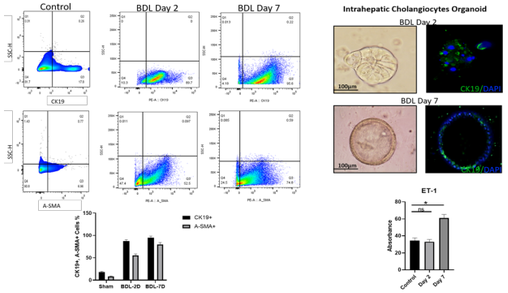

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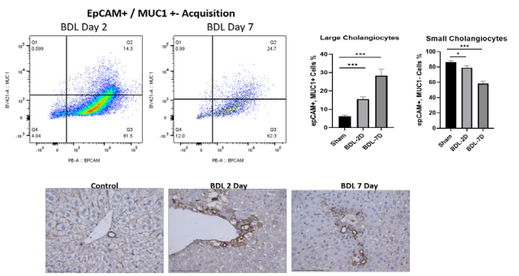

Figure 3.

5. Biliary and Pancreatic Surgery

PE-1

Long-Term Efficacy and Safety Outcomes of Folfirinox versus Gemcitabine as Adjuvant Therapy for Pancreatic Cancer

Ulil Albab Habibah

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Aims: Pancreatic cancer is a highly aggressive malignancy with a poor prognosis. Adjuvant chemotherapy is critical in improving survival outcomes for patients after surgical resection. This systematic review evaluates the efficacy and safety of folfirinox compared to gemcitabine as adjuvant therapies in patients with resected pancreatic cancer, synthesizing evidence from randomized controlled trials (RCTs).

Methods: A comprehensive systematic review was conducted, identifying 87 studies published between 2000 and 2024. After applying strict eligibility criteria, 82 studies were excluded. Five RCTs met the inclusion criteria, involving 1,710 patients (folfirinox: n = 855; gemcitabine: n = 855). Primary outcomes analyzed were disease-free survival (DFS), overall survival (OS), and safety profiles. Secondary outcomes included quality of life (QoL) assessments and subgroup analyses based on prognostic factors such as tumor grade, disease stage, and treatment center characteristics.

Results: Folfirinox demonstrated significant superiority in efficacy compared to gemcitabine in improving DFS and OS. The median DFS for the folfirinox group was 21.4–21.6 months, markedly longer than 12.8 months in the gemcitabine group. Five-year OS rates were also notably higher for patients receiving folfirinox (43.2%–63.4%) compared to gemcitabine (31.4%–48.6%). However, folfirinox was associated with a higher incidence of grade 3–4 adverse events, including febrile neutropenia, fatigue, and gastrointestinal toxicity. QoL analyses revealed that folfirinox delayed the deterioration of physical and social functioning compared to gemcitabine. Subgroup analyses indicated that survival benefits were more pronounced in patients treated at high-volume centers and those with lower tumor grades and earlier disease stages.

Conclusions: Folfirinox significantly improves DFS and OS compared to gemcitabine in patients with resected pancreatic cancer, establishing it as the preferred adjuvant chemotherapy regimen. Nevertheless, its higher toxicity profile necessitates careful patient selection and management to balance efficacy with safety. Future studies are warranted to optimize treatment strategies, minimize adverse effects, and further enhance patient outcomes.

Keywords: Folfirinox, Gemcitabine, Pancreatic Cancer

PE-2

Report of Two Cases Video-Assisted Retroperitoneal Debridement: New Approach in Management of Necrotizing Pancreatitis

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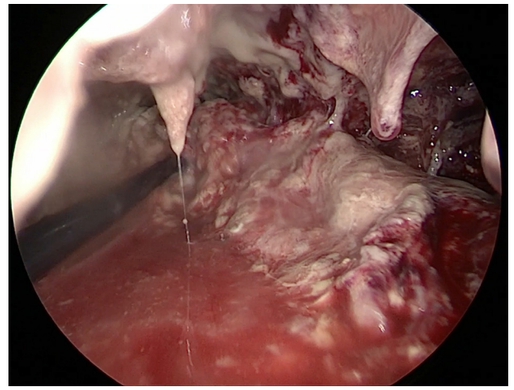
Aims: Necrotizing pancreatitis carries a high mortality and necessitates intervention such as endoscopic, radiologic or surgical intervention to achieve sepsis control. The surgical strategy for acute pancreatitis necrosis has evolved, with open necrosectomy is no longer considered the first approach. A surgical step-up approach consisting of percutaneous drainages and Video – assisted retroperitoneal debridement is now the favored surgical approach.

Methods: We report our experience with 2 patients diagnosed with pancreatic necrosis who underwent Video assisted Retroperitoneal Debridement after percutaneous drainage at Binh Dan hospital.

Results: 2 patients with necrotizing pancreatitis were previously treated with percutaneous drainage using 3 drains into the collection, but their clinical condition did not improve, so video-assisted retroperitoneal debridement (VARD) was performed. One patient underwent surgery via a left retroperitoneal approach, and the other via a right retroperitoneal approach. The first patient developed a colonic fistula on the 12th postoperative days. Both patients eventually recovered after discharge. The hospital stays were 40 days and 25 days, respectively.



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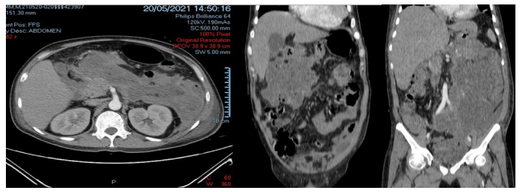

Figure 2.

Conclusions: Our current case report demonstrates the effectiveness of the VARD procedure for patients with acute pancreatic necrosis.

Keywords: Necrotizing Pancreatitis, Surgical Step up Approach, Video - Assisted Retroperitoneal Debridement

PE-3

Efficacy of Biliary Stent Placement in Malignant Biliary Tract Obstruction: A Prospective Study in India

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Aims: To evaluate efficacy of biliary stent placement in patient with biliary Obstruction.

Methods: A prospective observational study was conducted for three years of duration from February 2021 to January 2024. Patients with biliary Obstruction who undergone stent drainage were included in this study. In present study patients with percutaneous biliary stent placement and endoscopic stent placement were included. Liver function test results were recorded before and after stent placement. statistical analysis was done by Microsoft excel 2019 and spss software.

Results: A total 48 patients were included among them 28 were male and 20 were female. Mean age was observed to be 58 ±7. Most common cause of biliary obstruction was observed to be cholangiocarcinoma (37.5 %, n= 18) followed by hepatic carcinoma (20%, n=10). Most common site of obstruction lesion was observed to be common bile duct (50% = 24) followed by hepatic bile duct (35.41% n=17). Percutaneous biliary stent placement was performed in 17 patients (35.4%), while endoscopic stent placement was conducted in 31 patients (64.6%). Most common presenting sign was obstructive jaundice followed by pruritus and loss of appetite. Serum bilirubin levels were 289.5 ± 138.2 µmol/L prior to the procedure, which significantly decreased to 140.5 ± 82.2 µmol/L at one-week follow-up (P<0.001). Liver enzymes like alkaline phosphatase and alanine aminotransferase were significantly decreased. After procedure, complications developed in 4 patients (8.3%), including acute cholangitis in 2 patients, bleeding in 1 patient, and a liver abscess in 1 patient. Biliary stent placement was successful in all patients. However, 36 to 82 days after the procedure, stent blockage was reported in 2 patients (4.1%).

Conclusions: The biliary stent placement safely alleviates malignant biliary Obstruction, enhancing liver function and quality of life.

Keywords: Biliary Tract Obstruction, Biliary Tract Stent, Liver Function Test

PE-4

Ectopic Liver Tissue in the Gall Bladder: A Rare Entity

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Aims: Ectopic Liver Tissue (ELT) is a rare clinical entity that any surgeon faces in their surgical career. Due to the association or propensity to develop hepatocellular carcinoma, this disease has gained clinical importance and surgeons ought to be aware of the possible intervention and complications that can be associated with it. So, we aimed to disseminate this rare clinical finding.

Methods: The patient was operated and histopathology reported the presence of ectopic liver tissue present within the wall of the gall bladder. Scientific publications were searched regarding this clinical entity through google scholar and pubmed.

Results: The incidence has been reported to be 0.24 %- 0.47 % with the gall bladder being the most common site. Anatomically, ELT in gall bladder derives its blood supply either from vascular pedicle arising with or without its own vein from liver parenchyma; or from branches of cystic artery and sometimes through vascular structures embedded within the mesentery lying adjacent to the liver parenchyma. Surgically, it becomes important to delineate the blood supply because often the operating surgeon might encounter uncontrollable bleeding if the blood supply has been derived from liver parenchyma itself. Complications that can be associated with ectopic liver are torsion, bleeding into peritoneum, cirrhosis and sometimes lead to malignant degeneration to hepatocellular carcinoma due to metabolic inactivity owing to less efficient vascular and biliary ductal systems which some-times might be confused for occult metastases from a primary hepatoma. Gall bladder associated ELT is best managed by En bloc resection via laparoscopic cholecystectomy which suffice if the biopsy comes out to be negative. However, as malignant degeneration chances still exist in about 3% of cases, some patients might need to undergo second surgery for negative resection margin and regional lymphadenectomy.

Conclusions: Ectopic Liver tissue in the gall baldder is a rarely encountered clinical phenomenon. Intraoperative bleeding should be carefully monitored when the blood supply derives from liver parenchyma. Complications like peritoneal bleed, cirrhosis and malignant degeneration should be accounted for.

Keywords: Ectopic Liver Tissue, Hepatocellular Carcinoma

PE-5

Biliary Adenoma with Reactive Lymphoid Hyperplasia in a 68-Year-Old Man with Chronic Hepatitis B Patient: A Case Report

Min Ji Kim

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Aims: Biliary adenoma is an extremely rare condition worldwide, with research primarily conducted through case reports. This study aims to retrospectively analyze cases of biliary adenoma diagnosed through postoperative histopathological examination at our institution.

Methods: This study presents a rare case of a 68-year-old man with chronic hepatitis B patient, who was preoperatively diagnosed with a nodule in the left hepatic lobe, with MRI findings consistent with HCC (There is diffusion restriction on DWI, moderate high signal intensity on T2-weighted images, hyperintensity in the arterial phase, and hypointensity in the hepatobiliary phase). The patient underwent a liver tumor resection.

Results: Histopathological examination following left lobectomy confirmed bile duct adenoma accompanied by reactive lymphoid hyperplasia.

Conclusions: Biliary adenoma is a very rare benign tumor with its clinical and pathological characteristics not yet clearly established. By reporting this rare case of biliary adenoma, we aim to share clinical experience and contribute to the differentiation from hepatocellular carcinoma, as well as the establishment of treatment guidelines.

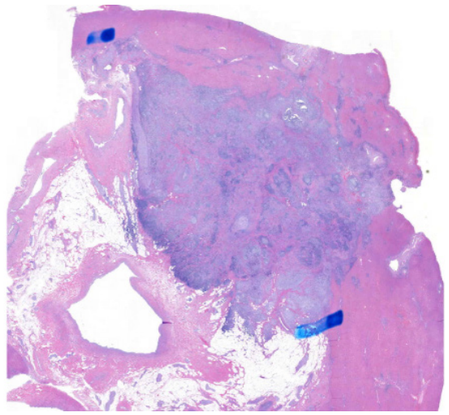
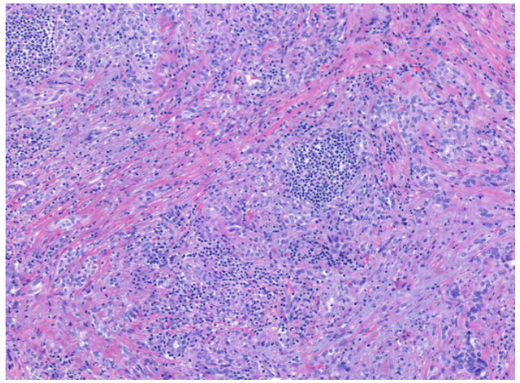


Figure 1.



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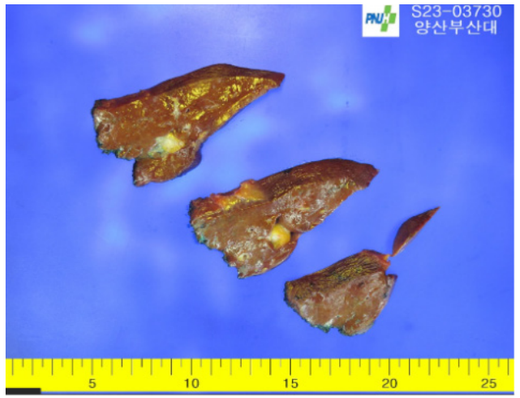

Figure 3.

Keywords: Bile Duct, Hepatitis B

PE-6

Effectiveness of Giving Probiotics and Sinbiotik on the Survival of Post-Pancreatectomy Patients

Putri Ayu[1], Roland Helmizar[2], Siska Azizah[3], Rahmat Fauzan[4]

Economics, Andalas University, Indonesia[1], Internal Medicine, Baiturrahmah University, Indonesia[2], health, Baiturrahmah University, Indonesia[3], Education, Padang State University, Indonesia

Aims: Pancreatectomy surgery is one of the efforts to treat severe pancreatic disease. One of the treatments carried out to reduce post-operative risk is the administration of probiotics. This study aims to identify the effectiveness of probiotic administration on the survival of patients after pancreatectomy surgery.

Methods: The method used is a Systematic Literature Review

using the PRISMA diagram. The first step is identification which is carried out by searching for topics in search engines sourced from PubMed, Scopus and Cochrane Library. The keywords used are "Probiotics", "Synbiotics", "Post-operation", "Patient" and "Pancreatectomy". then delete the same documents. The second step is screening with the criteria of deleting journals that do not discuss post-pancreatectomy patients and those that do not have quantitative results. then eligibility is carried out and continued with included. So that 10 journals are obtained that match the desired topic.

Results: The results show that out of 10 journals there are 7 articles using probiotics, the remaining 3 are synbiotics. It is generally found that probiotic or synbiotic embryos can reduce postoperative complications, such as infections and gastrointestinal disorders, and accelerate patient recovery. However, not all articles show significant results. Some articles show an increase in survival of 5-10% for patients who received probiotics compared to those who did not (control patients).

Conclusions: Further studies are needed on the effectiveness of probiotics or Synbiotics in providing effective clinical recommendations. So that, there is no relationship between the use of probiotics and severe complications such as multiple organ failure or sepsis.

Keywords: Probiotic, Sinbiotik, Pancreatectomy

PE-7

Sociodemographic Conditions, Behavior Risk, and Metabolic Risk Factors on the Quality of Life and Death for Pancreatic Cancer Patients in Indonesia Using the Global Burden of Disease

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[1]IP Trisakti, Indonesia, [2]Health, Baiturrahmah University, Indonesia

Aims: Pancreatic cancer is one of the diseases that causes death and decreased quality of life in Indonesia. This study aims to identify how sociodemographic factors, behavioral factors, and metabolic factors affect the death and disability of pancreatic patients in Indonesia.

Methods: The method used is descriptive graphics. The data was sourced from the Global Burden of Disease from the Institute of Health Mathematics. Data was taken from 1990-2021, for Indonesia. The sociodemographic variables used are age and gender. The habit variable is from smoking, and the metabolic risk variable is from blood sugar levels and body weight

Results: The results show that from 1990-1998 smoking was the main risk factor for death in Indonesia, with a contribution of around 17-18% in the 54-55 year age group. The elderly group 55+ years and the productive age group 15-49 years also revealed a significant impact on the cause of death, although lower than the older group. However, in 2000-2021 it showed that people with high fasting plasma glucose aged 55 years + were the highest cause of death, reaching 20-24%. The trend of High Fasting Plasma Glucose has increased in contribution, indicating that metabolic factors are starting to play a bigger role in pancreatic cancer. The higher the age, the higher the risk of death in pancreatic cancer sufferers. DALYs increase over time, with a trend similar to mortality rates. The contribution of obesity and high glucose levels has risen in recent decades, reflecting changes in increasingly unhealthy lifestyles in Indonesia

Conclusions: Interventions from health workers and the community are needed to provide education about anti-smoking programs, healthy lifestyles, and good diabetes management in Indonesia.

Keywords: Sociodemographic Conditions, Behavior Risk, Metabolic Risk, Pancreatic Cancer

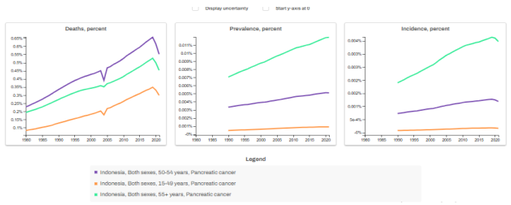

Figure 1.

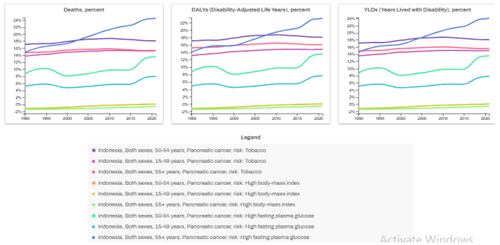

Figure 2.

PE-8

Identification of Sensitivity between EUS and MRCP for Malignancy-Induced Obstructive Jaundice Diagnosis: A Systematic Review

Derizal Derizal[1], Siska Azizah[2], Roland Helmizar[3]

[1]Ip Trizakti, Indonesia, [2]Health, Baiturrahmah University, Indonesia, [3]Internal Medicine, Baiturrahmah University, Indonesia

Aims: Biliary stone and biliary neoplasms are common etiologies of obstructive jaundicen a Endoscopic Retrograde Cholangiopancreatography (ERCP) is the gold standard for diagnosing malignancies causing obstructive jaundice. Other modalities include endoscopic ultrasonography guided fine needle aspiration (EUS-FNA) and ERCP in the diagnosis of patients with suspected malignancies causing obstructive jaundice.

Methods: This study used a systematic literature review of several reputable articles in the form PUBMED, EMBASE, EBSCO, PROQUEST, snowballing, global index medicus, GARUDA, SINTA and several digital libraries of universities in Indonesia until April 30, 2021. There were 5 studies that met the eligibility criteria. The main outcome measurements were sensitivity. Data were analyzed using Review Manager 5.4.1.

Results: The overall pooled sensitivity of ERCP for diagnosis of malignant biliary obstruction were 62.2% [95% CI 57.7–74.7%] and the overall pooled sensitivity of EUS-FNA for diagnosis of malignant biliary obstruction were 86.7% [95% CI 72.5–89.4%].

Conclusions: EUS-FNA was more superior to ERCP in the diagnosis of malignancy causing obstructive jaundice.

Keywords: EUS and MRCP, Malignancy, Pancreas Cancer

PE-9

Recent Developments in Diagnosis, Risk Factors, and Therapy of Pancreatic Cancer: A Review of the Literature

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Aims: One cancer kind with a bad prognosis and a high death rate is pancreatic cancer. Due to the limits of the current diagnostic techniques and the fact that the symptoms are sometimes non-specific, early detection remains a significant issue. To enhance patient prognosis, it is therefore necessary to comprehend risk factors, modern diagnostic techniques, and more potent therapy options. Based on a review of scientific publications, this study aims to examine the most recent advancements in pancreatic cancer detection, risk factors, and treatment.

Methods: In order to conduct this literature review, articles from the recent five years (2018–2023) were searched in scientific databases like PubMed and other. Studies that addressed pancreatic cancer diagnosis, risk factors, and treatment were included in the inclusion criteria; articles that did not specifically address pancreatic cancer or had an unclear methodology were excluded. The study was carried out by classifying the results according to the primary subjects, which include key risk factors, pancreatic cancer treatment advancements, and biomarkers for early diagnosis.

Results: According to studies, a number of biomarkers, including circulating tumor DNA (ctDNA), CA 19-9, and artificial intelligence-based medical imaging techniques, are starting to be used to increase the precision of early detection (Park et al., 2021; Singhi et al., 2019). Obesity, diabetes mellitus, family history, and exposure to carcinogens are the primary risk factors for pancreatic cancer development (Klein, 2021; Rawla et al., 2019). In the meanwhile, the most recent advancements in treatment combine immunotherapy, molecularly targeted therapy, and chemotherapy based on nanotechnology, which may improve patient survival (O'Reilly et al., 2020; Bear et al., 2022).

Conclusions: Advances in the diagnosis and treatment of pancreatic cancer hold promise for enhancing early detection and the efficacy of treatment. Nevertheless, additional investigation is required to validate the therapeutic advantages of this novel technique. It is anticipated that incorporating a multidisciplinary approach into research and treatment will lower the future death rate from pancreatic cancer.

Keywords: Pancreatic Cancer, Biomarkers, Early Detection, Targeted Therapy

PE-10

Percutaneous Transhepatic Cholangioscopy Applying Bernoulli Effect with the Amplatz Sheath for Hepatolithiasis Treatment

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Department of Hepato-Pancreato-Biliary Surgery, Binh Dan Hospital, Vietnam

Aims: *PTCS is a minimally invasive technique* for direct visualization and intervention within the biliary system, performed under ultrasound and fluoroscopic guidance to ensure precise access and navigation. The Amplatz sheath facilitates repeated access, reduces trauma to the bile ducts, and enhances procedural efficiency due to *"Bernoulli effect"*

This technique provides a safe and effective alternative to conventional endoscopic approaches, especially in patients with altered biliary anatomy or recurrent cholangitis.

Methods: A cross-sectional descriptive study was conducted on patients of hepatolithiasis who underwent percutaneous transhepatic cholangioscopy using Amplatz sheath at Binh Dan Hospital from January 2024 to December 2024

Results: Twenty cases of hepatolithiasis were treated with percutaneous lithotripsy using an Amplatz sheath. Female patients accounted for 65% of cases, with an average age of 51,5 ± 3,2 years. 18/20 patients (90%) had a history of bile duct stone surgery. 11 patients (55,0%) had bile duct strictures. The mean stone size was 31,5 ± 15,1 mm, ranging from 12 mm to a maximum of 112 mm. Four cases (20,0%) underwent one stage percutaneous transhepatic cholangioscopy. The clearance rate for intrahepatic stones was 80%. The average

lithotripsy duration was 158,1 ± 110 minutes, ranging from 45 to 480 minutes. Postoperative complications occurred in 3 out of 20 cases (15%), including 2 cases of self-limiting pleural effusion and 1 case of minor hemobilia

Conclusions: **Percutaneous Transhepatic Cholangioscopy (PTCS)** is a minimally invasive technique suitable for treating cases of diffuse and recurrent biliary stones, as well as non-dilated common bile ducts, in the absence of liver atrophy or concomitant cholangiocarcinoma. *The use of the Amplatz sheath* offers several advantages in this procedure. It enhances the effectiveness of biliary stone clearance through *the Bernoulli effect*. Additionally, it protects the percutaneous tract, allowing a one-step PTCSL approach when feasible. The sheath also *facilitates anterograde access, reduces hospital stay duration, and lowers the risk of sepsis*, contributing to improved patient outcomes.

Keywords: Percutaneous Transhepatic Cholangioscopy (PTCS), Amplatz Sheath, The Bernoulli Effect, Percutaneous Transhepatic Cholangioscopic Lithotripsy (PTCSL)

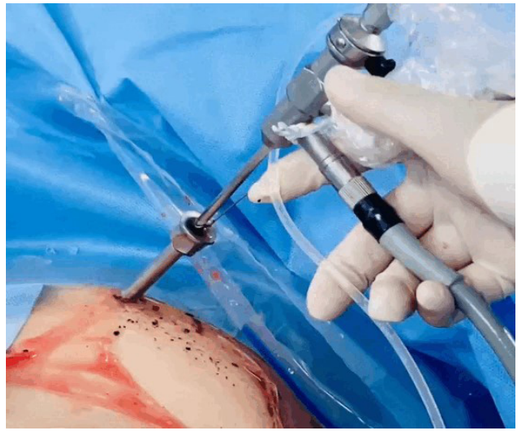

Figure 1. PTCSL.

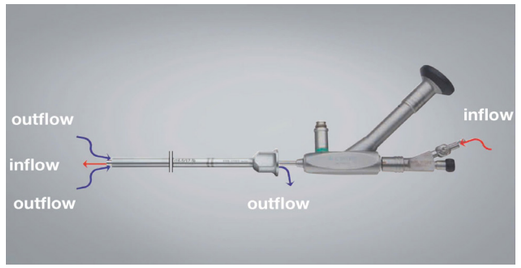

Figure 2. PTCS

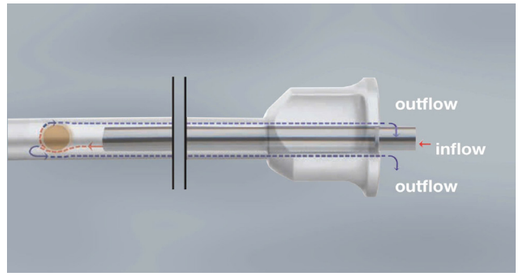

Figure 3. Bernoulli effect.

PE-11

Understanding the Lived Experiences of Patients with Pancreatic Cancer: A Systematic Literature Review on Emotional, Social, and Healthcare Challenges

Muhammad Irzaq[1], Rani Marsyanda[2]

[1]Department Art and Language, Alumnus of Padang State University, Indonesia, [2]Department of Mathematic Education, Sultan Thaha Syaifuddin, Islamic State University, Indonesia

Aims: A very aggressive cancer with a dismal prognosis, pancreatic cancer has a substantial negative impact on patients' quality of life. Improving patient-centred treatment requires an understanding of these individuals' life experiences. This systematic literature review aims to compile qualitative studies on the emotional, psychological, social, and healthcare-related difficulties faced by patients with pancreatic cancer.

Methods: Major databases such as PubMed and Scopus were thoroughly searched using keywords like "pancreatic cancer" and "patient experience". Included were studies released throughout the previous ten years. Thematic analysis was used to find important themes in the chosen studies.

Results: The results show that because of the aggressive nature of the disease and the uncertain prognosis, patients suffer from severe anxiety, sadness, and terror. According to Wancata et al. (2022), for example, patients frequently experience significant emotional difficulties during their course of treatment. Patients say they have trouble getting a prompt diagnosis, comprehending their options for therapy, and keeping lines of communication open with medical professionals. Patients and their spouses have trouble navigating the healthcare system and making wise decisions (Zhang et al., 2024). The illness impacts patients' relationships, jobs, and general social functioning, which frequently results in financial hardship and social isolation. Patients with advanced pancreatic cancer experience major disturbances in their everyday routines and social relationships (Chen et al., 2025).

Conclusions: The results highlight the need for better patient-provider communication, comprehensive psychosocial support, and increased access to healthcare for those with pancreatic cancer. Comprehending patients' experiences will help medical practitioners deliver more compassionate and patient-focused treatment, which will eventually enhance the quality of life for individuals afflicted by the illness.

Keywords: Pancreatic Cancer, Lived Experiences, Emotional And Social, Healthcare Challenges

PE-12

Gastric Partitioning Compared to Conventional Gastrojejunostomy as Palliative Surgeries in Patients with Gastric Outlet Obstruction Due to Unresectable Gastric or Pancreatic Cancers: A Pair-Wise and Individual Patient Data Meta-Analysis

Mohamed Hamouda Elkasaby[1], Atef A Hassan[1], Ahmed Mohamed Sherif Ali[2]

[1]Faculty of Medicine, Al-Azhar University, Cairo, Egypt; [2]Faculty of Medicine, Mansoura University, Mansoura, Egypt

Aims: Gastric outlet obstruction (GOO) is a severe complication of unresectable gastric and pancreatic cancers. Conventional gastrojejunostomy (CGJ) is a standard surgical intervention. Stomach-partitioning gastrojejunostomy (SPGJ) has emerged as an alternative to improve gastric emptying and enhance clinical outcomes. We conducted a meta-analysis comparing SPGJ and CGJ in patients with GOO due to unresectable gastric or pancreatic cancers.

Methods: Electronic databases were searched up to February 8, 2025. Outcomes included DGE, major postoperative complications, need for reintervention, short-term mortality, operation time, gastric outlet obstruction scoring system (GOOS), length of hospital stay (LOS), adherence to postoperative chemotherapy, and overall survival. For continuous outcomes, mean differences (MD) with 95% confidence intervals (CI) were calculated. For dichotomous outcomes, relative risks (RR) with 95% CI were reported. Reconstructed individual patient data (IPD) from Kaplan-Meier curves was utilized for survival analysis.

Results: A total of 11 studies comprising 456 patients were included. SPGJ was associated with significantly reduced DGE (RR = 0.24, 95% CI: 0.12–0.47; Fig 1) and postoperative major complications (RR = 0.26, 95% CI: 0.12–0.54; Fig 2) compared to CGJ. No significant differences were found in the need for reintervention (RR = 0.59, 95% CI: 0.21–1.64), short-term mortality (RR = 0.99, 95% CI: 0.42–2.33), or LOS (MD = -1.47 days, 95% CI: -3.10 to 0.16). GOOS scores were comparable between groups. Overall survival was also similar between SPGJ and CGJ (HR = 1.06, 95% CI: 0.66–1.70; Fig 3)

Conclusions: Our meta-analysis supports SPGJ as a superior option to CGJ for managing malignant GOO, offering significant reductions in DGE and postoperative complications, similar GOOS scores, and comparable safety regarding reintervention, short-term and long-term mortality, and LOS. High-quality RCTs are needed to confirm these findings and guide clinical practice.

Keywords: Gastric Outlet Obstruction, Unresectable Gastric or Pancreatic Cancers, Gastric Partitioning, Conventional Gastrojejunostomy

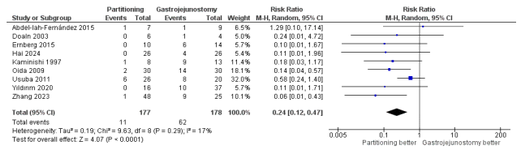

Figure 1. DGE.

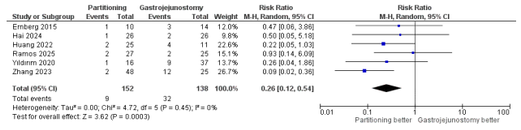

Figure 2. Compliacations.

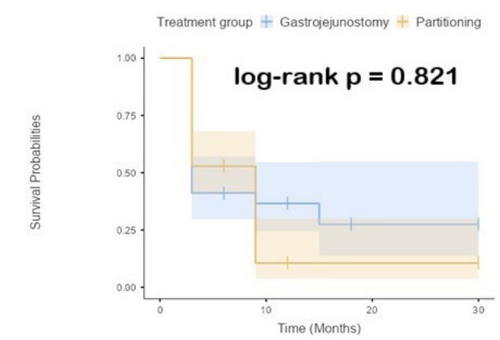

Figure 3. Picture1.

PE-13

Near-Infrared Fluorescence Cholangiography Using Indocyanine Green in Laparoscopic Cholecystectomy; A Meta-Analysis of Visualization Rates and Complications

Mohamed Hamouda Elkasaby[1], Atef A Hassan[1], Ahmed Mohamed Sherif Ali[2]

[1]Faculty of Medicine, Al-Azhar University, Cairo, Egypt; [2]Faculty of Medicine, Mansoura University, Mansoura, Egypt

Aims: Laparoscopic cholecystectomy (LC) is one of the most performed surgeries worldwide. Biliary tract injuries are among

the most feared complications after LC. The primary cause of biliary injuries during LC is the incorrect identification of the biliary tract anatomy. Near-infrared fluorescence (NIRF) imaging, following intravenous (IV) injection of indocyanine green (ICG), shows promise for simplifying the intraoperative visualization of biliary anatomy. This technique enables real-time identification of the cystic duct and common bile duct, potentially enhancing the outcomes of LC. This systematic review and meta-analysis aimed to investigate the effects of NIRF-ICG on LC outcomes.

Methods: This meta-analysis followed the Cochrane Handbook for Systematic Reviews of Interventions guidelines. We searched PubMed, Embase, Cochrane Library, Web of Science, and Scopus until December 23rd, 2024. We included randomized-controlled trials and retrospective studies comparing NIRF-ICG LC and conventional LC. Statistical analysis was performed using Review Manager 5.3 software.

Results: Results: Fifteen studies with 1581 patients (41.1%) in the NIRF-ICG group and 2264 (58.9%) in the control group were included. The NIRF-ICG was associated with statistically significant reduced overall complications, bile leakage, and duct drainage (risk ratio (RR) = 0.62, 95% CI: [0.40, 0.95], *P*=0.03; Fig 1), (RR = 0.34, 95% CI: [0.14, 0.83], *P*=0.02; Fig 2), and (RR = 0.64, 95% CI: [0.44, 0.91]), *P*=0.01; Fig 3), respectively. Common bile duct (CBD), cystic duct- CBD junction, and common hepatic duct visualization rates were better with the NIRF-ICG, (RR= 3.67, 95% CI: [2.62, 5.15], *P*<0.001), (RR = 3.00, 95% CI: [2.03, 4.43], *P*<0.001), and (RR = 2.87, 95% CI: [1.94, 4.25], *P*<0.001), respectively. There was no significant difference in cystic duct visualization rate (RR = 1.40, 95% CI: [0.71, 2.78], *P*=0.33).

Conclusions: NIRF following administration of ICG in LC offers better visualization of biliary tract anatomy and is associated with reduced overall complications, bile leakage, and bile duct drainage.

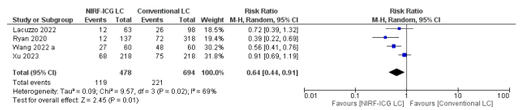

Figure 3. Duct Drainage.

Keywords: Laparoscopic Cholecystectomy, Near-Infrared Fluorescence Cholangiography, Indocyanine Green

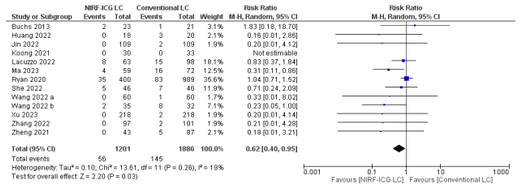

Figure 1. Complications.

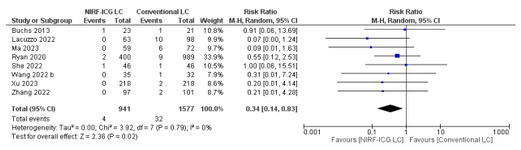

Figure 2. Bile leakage.

PE-14

Mini-incision Cystogastrostomy for Management of Giant Pancreatic Pseudocysts: Preliminary Results on a Case Series

Le Trung Hieu, Le Van Thanh, Vu Van Quang, Nguyen Van Quynh, Tran Manh Thang

Department of HBP Surgery, 108 Military Central Hospital, Vietnam, Department of HBP Surgery, 175 Military Hospital, Vin University, Vietnam

Aims: Pancreatic pseudocysts, complications of pancreatitis, often necessitate intervention when symptomatic or large. While endoscopic and open surgical cystogastrostomy are established treatments, mini-incision cystogastrostomy (MIC) is a hybrid technique that combines surgical precision with minimal invasiveness, potentially benefiting resource-limited settings.

Methods: A retrospective study of five patients with giant pancreatic pseudocysts (14–19 cm diameter) treated with MIC between September 2020 and June 2024 was conducted. Preoperative imaging, including abdominal ultrasound and CT scans, guided surgical planning. A small epigastric incision allowed direct visualization for secure cystogastrostomy. Data on demographics, surgical details, and postoperative outcomes were analyzed, and findings were compared with literature on alternative techniques.

Results: The cohort comprised four males and one female (age range: 18–50 years). The mean operative time was 45 minutes (range: 35–60 minutes), and no intraoperative complications occurred. Patients experienced complete symptom resolution, with a mean hospital stay of 4.6 days (range: 4–6 days). Follow-up over 24 months revealed no recurrences or complications. MIC provided secure anastomosis under direct visualization, combining the advantages of minimal invasiveness with surgical efficacy.

Conclusions: MIC is a feasible and effective option for giant pancreatic pseudocysts, particularly where advanced endoscopic tools are unavailable. This technique balances the precision of surgery with reduced invasiveness, supporting enhanced recovery and symptom resolution.

Keywords: Mini-Incision Cystogastrostomy, Giant Pancreatic Pseudocysts

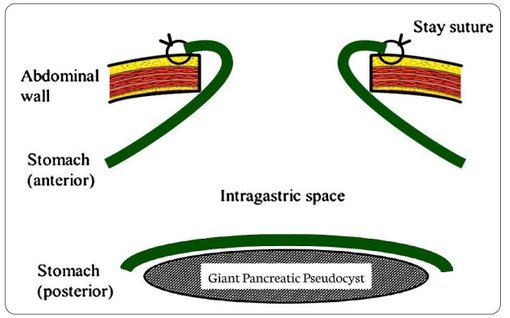

Figure 1.

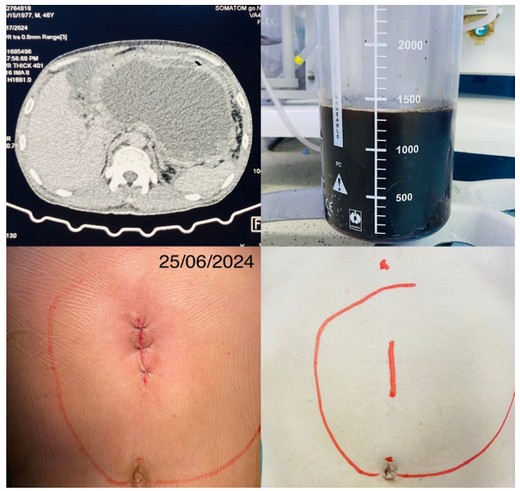

Figure 2.

PE-15

Modified Laparoscopic Left Lateral Segmentectomy for the Management of Left-Sided Hepatolithiasis

Le Trung Hieu, Le Van Thanh, Vu Van Quang, Nguyen Van Quynh, Tran Manh Thang

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Aims: Hepatolithiasis remains a significant health burden in the Asia-Pacific region, predominantly affecting the left hepatic segments. While liver resection is the primary treatment, high recurrence and bile leakage rates persist. This study aimed to evaluate the safety and efficacy of a modified laparoscopic left lateral segmentectomy technique.

Methods: A retrospective review of 21 patients undergoing laparoscopic left lateral segmentectomy with a transection line right of the falciform ligament for left-sided hepatolithiasis between August 2023 and November 2024 was conducted. Patient demographics, surgical details, postoperative outcomes, residual stone rates, and recurrence rates were analyzed.

Results: Mean operative time was 136.3 ± 41.5 minutes, with an average blood loss of 115.0 ± 52.3 ml. Postoperative complications occurred in 9.5% of patients, including Clavien-Dindo grade I (4.7%) and IIIa (4.7%). The mean postoperative hospital stay was 7.5 ± 3.4 days.

Conclusions: The modified laparoscopic left lateral segmentectomy with a transection line on the right side of the falciform ligament is a safe, feasible, and effective method for managing left-sided hepatolithiasis and may improve surgical outcomes.

Keywords: Modified Laparoscopic Left Lateral Segmentectomy, Left-Sided Hepatolithiasis

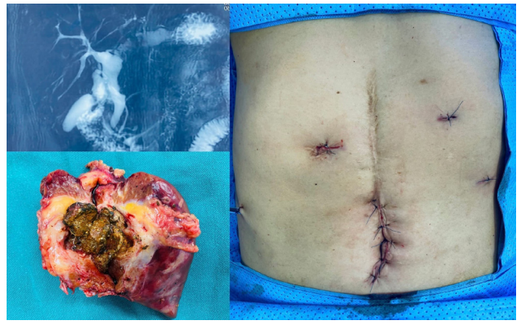

Figure 1.

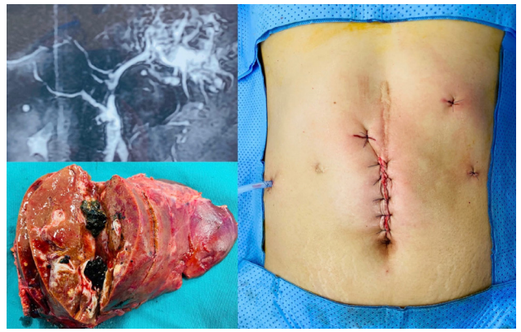

Figure 2.

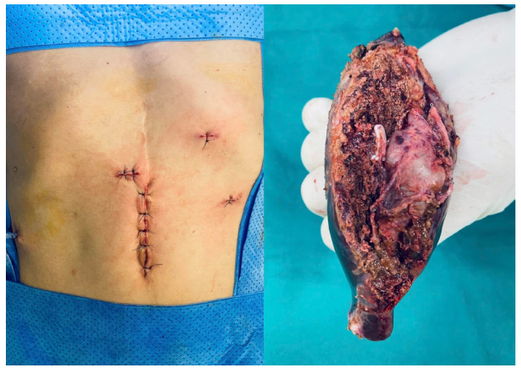

Figure 3.

PE-16

Percutaneous Gelfoam Slurry Injection in the Management of Hemobilia Following Percutaneous Biliary Intervention: A Case Series and Review of Literature

Ho Chi Linh[1], Pham Hai Trieu[2], Nguyen Ta Quyet[3]

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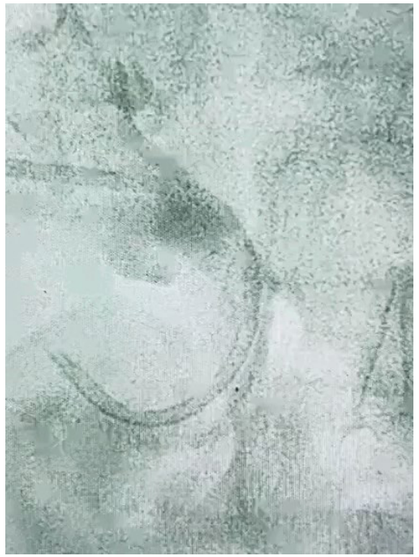
Aims: Percutaneous biliary intervention can be associated with high rates of different adverse events, including hemobilia. Conventional management of hemobilia generally includes surgery or endovascular embolization. However, its application may be limited by logistical delays, particularly in emergent scenarios where immediate hemostasis is required.

Methods: In this case series, we retrospectively reviewed eight cases of acute hemobilia following percutaneous biliary interventions. All patients were successfully treated with percutaneous Gelfoam slurry injection into the biliary duct.

Results: Over a two-year period, percutaneous Gelfoam slurry injection was performed for the management of hemobilia in eight patients, following percutaneous transhepatic biliary drainage, percutaneous transhepatic cholangioscopic lithotripsy, and percutaneous transhepatic biliary stenting in 3, 3, and 2 cases, respectively. All cases presented with immediate hemorrhage during the initial procedure. Major hemobilia was observed in three cases, one of which resulted in hemodynamic collapse. In one patient, follow-up cholangioscopy approximately three weeks after surgery confirmed the absence of Gelfoam within the biliary tract. One patient died 15 days after the procedure due to pneumonia in the setting of end-stage pancreatic cancer; however, hemobilia had resolved prior to death.

Conclusions: Percutaneous gelfoam slurry injection into the biliary duct represents a promising and minimally invasive technique for the rapid control of major hemobilia following percutaneous biliary interventions. This case series highlights its potential role as an emergency measure when conventional methods are either impractical or unavailable.

Keywords: Gelfoam Slurry, Percutaneous Biliary Intervention, Hemobilia



PE-17

Comparative Analysis on the Efficacy and Accuracy of EUS, ERCP, MRI, and CT Scans in the Management of Pancreatic Disease

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Aims: Pancreatic diseases, particularly pancreatic cancer and chronic pancreatitis, require precise imaging for early diagnosis and effective management. EUS, ERCP, MRI, and CT scans play distinct roles in evaluating pancreatic conditions. However, discrepancies in their diagnostic accuracy and clinical efficacy necessitate a comparative analysis. This study seeks to systematically evaluate the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each modality. By incorporating a robust methodological approach, we aim to determine the most effective imaging technique for pancreatic disease management.

Methods: This study employs a systematic review with a comparative analysis approach, adhering to PRISMA guidelines. Databases from PubMed, Scopus, and Web of Science were searched for relevant peer-reviewed articles published in the last ten years. Dependent variables includes diagnostic accuracy (sensitivity, specificity, PPV, and NPV) and efficacy in management (rate of successful diagnosis). Independent variables includes imaging modalities (EUS, ERCP, MRI, CT Scan), patient demographics (age, gender, comorbidities), and disease type (pancreatitis, pancreatic cancer, cysts, other benign lesions). Control variables includes operator experience, patient BMI, and hospital type.

Results: Descriptive statistics depoct that EUS had the highest mean sensitivity (92.5%) and specificity (88.3%) with low SD, indicating consistent accuracy across studies. CT scan had the lowest sensitivity (81.2%) and specificity (79.3%), showing it is less reliable compared to the other modalities. ERCP had a higher variability (SD of 2.0 and 2.5), meaning its performance fluctuates across studies. Regression analysis shows that EUS had the highest coefficient (β = 1.85, P<0.001), meaning it has the strongest positive impact on correct diagnosis. ERCP and MRI were statistically significant but had lower coefficients than EUS. CT scan had the lowest coefficient (β = 0.78), meaning it is the least reliable for correct diagnoses. BMI had a negative coefficient (-0.45), showing that higher BMI reduces imaging accuracy. Operator experience positively impacted diagnostic accuracy (β = 0.62, P<0.001).

Conclusions: EUS demonstrated superior diagnostic accuracy and efficacy in managing pancreatic diseases, making it the preferred modality for early detection. ERCP remains essential for therapeutic intervention, while MRI provides a non-invasive alternative with high accuracy. CT scans, although widely available, exhibit lower specificity and sensitivity compared to other modalities. Further studies should explore cost-effectiveness and patient accessibility factors to enhance decision-making in clinical practice.

Keywords: Pancreatic Disease, Diagnostic Accuracy, Imaging Modalities, EUS

Variable	Coefficient (β)	Standard Error	p-value	Interpretation
EUS	1.85	0.12	<0.001	EUS significantly improves diagnostic accuracy.
ERCP	1.12	0.15	0.008	ERCP is beneficial but less effective than EUS.
MRI	1.38	0.14	0.002	MRI provides a good diagnostic alternative.
CT Scan	0.78	0.18	0.035	CT scan has the lowest impact on diagnostic accuracy.
BMI	-0.45	0.09	0.021	Higher BMI negatively affects imaging accuracy.
Operator Experience	0.62	0.07	<0.001	More experienced operators produce better results.

Figure 1. Comparative Analysis on the Efficacy and Accuracy of EUS, ERCP, MRI, and CT Scans in the Management of Pancreatic Disease.

PE-18

Magnet-Assisted Biliary Reconstruction: A Paradigm Shift in Minimally Invasive Hepatobiliary Surgery

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Aims: Traditional hepaticojejunostomy remains the cornerstone for biliary reconstruction following complex bile duct injuries; however, it is associated with significant postoperative morbidity, anastomotic stricture formation, and prolonged recovery. Magnet-assisted biliary anastomosis (MABA) has emerged as a novel, minimally invasive alternative, leveraging controlled magnetic compression anastomosis (MCA) to achieve precise and reproducible ductal continuity without the need for extensive suturing. This systematic review critically evaluates the safety, efficacy, and long-term outcomes of MABA, with a focus on its potential to replace conventional surgical techniques in hepatobiliary reconstruction.

Methods: A systematic literature review was conducted following PRISMA guidelines across PubMed, Embase, Scopus, and the Cochrane Library. The search strategy incorporated MeSH terms and free-text keywords, including *magnet-assisted anastomosis*, *biliary stricture management*, *magnetic compression anastomosis*, and *hepaticojejunostomy alternatives*. Inclusion criteria encompassed randomized controlled trials, cohort studies, and case-control studies evaluating MABA in both benign and malignant biliary pathologies. Exclusion criteria included animal studies, case reports with <5 patients, and non-peer-reviewed publications. Two independent reviewers extracted data on technical success, anastomotic patency, complication rates, and long-term biliary function. A meta-analysis was performed where data homogeneity permitted, and risk of bias was assessed using the Newcastle-Ottawa Scale and Cochrane risk-of-bias tool.

Results: Thirty-five studies met inclusion criteria, comprising 1,482 patients undergoing MABA for benign biliary strictures (n=927), post-cholecystectomy bile duct injuries (n=389), and malignant biliary obstructions (n=166). The pooled analysis demonstrated a high anastomotic success rate (89.4%) with significantly reduced operative duration (mean reduction of 52 minutes; P<0.001) compared to hepaticojejunostomy. Anastomotic patency at 24 months post-reconstruction was 92.6%, outperforming traditional surgical techniques. The incidence of anastomotic stricture was notably lower in the MABA group (4.7%) versus hepaticojejunostomy (12.1%), with a hazard ratio of 0.39 (95% CI: 0.21–0.68). Postoperative complications, including bile leak (3.2%) and cholangitis (5.5%), were comparable between groups, while magnet migration occurred in 2.1% of cases. Notably, biodegradable magnetic stents exhibited superior biointegration, reducing the risk of residual foreign

body reactions.

Conclusions: Magnet-assisted biliary reconstruction represents a transformative advancement in hepatobiliary surgery, offering a minimally invasive, suture-free alternative to conventional hepaticojejunostomy. The technique demonstrates superior anastomotic patency, reduced operative morbidity, and enhanced postoperative recovery. The integration of bioresorbable magnetic implants and endoscopic-assisted deployment further refines its clinical applicability. While current evidence underscores its feasibility and safety, large-scale, multi-center randomized trials are warranted to establish definitive clinical guidelines and long-term outcomes. The confluence of magnetic surgical innovation with hepatobiliary reconstruction heralds a paradigm shift toward precision-based biliary surgery.

Keywords: Magnetic Compression Anastomosis (MCA), Magnet-Assisted Biliary Anastomosis (MABA), Biointegration, Hepaticojejunostomy

PE-19

Integration of Multiple Preoperative Serum Biomarkers Using Decision Tree Analysis Enhances Outcome Prediction in Resectable Gallbladder Cancer

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[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Naval Medical University, Shanghai, China; [2]Department of Hepatobiliary Surgery, Affiliated Hospital of Nantong University, Nantong, China; [3]Department of Liver Transplantation And Hepatic Surgery, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, China

Aims: Current prognostic assessment for gallbladder cancer (GBC) relies heavily on postoperative pathological findings. This study aimed to develop practical preoperative risk stratification models using readily available biomarkers to predict surgical outcomes in resectable GBC.

Methods: A retrospective analysis included 308 patients undergoing curative resection for GBC across two hepatobiliary centers (discovery cohort: n=216; validation cohort: n=92). Decision tree models incorporating preoperative biomarkers were developed through classification and regression tree analysis. Model performance underwent evaluation using C-index calculation and calibration plots.

Results: The overall survival model identified CEA, CA12-5, and total bilirubin as key determinants, while CEA, CA19-9, and total bilirubin proved crucial for recurrence-free survival prediction. In the validation cohort, the models effectively stratified patients into distinct risk groups with significantly different 3-year overall survival rates (81.0%, 67.1%, and 0% for low-, intermediate-, and high-risk groups; $P<0.001$) and recurrence-free survival rates (82.9%, 48.1%, and 0%, respectively; $P<0.001$). Model performance remained robust across various clinical subgroups, demonstrating excellent calibration (integrated Brier score: 0.236 for overall survival, 0.280 for recurrence-free survival).

Conclusions: These novel decision tree models effectively stratify patients with resectable GBC into distinct prognostic groups using readily available preoperative biomarkers. Integration with clinical parameters enables more accurate risk assessment, potentially facilitating individualized treatment strategies and improving patient selection for surgical intervention.

Keywords: Gallbladder Cancer, Decision Tree Analysis, Outcome Prediction

PE-20

Single Port Robotic Assisted Cholecystectomy and Common Bile Duct Exploration: Initial Experience

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Aims: Analisis of the feasibility, safety and short-term outcome of single port robotic-assisted cholecystectomy with common bile duct (CBD) exploration for complicated biliary stone with the Da Vinci SP system.

Methods: From June 2024 to December 2024, five consecutive patients (3 M, 2 F) underwent single port robotic-assisted cholecystectomy and CBD exploration in our Center, four as emergency and one as elective procedures. Data on patient demographics, perioperative investigations, surgical procedures and postoperative outcomes were retrospectively analyzed.

Results: Five consecutive patients were identified, including three males and two females. The median age was 74 (49–89) years. Four patients underwent emergency surgical procedures and one underwent elective surgery.Median BMI was 23.3(20-24.2). Median total bilirubin was 37umol/L (16–56). Median CBD diameter was 10mm (7-15). Median operative time was 176 (76–365) minutes. Total bleeding was within 10ml. The clearance rate of common bile duct stones was 100%. No peritoneal or biliary drainage was used. No postoperative complications were recorded and the median postoperative length of stay was 5 (1–8) days.

Conclusions: Our initial experience confirmes single port robotic assisted cholecystectomy and CBD exploration as a feasible, safe and effective treatment for synchronous GB and CBD lithiasis. Additionally, single port robotic system provides better cosmetic results than conventional robotic systems, and may reduce the learning curve for complex procedures.

Keywords: Biliary Lithiasis, Common Bile Duct Exploration, Single Port Robotic Surgery

PE-21

Uncommon Presentation: Case Report of Pancreatic Tumor in a Young Patient

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General Surgery, Physician, Philippines

Aims: Pancreatic tumors in children are rare, with a prevalence estimated at 1–2 cases per ten million children and adolescents in the United States. In our locality, no available record exists dealing with pancreatic tumors in the pediatric setting, including our institution. This case report highlights a rare instance of a mid-adolescent patient presenting with severe left upper quadrant abdominal pain, ultimately leading to the discovery of a pancreatic mass. The limited literature posed challenges for preoperative planning and decision-making.

Methods: Work up included routine laboratories and imaging for clearance and a CT scan with pancreatic protocol. The surgical plan was open frozen section biopsy, distal pancreatectomy with splenectomy. Calculated caloric intake was made for nutritional build-up. Incentive spirometry was started, and patient was referred to rehabilitation for functional build-up. After resectability has been established, risk stratification and clearance for surgical intervention was requested. The patient underwent exploratory laparotomy with distal pancreatectomy, splenectomy with intraoperative frozen section.

Results: Final histopathology result revealed a diagnosis of Pancreatic Neuroendocrine Tumor, Oncocytic variant, WHO Grade II. Pancreatic neuroendocrine tumors (NET), also known as islet cell tumors, account for 2% of all pancreatic neoplasms and 5%–10% of all pediatric pancreatic tumors.

Conclusions: Pancreatic cancer is typically regarded as a disease that occurs in adulthood. A high clinical suspicion is warranted for pediatric cases highlighting the importance of screening protocols for individuals with hereditary conditions or a family history linked to pancreatic cancer for this age group.

Keywords: Pancreas, Tumor, Pediatrics

PE-22

Clinical Pattern & Postoperative Outcome of Whipples Patient for Solid Pseudopapillary Tumour of Pancreas in Tertiary Care Hospital In Bangladesh- A Retrospective Observational Study

Anharur Rahman

Surgery, Associate Professor, Bangladesh

Aims: Solid pseudopapillary tumor of the pancreas is rare neoplasm with low malignancy and favorable prognosis post-surgery. Aim to asses clinical pattern & postoperative outcomes of SPT patients undergoing Whipple procedure at Bangabandhu Sheikh Mujib Medical University, Lab Aid Hospital.

Methods: This retrospective observational study included 35 patients diagnosed with SPT over five years. Data on clinical presentations, imaging findings, surgical interventions. Postoperative outcomes were extracted from medical records. Descriptive statistics summarized demographics and clinical features. Inferential analyses, including chi-square tests and Kaplan-Meier survival analysis, evaluated associations between variables and outcomes. Multivariate regression identified predictors of postoperative complications and survival.

Results: Among 35 patients, 85.7% were female with a median age of 28 years (18-45). Presentations included abdominal pain (60%), palpable mass (25%), and incidental findings (15%). The Whipple procedure was performed in 40%, and distal pancreatectomy in 60%. Postoperative complications occurred in 34%, including pancreatic fistula (20%), delayed gastric emptying (10%), and infections (4%). The five-year overall survival rate was 95%, with no tumor recurrence. Complete surgical resection significantly improved survival ($P<0.01$, HR=0.2, 95% CI: 0.05-0.8). Patients without complications had higher quality of life scores (85 vs. 70, $P<0.05$). Average hospital stay 15 days (SD $\pm$5). Surgical margin status ($P=0.02$, OR=3.5) and tumor size ($P=0.03$, OR=2.1) were significant predictors of morbidity. Kaplan-Meier analysis showed longer disease-free survival for negative surgical margins ($P=0.01$).

Conclusions: The Whipple procedure effectively treats SPT of the pancreas in Bangladesh, with excellent survival & low recurrence.Outcomes are improved by complete resection and managing postoperative complications.

Keywords: Solid Pseudopappilary Tumour, Whipple's Surgery, Clinical Pattern

PE-23

Evaluated the Effectiveness of Rutin in Treating Diabetes Mellitus Using an Experimental Rat Model

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Aims: Diabetes mellitus is a metabolic disorder marked by elevated blood glucose levels and biochemical changes related to glucose and lipid peroxidation. This condition generates free radicals that cause lipid peroxidation, which serves as a marker for oxidative stress in the body. A common method to measure lipid peroxidation is by assessing malondialdehyde levels. The body's defense system includes antioxidant en-

zymes that help neutralize free radicals. Among these enzymes are reduced glutathione and superoxide dismutase. Rutin, a bioflavonoid derived from the flavonol quercetin and the disaccharide rutinose, is present in various plants and fruits such as citrus fruits, apples, and buckwheat. Known for its anti-inflammatory, antiproliferative, and antioxidant properties, rutin mitigates oxidative stress by scavenging reactive oxygen species (ROS). By lowering ROS levels, rutin can reduce oxidative stress in neurons and help manage neuropathy, including auditory neuropathy, in diabetic patients.

Methods: Forty diabetic rats were randomly divided into the following groups: group 1 (control), group 2 (diabetic rats), and groups 3–5 (rats treated with rutin at doses of 50, 100, and 150 mg/kg, respectively). We assessed the impact of the treatment by measuring levels of malondialdehyde (MDA), total superoxide dismutase (SOD), and reduced glutathione (GSH).

Results: The rutin-treated groups showed significant improvements in diabetes mellitus compared to the diabetic control group (P<0.05). Treatment with rutin led to notable enhancements in SOD and GSH and reductions in MDA activity.

Conclusions: Rutin demonstrates potential as a treatment for diabetes mellitus, though further clinical trials are needed to establish its efficacy in a rat model.

Keywords: Rutin, Diabetes Mellitus, Blood Glucose

PE-24

The Role of Microrna in Biliary Atresia Pathogenesis

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ACS Medical College and Hospital, India

Aims: Biliary atresia is a severe neonatal condition with unknown etiology. Emerging evidence suggests microRNAs (miRNAs) may regulate disease progression.

Methods: Serum miRNA profiles from 100 infants with biliary atresia were compared to healthy controls. Functional studies were performed using animal models.

Results: miR-34a and miR-21 were significantly upregulated in biliary atresia and promoted fibrosis in animal models. Inhibitors of these miRNAs reduced fibrosis by 40%.

Conclusions: Targeting dysregulated miRNAs offers a novel therapeutic avenue for biliary atresia, improving outcomes for affected infants.

Keywords: Biliary Atresia, Neonatal Liver Disease, Molecular Therapy

PE-25

3D-Printed Pancreatic Scaffolds for Diabetes Treatment

Nandha Kumar

ACS Medical College and Hospital, India

Aims: Pancreatic islet transplantation is limited by donor shortages. 3D-printed scaffolds aim to create functional pancreatic tissue for diabetes treatment.

Methods: Scaffolds with biocompatible hydrogels seeded with insulin-producing beta cells were tested in vitro and in diabetic mouse models.

Results: The scaffolds maintained 80% cell viability and normalized glucose levels in mice for 12 weeks.

Conclusions: 3D-printed pancreatic scaffolds represent a groundbreaking approach to treating diabetes, reducing reliance on donor organs.

Keywords: PANCREATIC SCAFFOLDS, REGENERATIVE MEDICINE, 3D PRINTING,

PE-26

Pancreatic Tuberculosis Masquerading as Pancreatic Cancer: A Rare Case Report

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Aims: Tuberculosis is highly prevalent in developing countries, however isolated pancreatic tuberculosis is rare. Due to its rarity, most available literature is limited to case reports and case series.

Methods: The authors wish to report a 79 years old fit gentleman who was an ex-hospital staff presented with abdominal discomfort and constitutional symptoms for a year duration. Investigation including ct imaging geared toward pancreatic head malignant tumor.

Results: He underwent whipple procedure after biliary drainage procedure and surgery went well with no major complications. Histopathological report comes back consistent with inflammatory mass of tuberculosis in origin. Patient was started on anti-tubercular medications.

Conclusions: Pancreatic tuberculosis can mimic malignancy in both clinical and radiological aspect. Histology confirmation is needed to establish diagnosis. Early recognition and diagnosis coupled with multimodal treatment can improve outcome.

Keywords: Pancreatic Tuberculosis, Pancreatic Cancer, Tuberculosis

PE-27

Totally Laparoscopic Pancreaticoduodenectomy: First Case Reported in Mongolia

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Aims: Approximately 48,960 people in the USA will be diagnosed with pancreatic cancer in 2015 and 40,560 will die for this reason; In Mongolia, the new cases of pancreatic cancer in 2021 were 850, with 460 deaths; Less than 20% of cases were considered resectable at the time of diagnosis. The Whipple procedure is currently the only curative treatment option for periampullary cancers since the first communication by Whipple in 1935, and up until now is a common procedure in several reference centres around the world. In 1994, Gagner reported the first totally laparoscopic pancreaticoduodenectomy. The objective of this study was to make known our initial experience with a pancreatoduodenectomy performed entirely laparoscopic ally, and the surgical technique we used in the first central Hospital of Mongolia.

Methods: The case concerns a 58 year-old man with jaundice and loss of weight of 3 months onset. Weight 64 kg, height: 160 cm Her biopsy reported adenocarcinoma of Váter's ampulla, and as it was considered resectable, she underwent a laparoscopic pancreaticoduodenectomy.

Results: Totally laparoscopic pancreaticoduodenectomy surgery

Conclusions: From our point of view, this type of procedure should be performed in centres with experience in open pancreatic surgery, with training in advanced laparoscopic surgery and following a strict protocol. The real advantages of this approach for the Whipple procedure are principally the reduced transoperative blood loss and shorter hospital stay. The long-term outcomes of this type of surgery as treatment for pancreatic and bile duct tumours remain unknown.

Keywords: Bile Duct, Whipple, Laparoscopy

PE-28

Economic Analysis of Cost-Benefit in Pancreatic Cancer Treatment, Therapeutic Efficacy, and Socioeconomic Outcomes

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Aims: Pancreatic cancer is one of the most lethal malignancies with a low survival rate. The economic burden associated with its treatment is substantial, necessitating an in-depth analysis of cost-benefit and therapeutic efficacy. This study aims to quantify these aspects and assess the socioeconomic outcomes for patients undergoing different treatment modalities.

Methods: This study uses data from WHO, UNDP, World Bank, and published studies in medical journals. Variables include treatment costs, survival rates, quality-adjusted life years (QALYs), direct and indirect costs, SES, and demographic variables. In-depth analysis using multiple regression model (Cost-Benefit Analysis), logistic regression (Therapeutic Efficacy), and linear regression (Socioeconomic Outcomes).

Results: The average cost of pancreatic cancer treatment was found to be $100,000 (SD=$30,000), median survival rate post-treatment was 12 months (5-year survival rate: 10%), and average QALYs were 1.5 years. CBA using regression model showed a significant positive correlation (P<0.05) between higher treatment costs and increased QALYs, indicating that more expensive treatments tend to provide better quality-adjusted life years. Therapeutic efficacy usin logistic regression indicated that patients undergoing combination therapies had a higher likelihood of survival (OR=2.5, P<0.01) compared to those receiving monotherapy. Socioeconomic outcomes revealed that lower socioeconomic status was associated with higher treatment costs and lower survival rates (β=-0.3, P<0.05).

Conclusions: This study underscores the importance of economic evaluations in pancreatic cancer treatment, demonstrating the need for cost-effective and equitable healthcare solutions. Future research should focus on longitudinal studies and the inclusion of more diverse populations to validate these findings.

Keywords: Health Economics, Pancreatic Cancer Treatment, Quality of Life

PE-29

Optimizing Biliary Drainage Success in Malignant Biliary Obstruction: A Machine Learning-Driven Approach Integrated with Endoscopic Ultrasound

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Aims: Malignant biliary obstruction (MBO), commonly associated with hepatopancreatobiliary cancers, often necessitates biliary drainage to alleviate symptoms. Endoscopic ultrasound (EUS) plays a pivotal role in both diagnosing and managing MBO. Incorporating machine learning (ML) with EUS offers a promising avenue to improve the accuracy of predicting drain-

age success. This study evaluates the predictive value of ML models combined with EUS for biliary drainage outcomes in MBO patients.

Methods: A retrospective analysis of 90 MBO patients undergoing EUS-guided biliary drainage (2021–2023) was conducted. Clinical, radiological, and procedural data were collected. ML models—logistic regression, random forest, and neural networks—were trained on 70% of the dataset and validated on 30%. Successful drainage was defined as a >50% bilirubin reduction within 7 days. Model performance was assessed using AUC, and key predictors were identified through statistical analysis.

Results: Among the 90 patients, the random forest model demonstrated superior accuracy (AUC: 0.89, 95% CI: 0.82–0.95) compared to logistic regression (AUC: 0.79, P=0.002) and neural networks (AUC: 0.84, P<0.001). Successful drainage was achieved in 72 patients (80%), with tumor size (OR: 1.45, P=0.004), stent placement (OR: 2.12, P<0.001), and baseline bilirubin (OR: 1.28, P=0.01) identified as key predictors. Complication rates were lower in patients with successful drainage (15% vs. 32%, P=0.03).

Conclusions: Integrating ML, particularly random forest models, with EUS significantly improves the prediction of biliary drainage success, offering a valuable tool for optimizing MBO management.

Keywords: Malignant Biliary Obstruction, Endoscopic Ultrasound, Machine Learning

PE-30

A Rare Case of Gallbladder Hypoplasia: Diagnostic Challenges and Surgical Management

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Aims: Gallbladder hypoplasia is a rare congenital anomaly first described by Lemery in 1701. It develops from failure of normal development of the cystic bud in utero which usually forms at 6 weeks age of gestation from the caudal part of the foregut. We present a case of a 46 year old male, previously a known case of contracted gallbladder with mild common bile duct dilatation presenting with 1 day history of epigastric to right upper quadrant pain, boring in character, radiating to the back. The patient was managed as a case of mild gallstone pancreatitis and underwent Endoscopic Retrograde Cholangiopancreatography (ERCP), which revealed gallbladder sludge. The patient was then scheduled for early laparoscopic cholecystectomy. Intraoperatively, we noted adhesions towards the supposed gallbladder fossa. Upon adhesiolysis, we noted an absent gallbladder. Further dissection and ultimately adjunctive measures, such as intraoperative ultrasound, were done, but even this did not reveal any evidence of a gallbladder. The patient was then discharged and was worked up with Magnetic Resonance Imaging - Magnetic Resonance Cholangiopancreatography, this revealed a 13 mm, thin, bud-like structure adjacent to the common hepatic duct. An impression of Gallbladder Hypoplasia was made.

Methods: A case report will be presented. The patient's data were retrieved and reviewed from the SegHIS database and the medical records of Southern Philippines Medical Center.

Conclusions: This case emphasizes the importance of thorough preoperative diagnostic workup in rare biliary anomalies like gallbladder hypoplasia. Accurate diagnosis is essential to avoid unnecessary intervention and to ensure optimal surgical management.

Keywords: Gallbladder, Hypoplasia, Management

PE-31

Distal Pancreatosplenectomy with Metastasectomy and Perioperative Chemotherapy in a 59-Year-Old Male with Pancreatic Tail Adenocarcinoma and Liver Oligometastasis

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Aims: Majority of pancreatic adenocarcinoma are metastatic at the time of diagnosis. Current guidelines do not recommend definitive surgery for metastatic pancreatic cancers. We report a case of a 59-year-old male with pancreatic tail adenocarcinoma with liver oligometastasis. Patient received two cylces of neoadjuvant FOLFORINOX which showed partial tumor response. Patient eventually underwent open distal pancreatectomy with splenectomy and metastasectomy of segments 5 and 6 liver nodules. Post-operatively another 4 cycles of FOLFORINOX were given. Surveillance imaging 8 months after the surgery showed absence of tumor recurrence and no evidence of metastatic disease. Tumor marker (CA19-9) also decreased after the surgery and chemotherapy.

Conclusions: Resection of the primary tumor and metastatic lesions in stage IV pancreatic adenocarcinoma may be considered in highly selected patients. Patients with at least partial tumor response after neoadjuvant chemotherapy, as well as the decreasing level of CA19-9 may be considered in offering definitive surgery with metastasectomy for patients with pancreatic adenocarcinoma with liver oligometastasis.

Keywords: Metastatic Pancreatic Adenocarcinoma, Liver Oligometastasis, Distal Pancreatectomy

PE-32

Features of Relaparoscopy in Case of Bile Leakage after Surgery on the Liver and Bile Ducts

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Aims: To determine the features of performing relaparoscopy in patients with bile leakage after operations on the liver and bile ducts.

Methods: The study is based on the analysis of laparoscopic correction of postoperative bile leakage in 11 patients who had previously undergone liver surgery (n=3) and bile duct surgery (n=8). Liver surgery included open echinocolectomy, bile duct surgery included laparoscopic (n=3) and traditional cholecystectomy (n=5). Women accounted for 63.6%, men – 36.4%. Diagnosis of bile leakage was based on the release of bile from the drainage tube and radiological examination methods such as ultrasound, CT and MRI.

Results: In 6 (63.6%) cases of postoperative bile leakage from the gallbladder bed and Luschka ducts, coagulation of the gallbladder bed (n=4) and reclipping of the Luschka ducts (n=2) were performed during relaparoscopy. In 1 (9.1%) case, the cause of postoperative bile leakage was the loss of clips from the cystic duct. In this case, reclipping of the cystic duct was performed with sanitation and drainage of the abdominal cavity. Combined biendoscopic intervention was performed in 1 (9.1%) patient with postoperative bile leakage and stenosis of the major duodenal papilla. At the first stage, relaparoscopy with sanitation and drainage of the abdominal cavity was performed, at the second - endoscopic papillosphincterotomy. In the postoperative period, purulent-septic complications in the main group occurred in 1 (9.1%) patient. The postoperative hospital stay was 6.9±1.3 days.

Conclusions: According to indications, relaparoscopic correction of bile leakage after operations on the liver and bile ducts is the method of choice.

Keywords: Relaparoscopy, Postoperative Bile Leakage, Liver and Bile Duct Surgeries

6. HBV, Basic

PE-1

Mitigating Hepatitis B Mother-to-Child Transmission through Early Detection and Prophylaxis; A Prospective Study at a Tertiary Care Center

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Aims: Hepatitis B virus is the most common viral cause of hepatitis globally. In India, HBsAg prevalence ranges from 1.1% to 12.2%, with an average of 3-4%. Perinatal transmission is the most common route of HBV infection often leading to lifelong infections in the affected. Vertical transmission risk in the case of HBsAg seropositivity is nearly 10-40%, whereas, in both HBsAg and HBeAg, seropositivity, increases to 70- 90%.

Methods: A prospective study was conducted in the attached hospital to Bundelkhand Medical College, Sagar India from May 2023 to April 2024, among all pregnant women who attended the ANC clinic. Serum samples were subjected to HBsAg detection by ICT-based rapid antigen and positive results were re-confirmed by ELISA test. Samples were taken of neonates of such positive mothers who received tenofovir prophylaxis, in the early neonatal period and subjected to ELISA test for detection of vertical transmission. HBeAg testing was also performed along with viral load testing for HBV DNA in all neonates who came positive.

Results: Among the 9022 screened ANC cases, 50 were found seropositive by ICT, and all of them were asymtomatic. They were further confirmed by ELISA wherein 47 were found seropositive for HBsAg with an estimated Sero-prevalence of 0.52%. Vertical transmission was found in 4 (8.5 %) of cases, perinatal mortality was in 2.12% and Miscarriage was found in 4.2 % of cases.

Conclusions: HBsAg-positive pregnant women are mostly asymptomatic hence screening of all irrespective of risk factors is helpful in diagnosis and proper management, to reduce the future burden of disease on society and healthcare resources. We need to gain insight into the methods of prevention of perinatal transmission with Immuno-prophylaxis of babies shortly after birth since current levels of transmission remain concernable.

Keywords: Mother-to-Child Transmission, HBV, Liver Diseases, Liver

PE-2

Suppression of HBV Transcription and Replication by Host Rna-Binding Protein #RB11

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Background/Aim: Hepatitis B virus (HBV) remains a global health issue, causing hepatocellular carcinoma despite the availability of useful vaccines. Although current antiviral treatments suppress the viral replication, eradicating the infection is very challengeable due to the persistently infected covalently closed circular DNA (cccDNA) in the cells and drug resistance resulting from long-term treatment. Therefore, efforts developing new therapeutic agent are undergoing currently. Here, we identified a cellular factor, #RB11, as a potent inhibitor of the HBV replication, and defined a mode of action on its inhibitory activity.

Methods: HepG2-NTCP cells were infected with HBV and then transfected with #RB11 plasmid. From the cells, the levels of HBV DNA, core protein, and HBsAg/HBeAg secretion were determined by RT-qPCR, Western blotting, and ELISA. #RB11 knock-down using siRNA was performed to determine the role of #RB11 on HBV replication as above. Transcriptional activities of #RB11 and binding activities of HNF4α and HNF1α on EnhI/Xp and EnhII/Cp were determined using luciferase reporter and ChIP assays, respectively. *In vivo* antiviral effect of #RB11 was determined in HBV-infected mice model.

Results: Expression level of #RB11 was lower in HBV-infected cells compared to that of uninfected cells. Overexpression of the #RB11 in both HepG2-NTCP and C57/BL6 mice infected with HBV inhibited the viral transcription/replication, core expression, and secretion of HBsAg and HBeAg. In contrast, knock-down of #RB11 increased the secreted levels of HBV antigens from the cells. Additionally, #RB11 reduced the binding activity of hepatocyte nuclear factors HNF4α and HNF1α to EnhI and EnhII, following inhibition of HBV transcription. Importantly, #RB11 vector delivery markedly suppressed the viral replication in HBV-infected mouse models.

Conclusion: Our data demonstrates that a novel host-restriction factor, #RB11, inhibits viral transcription via interfering interaction between host transcription factors and enhancers, and may be applicable for treating HBV infection.

This work was supported by the intramural fund (#2022-NG-003-02) from Korea National Institutes of Health.

Keywords: HBV, RNA Binding Protein, #RB11

PE-3

Prevalence and Co-Infection of Hepatitis-B, Hepatitis-C, HIV, and Syphilis among Individuals in a Tertiary Care Hospital of Nepal

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Aims: The vertical and horizontal transmission of hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis remains a significant public health problem globally. High-risk populations and blood donors are primarily focused in Nepal due to vulnerability and transmission potential of these infections. This study aimed to determine the prevalence and co-infection of HBV, HCV, HIV, and syphilis among individuals attending the KIST Medical College and Teaching Hospital (KISTMCTH).

Methods: A retrospective study was conducted in the Microbiology Department of KISTMCTH. Blood samples (3 mL) were collected from individuals, and serum was separated for analysis. HBV (HBsAg), HCV (anti-HCV), and HIV (anti-HIV) were screened by respective rapid test kits, and confirmed by chemiluminescent immunoassay. Syphilis was initially screened by the rapid plasma reagin method and confirmed by the Treponema pallidum hemagglutination assay (TPHA) card test. A p-value of less than 0.05 was considered statistically significant.

Results: The seroprevalence of syphilis, HBV, HCV, and HIV was 1.63% (135/8,306), 0.49% (137/28,159), 0.28% (60/21,219), and 0.13% (34/26,980), respectively. The higher incidences of HBV (0.30%, 85/21,966), HCV (0.23%, 55/15,398), HIV (0.10%, 33/21,119), and syphilis (1.52%, 126/7,970) were observed in the individuals belonging to the age group 18-59 years. Males had higher incidences of HBV (0.29%, 82/11790), HCV (0.22%, 46/11077), HIV (0.07%, 20/11282), and syphilis (0.87%, 72/1010) compared to females. Co-infections of HBV-HIV and HCV-HIV were found in 0.0018% (n=1) and 0.0041% (n=2) of individuals, respectively.

Conclusions: A notable prevalence of HBV, HCV, HIV, and syphilis, with co-infection of HBV-HIV and HCV-HIV, particularly among males and individuals aged 18–59 years, highlights the need for targeted screening, prevention, and awareness programs to reduce transmission and co-infection risks.

Keywords: Seroprevalence, Hepatitis B, Hepatitis C, Syphilis

PE-4

Next Generation Sequencing Analysis of HBV Mutations in Liver Biopsy Samples from HBeAg-Negative Chronic Hepatitis B Patients

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Aims: HBV genomic variants are linked to chronic hepatitis B (CHB) progression, but the impact of liver tissue mutations remains unclear. This study assessed the correlation between X/precore mutations, HBV replication, and CHB progression in HBeAg-negative patients.

Methods: A total of 111 HBeAg-positive CHB patients were enrolled. Twelve key X/precore mutations (G1613A, C1631T, C1653T, T1674C, T1753V, T1754V, A1762T, G1764A, C1773T, A1846T, G1896A, and G1899A) were identified in liver tissue samples using an NGS-based assay. Serum HBV antigens (HBsAg, HBeAg, and HBcrAg) and intrahepatic HBV markers (cccDNA and pregenomic RNA) were quantified using commercial assays and qPCR. Liver inflammation and fibrosis were assessed by liver biopsy using the METAVIR scoring system.

Results: BCP/X mutations were more prevalent in older patients, with mutation burden increasing with age. The average mutation count was 7.3, 7.1, and 5.3 in inactive carriers, grey-zone, and HBeAg-negative immune-active phase patients, respectively, with lower counts in immune-active phase patients. Mutation profiles showed that BCP mutations (A1762T and G1764A) were associated with lower serum HBcrAg and HBsAg levels, while the PC mutation (G1896A) was linked to higher serum HBV DNA levels. However, no specific mutations were correlated with elevated AST/ALT, inflammatory activity, or intrahepatic cccDNA and pregenomic RNA. Despite lower cccDNA and HBV DNA in patients with higher mutation counts (≥6), these patients were more likely to have significant fibrosis compared to those with fewer mutations (<6).

Conclusions: The naturally occurring BCP/X mutation patterns identified in liver tissue are complex and influence the intrahepatic HBV pool and its transcription in HBeAg-negative patients. Our findings suggest that comprehensive analysis of the entire HBV mutation profile, rather than focusing on individual mutations, may offer insights into antiviral strategies and the prediction of disease progression in HBeAg-negative CHB.

Keywords: HBV Mutation, Next Generation Sequencing, Chronic Hepatitic B

PE-5

Epigenetic Modifications in HBV-Associated Hepatocarcinogenesis: A Systematic Review

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Aims: Hepatitis B virus (HBV) infection remains a leading cause of hepatocellular carcinoma (HCC) globally. Emerging evidence suggests that epigenetic modifications, including DNA methylation, histone modification, and non-coding RNA regulation, play pivotal roles in HBV-associated hepatocarcinogenesis by altering gene expression without modifying the genetic code. This systematic review aims to comprehensively evaluate current knowledge on the epigenetic mechanisms underlying HBV-induced HCC and explore therapeutic strategies targeting these modifications.

Methods: A systematic literature search was conducted across PubMed, Web of Science, and Scopus databases from inception to January 2025, following PRISMA guidelines. Studies included preclinical investigations, clinical trials, and systematic reviews focusing on epigenetic alterations—DNA methylation, histone modifications, and non-coding RNA regulation—in HBV-associated HCC. Data were extracted regarding study design, key findings on epigenetic dysregulation, and therapeutic implications. Risk of bias was assessed using the Cochrane Collaboration's tool for randomized studies and the ROBINS-I tool for non-randomized studies.

Results: A total of 72 studies were included, comprising 35 preclinical studies and 37 clinical and translational investigations. Hypermethylation of tumor suppressor genes (e.g., CDKN2A, RASSF1A) and hypomethylation of oncogenes were frequently observed in HBV-related HCC. Histone modification patterns, such as increased H3K27 acetylation and decreased H4K16 acetylation, were associated with altered chromatin structure and oncogene activation. HBV X protein (HBx) was identified as a critical modulator of epigenetic dysregulation through interaction with DNA methyltransferases and histone-modifying enzymes. Non-coding RNAs, including miR-122 and lncRNAs such as HULC, further contributed to tumorigenesis by regulating key oncogenic pathways. Emerging therapeutic strategies, including epigenetic drugs like DNA methylation inhibitors (e.g., 5-azacytidine) and histone deacetylase inhibitors, demonstrated promise in preclinical models.

Conclusions: Epigenetic modifications play a central role in HBV-associated hepatocarcinogenesis, influencing gene expression and tumor progression. Understanding these molecular mechanisms offers new avenues for biomarker discovery and therapeutic intervention. Targeting epigenetic regulators holds promise for improving outcomes in HBV-related HCC and warrants further investigation in clinical trials.

Keywords: Hepatitis B Virus, Hepatocellular Carcinoma, Epigenetic Modifications, Dna Methylation

7. HBV, Clinical

PE-1

Atherosclerotic Cardiovascular Risk in Patients with Chronic Hepatitis B: Tenofovir Disoproxil fumarate vs Tenofovir Alafenamide: A Korean Nationwide Study

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Aims: Despite of comparable antiviral efficacy between tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF), concerns about TAF's impact on lipid profiles and its potential increase atherosclerotic cardiovascular disease (ASCVD) risk persist. This study aimed to compare the long-term ASCVD risk in patients treated with either TAF or TDF for chronic hepatitis B (CHB).

Methods: We retrospectively analyzed treatment-naïve CHB patients who received TAF or TDF between 2017 and 2022, using Korean National Health Insurance Service claims data. ASCVD cumulative incidence was estimated by Kaplan-Meier method and compared using the log-rank test. Propensity score (PS)-matched analysis and Cox regression analysis were performed to identify risk factors for ASCVD.

Results: Among 44,714 patients with CHB, 16,120 (36.1%) received TAF and 28,594 (63.9%) received TDF. Over a median follow-up period of 3.0 years, ASCVD occurred in 817 patients (630 in TDF-treated and 187 in TAF-treated patients), with an annual incidence of 6.18/1,000 patient-years (PYs). The TAF group had a significantly lower risk of ASCVD compared to the TDF group (4.60 vs. 6.88/1,000 PYs; $P<0.001$). This trend remained after PS-matching (4.67 vs. 6.67/1,000 PYs) with a hazard ratio of 0.70 ($P<0.001$) among PS-matched 15,169 pairs. Older age, hypertension, current smoking, and elevated AST were risk factors for ASCVD development.

Conclusions: Despite concerns about lipid metabolism, TAF did not increase ASCVD risk compared to TDF, providing reassurance for clinician in selecting antiviral therapies for patients with CHB.

Keywords: Atherosclerotic Cardiovascular Disease, Chronic Hepatitis B, Tenofovir Alafenamide Fumarate, Tenofovir Disoproxil Fumarate

PE-2

Trends, Inequalities, and Projections of Acute Viral Hepatitis in the Elderly: Results from the Global Burden of Disease Study 2021

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Aims: This study aimed to analyze the global burden of acute viral hepatitis among individuals older than 70 years from 1990 to 2021, utilizing data from the Global Burden of Disease (GBD) 2021 study.

Methods: Using GBD 2021 data, we calculated incidence and disability-adjusted life years (DALYs), analyzing trends with estimated annual percentage change (EAPC). We also made projections, health inequality analysis and estimated the relationship between the sociodemographic Index (SDI) and acute viral hepatitis disease burden.

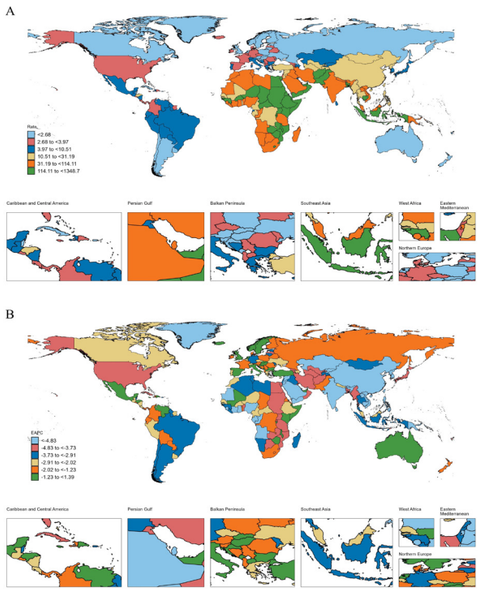

Figure 1.

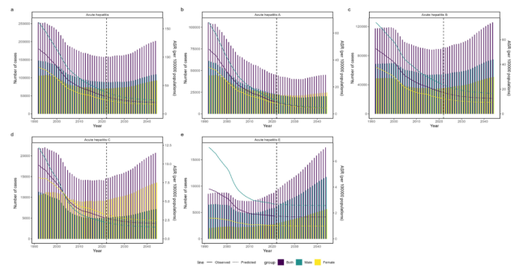

Figure 2.

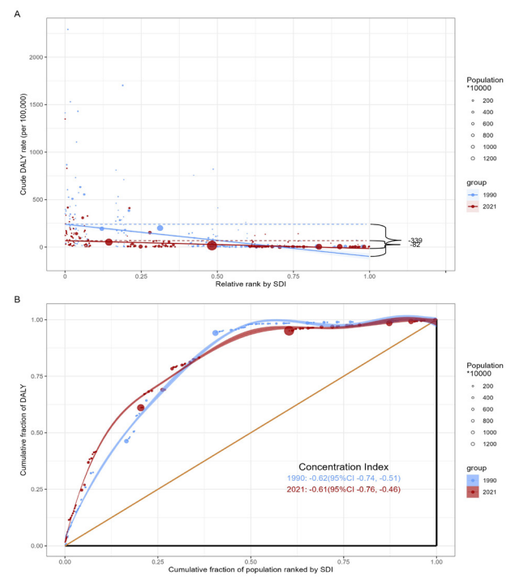

Figure 3.

Results: From 1990 to 2021, the global trend for acute viral hepatitis among older adults showed a significant decline in DALYs, with an increase observed in the incidence number. The highest DALY rates were observed in Eastern Sub-Saharan Africa and countries, such as Somalia, Afghanistan, and Ethiopia. Hepatitis B was the leading cause, followed by hepatitis A, C, and E. While both sexes experienced a decline in the hepatitis burden, males showed a more substantial reduction in DALYs. Projections indicated continued declines in DALY rates but rising incidence numbers over the next two decades. There was a negative association between the SDI levels and burden of acute viral hepatitis. Cross-country inequality analysis highlighted improved disparity measures, yet significant inequalities remain.

Conclusions: Despite a decreasing trend in DALYs, the rising incidence number of acute viral hepatitis among older adults, along with regional disparities and gender differences, underscored the urgent need for targeted public health interventions, which are vital for achieving the World Health Organization 2030 elimination goals.

Keywords: Acute Viral Hepatitis, Epidemiology, Disability Adjusted Life Year, Incidence

PE-3

Evaluation of Tenofovir Disoproxil Fumarate Treatment in Patients with Chronic Hepatitis B at Clinic 103 Cam Khe

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Aims: Chronic hepatitis B (CHB) is a major global health issue, leading to liver cirrhosis and hepatocellular carcinoma. Effective long-term treatment aims to suppress HBV replication, reduce liver damage, and prevent complications. Tenofovir disoproxil fumarate (TDF), a potent nucleotide reverse transcriptase inhibitor, is widely used due to its strong antiviral activity and high resistance barrier. However, concerns remain regarding its long-term safety, particularly its effects on renal function and bone health.

This study aims to evaluate the effectiveness and safety of tenofovir disoproxil fumarate (TDF) in patients with chronic hepatitis B (CHB).

Methods: A prospective study was conducted from January 2020 to January 2025 at Clinic 103 Cam Khe. Patients diagnosed with CHB and treated with TDF 300 mg were included in the study. Key parameters, including HBsAg, Anti-HBs, HBeAg, Anti-HBe, HBV DNA, AST, and ALT levels, were assessed at 6, 12, and 18 months, as well as at the 4-year follow-up. Virological response (HBV DNA <50 IU/ml), biochemical response (ALT reduction to <40 IU/ml in patients with pre-treatment ALT >40 IU/ml), and serological response were evaluated. Adverse effects were also monitored throughout the treatment period.

Results: Data from 63 patients receiving TDF treatment were analyzed. The virological response rates at 6, 12, and 18 months, and at the 4-year follow-up were 71%, 89%, 95%, and 100%, respectively. Anti-HBs seroconversion was observed in 9.3% of patients at the 4-year follow-up. No significant adverse effects necessitating treatment discontinuation were reported.

Conclusions: TDF demonstrated high efficacy and good tolerability in the treatment of CHB, making it a reliable therapeutic option.

Keywords: Tenofovir Disoproxil Fumarate, Hepatitis B Infection, Liver

PE-4

Comparison of the Effects of Tenofovir Disoproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF) on Liver Function in Patients with Hepatitis B

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Aims: Hepatitis B virus (HBV) infection remains a major global health concern, leading to chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). Antiviral therapy plays a crucial role in managing HBV, with nucleos(t)ide analogs being the cornerstone of treatment. Although, both Tenofovir Disoproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF) are widely used due to their potent antiviral efficacy and high genetic barrier to resistance, their impact on liver function remains an area of interest. Previous studies have suggested that TAF may have a more favorable safety, but further comparative data their effects are needed.

This study aims to compare the effects of TDF and TAF on liver function in patients with chronic hepatitis B (CHB), focusing on key biochemical markers and potential clinical implications.

Methods: 120 patients were randomly assigned to either the TAF treatment group or the TDF treatment group was conducted to compare the efficacy and safety. After of treatment, the following parameters were assessed: Viral suppression rate: Determined by measuring HBV DNA levels to evaluate the degree of viral control between the two groups. Alanine transaminase (ALT) normalization rate: Assessed based on changes in serum ALT levels. Adverse reactions and side effects: Recorded to compare the incidence of adverse events between the two groups.

Results: There was no significant difference in viral suppression between groups after 12 months of treatment ($p > 0.05$). Still, ALT normalization rate was higher, and the incidence of adverse reactions was lower in TAF group versus TDF group at 12 months after treatment ($p < 0.01$).

Conclusions: Both TAF and TDF are effective in the treatment of CHB. However, TAF is the preferred option due to its superior safety profile, particularly in terms of liver enzyme normalization and reduced adverse reactions. TAF as a safer alternative to TDF for long-term HBV management.

Keywords: Effects, Hepatitis B, Tenofovir Disoproxil Fumarate (TDF), Tenofovir Alafenamide (TAF), Liver Function

PE-5

Risk Factors for Relapse after Discontinuation of Tenofovir in HBeAg-Negative Patients

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Aims: Chronic hepatitis B (CHB) requires long-term nucleoside analog (NA) therapy to achieve virological suppression. However, relapse after treatment discontinuation is common, particularly in HBeAg-negative patients. Identifying relapse risk factors is essential for optimizing post-treatment monitoring and management.

To evaluate the relapse frequency and identify risk factors in HBeAg-negative CHB patients who discontinued tenofovir disoproxil fumarate (TDF) after achieving virological and biochemical responses.

Methods: A retrospective cohort study was conducted on HBeAg-negative CHB patients treated with NAs between January 2019 and December 2024. Patients who discontinued therapy after achieving undetectable HBV DNA and normal ALT levels were followed at 6, 12, and 24 months. Relapse was defined as HBV DNA reappearance or ALT elevation. The impact of age, fibrosis stage, and prior TDF use was analyzed.

Results: Among 61 patients, 49.1% relapsed after treatment cessation.

The relapse rate was significantly higher in patients aged ≥46 years (67.2%) compared to those <46 years (32.8%) ($P<0.01$).

Relapse rates increased with fibrosis severity: 47.5% (fibrosis stage 2), 52.5% (stage 3), and 95.1% (stage 4) ($P<0.01$).

Patients previously treated with TDF had a higher relapse risk, emphasizing the need for close monitoring.

Conclusions: Older age (≥46 years), advanced fibrosis (stage 4), and prior TDF treatment were significant predictors of relapse. Close follow-up, particularly in the first 12 months post-treatment, is essential for early relapse detection and management.

Keywords: Risk Factors, Relapse, Hbeag-Negative, Tenofovir, Discontinuation

PE-6

Analysis of the Relationship Between HBcrAg Levels and the Natural History of Chronic Hepatitis B Virus Infection

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Aims: Chronic hepatitis B virus (HBV) infection is a dynamic process reflecting the interaction between HBV replication and the host immune response. Understanding the natural history of HBV is a key issue in clinical practice. Recent studies have identified hepatitis B core-related antigen (HBcrAg) as a marker that reflects cccDNA or the natural history of the disease. This study aims to investigate the relationship between HBcrAg levels and the natural history of Chronic HBV Infection.

Methods: A total of 284 HBV patients with measured HBcrAg levels between Sep. 2022 and July 2024 were evaluated. These patients were categorized natural history by assessment of patients with chronic HBV infection based upon the presence of HBeAg, HBV DNA levels, alanine aminotransferase values (immune Active: IA, immune tolerant: IT). HBcrAg levels were assessed to determine the presence of hepatocellular carcinoma (HCC).

Results: The median follow-up duration was 7.2 months, with a median HBcrAg level of 3.5 (LogU/mL). Patients were categorized into HBeAg negative IA (n=118), HBeAg positive IA (n=112), HBeAg negative IT (n=34), HBeAg positive IT (n=3), and HBsAg loss (n=17) respectively (IA: immune activation, IT: immune-tolerant). HBcrAg levels significantly differed between HBeAg positive IT and IA ($P=0.0491$) and between HBeAg negative IT and IA ($P<0.0001$). AUROC analysis showed that HBeAg positive IA could be distinguished by HBcrAg levels, with a cut-off of 3.6. Additionally, HBcrAg can differentiate IA and IT status in both HBeAg-positive and HBeAg-negative patients, with a cut-off of 3.3 for HBeAg-positive and 2.4 for HBeAg-negative cases. No significant difference in HBcrAg levels was observed between patients who achieved HBeAg seroclearance and those who did not ($P=0.2150$) in HBeAg positive patients. In HBeAg negative IA patients, those with elevated HBcrAg levels (>3.2) showed a statistically significant association with the presence of HCC ($P=0.0055$).

Table 1. Demographics

Baseline Characteristics at the Time of HBcrAg Sampling	
Variables	Value (N=284)
HBcrAg (LogU/ml) (median, ± range)	3.5 (2.1-7.1)
Age (median, range)	60 (19-91)
<60 (n)	149
≥60 (n)	135
Gender	
male (n)	168
female (n)	116
Natural History	
HBeAg(+) IA	112
HBeAg(+) IT	3
HBeAg(-) IA	118
HBeAg(-) IT	34
HBsAg(-)	17
LC	
No	172
Yes	112
HCC History	
No	234
Yes	50
ALT (U/L) (mean ± sd)	25 ± 17.9
PLT (10^9/L) (mean ± sd)	188 ± 68
HBV DNA (copies/ml)	
>100000	12
<10000	265
others	6
Antiviral Therapy	
No	69
Yes	213
Temporary Hold	2

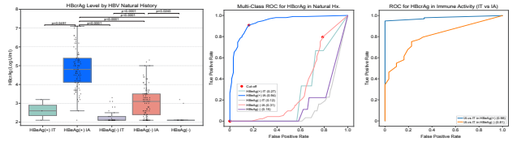

Figure 1. HBcrAg_Cutoff.

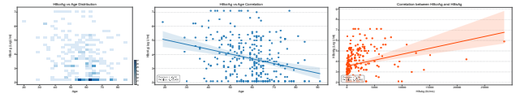

Figure 2. HBcrAg_Correlation.

Conclusions: HBcrAg may be a useful marker for distinguishing immune status, especially during active and tolerance phases, and for identifying the natural progression of the disease. Additionally, it helps predict the development of liver cancer in HBeAg-negative patients and may serve as a predictor for liver cancer occurrence in patients receiving antiviral therapy.

Keywords: HBV, Natural History, HBCRAG, Hepatocelluar Carcinoma

PE-7

Protective Effect of Nucleos(t)ide Analogue Therapy on the Incidence of Alzheimer's Disease in Patients with Chronic Hepatitis B Virus Infection

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Aims: Long-term therapy with nucleos(t)ide analogs (NUCs) is inevitable for chronic hepatitis B (CHB) patients. However, how NUC therapy on the developing Alzheimer's disease (AD) in these patients remains controversial.

Methods: This retrospective cohort study used the Korean National Health Insurance Service claims database from January 1, 2013, to December 31, 2013, treatment naïve CHB patients and those without previously diagnosed with AD. Participants were followed from the index date until either the diagnosis of AD or the study's conclusion on December 31, 2021. The primary outcome was the incidence of AD, compared between the group with initiated NUC therapy (n=18,365) at cohort entry and the group without NUC therapy (n=212,820).

Results: During the study, 416 patients were diagnosed with

AD. After propensity-score matching (18,365 pairs), the 5- to 7-year follow-up showed a significantly lower hazard ratio (HR) in the NUC-treated group compared to the untreated group (HR 0.31-0.40), with HRs remaining constant over time. Subgroup analysis showed more pronounced benefits of NUC therapy in patients under 65 years (HRs: 0.22 vs. 1.23; $P<0.05$) and those without dyslipidemia (HRs: 0.14 vs. 1.09; $P<0.05$). Protective effects were also observed across subgroups with hypertension, chronic kidney disease, heart disease, and a history of brain trauma, consistent with AD risk factor trends.

Conclusions: Our study analyses suggest that NUC therapy appears to have a protective effect against the development of AD in patients with CHB.

Keywords: Chronic Hepatitis B Virus, Nucleos(t)Ide Analogs, Alzheimer's Disease, Incidence

PE-8

Time Varying Effect of Nucleos(t)ide Analogue Therapy with Parkinson Disease in Chronic Hepatitis B Patients

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Aims: Prolonged therapy using nucleos(t)ide analogs (NUC) is inevitable in patients with chronic hepatitis B (CHB) infection, but its long-term impact on Parkinson's disease (PD) risk remains unclear. This study evaluated the association between NUC therapy and PD incidence in a nationwide CHB cohort.

Methods: The study population comprised the National Health Insurance Service claims database from January 1, 2013, to December 31, 2013, only included treatment naïve CHB patients and those without previously diagnosed with PD. Participants were followed until PD diagnosis or study completion. The primary outcome was PD incidence, comparing patients who initiated NUC therapy at cohort entry with those who did not.

Results: Over the 7.9-year study period, the incidence rate of PD in NUC-treated patients was 1.48 per 1,000 persons, compared to 1.95 per 1,000 persons in the untreated group. In an adjusted competing risk model, the 3-year follow-up showed a statistically significant reduction in risk (hazard ratio [HR]: 0.61; 95% confidence interval [CI]: 0.39–0.97). In the propensity score-matched cohort of 18,365 pairs, the cumulative incidence during 2 to 4 years of follow-up was significantly lower in the NUC-treated group compared to the untreated group. However, no statistically significant difference in cumulative PD incidence was observed between the groups at the early or late stages of the follow-up period.

Conclusions: NUC therapy initially reduced PD incidence, but this protective effect diminished over time, indicating a time-varying effect. Regular PD screening may be needed for long-term NUC users.

Keywords: Chronic Hepatitis B Virus, Nucleos(t)Ide Analogs, Parkinson Disease, Incidence

PE-9

Nationwide Analysis of Renal Outcomes in Chronic Hepatitis B Patients Treated with Tenofovir Alafenamide vs. Entecavir

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Aims: Patients with chronic hepatitis B (CHB) are at a higher risk of chronic kidney disease (CKD) compared to the general population. This study compared renal outcomes in treatment-naive CHB patients receiving tenofovir alafenamide (TAF) or entecavir (ETV) using South Korea's nationwide health insurance database.

Methods: Two cohorts were analyzed: patients with normal renal function (cohort 1) and those with CKD but not end-stage renal disease (ESRD) (cohort 2). Propensity score matching (PSM) balanced baseline characteristics.

Results: Before PSM, ETV users had higher CKD (10.88 vs. 4.48 per 1000 person-years, incidence rate ratio [IRR] 2.43, 95% CI 2.13–2.77) and ESRD rates (40.33 vs. 22.13, IRR 1.82, 95% CI 1.26–2.63) than TAF users. Post-PSM, CKD and ESRD incidence showed no significant difference (CKD IRR 1.20, 95% CI 0.69–2.10; ESRD IRR 1.49, 95% CI 0.81–2.75). Cox regression confirmed that the antiviral agent was not a significant predictor of CKD or ESRD.

Conclusions: In conclusion, TAF and ETV demonstrated similar renal safety profiles in CHB patients. These findings provide robust evidence for clinical decision-making, particularly for patients at risk of renal impairment.

Keywords: Chronic Hepatitis B, Kidney Disease, Tenofovir Alafenamide, Renal Insufficiency, Propensity Score Matching

PE-10

Hepatitis B Prevalence and Its Impact on Liver Cancer Risk

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Aims: To assess the prevalence of HBV infection and its impact on liver cancer risk, with a focus on HDV co-infection and associated risk factors.

Methods: A cross-sectional retrospective analysis was conducted on 3,605 residents who underwent early screening between June and December 2024. Data collected included demographic information, HBV infection status (HBsAg, Anti-HDV IgG), and liver cancer diagnoses. Statistical analyses were performed using Microsoft Excel and SPSS.

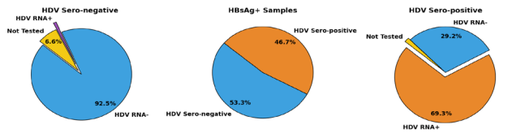
Results: The prevalence of hepatitis B virus (HBV) infection among the screened population was 5.2% (188 individuals), with a slightly higher rate in females (5.6%) compared to males (4.6%). Among those infected with HBV, 78% were co-infected with hepatitis D virus (HDV), and 75% of these cases had active HDV infection (HDV-RNA positive), indicating a significant risk of liver disease progression.

Between 2018 and 2024, 43% of all cancer cases in Dornod Province were diagnosed as liver cancer, with 39.5% of these cases linked to HBV and HDV co-infections. The high proportion of viral hepatitis-associated liver cancer underscores the strong relationship between chronic HBV/HDV infections and liver malignancy in this region.

The average age of liver cancer patients was 65 years, with male patients having a lower average age (61 years) compared to female patients (69 years). These findings highlight the persistent burden of viral hepatitis and its significant contribution to liver cancer in Dornod Province. The high co-infection rate with HDV, along with the substantial proportion of liver cancer cases linked to viral hepatitis, emphasizes the need for enhanced screening, early detection, and prevention strategies to reduce liver disease morbidity and mortality.

Conclusions: While HBV prevalence in Dornod aligns with national averages, the HDV co-infection rate (78%) is significantly higher. Liver cancer remains a leading cause of death in the region, largely driven by viral infections. Strengthening early detection and prevention strategies is critical to reducing liver cancer mortality in this high-risk population.

Keywords: Hepatitis B Virus (HBV), Hepatitis D Virus (HDV), Liver Cancer Risk, Hbv Prevalence



PE-11

Characterization of Changes in Noninvasive Fibrosis Markers Over 8 Years of Tenofovir-based Treatment in Patients with Chronic Hepatitis B

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Aims: Blood-based noninvasive tests (NITs) are frequently used to assess liver fibrosis severity or monitor fibrosis progression. However, limited data exist on the evolution of these markers of patients with chronic hepatitis B (CHB) receiving long-term nucleos(t)ide analogue therapy. We serially evaluated 3 blood-based NITs to characterize changes in fibrosis over 8 years in patients with CHB receiving tenofovir-based therapy.

Methods: In 2 similarly designed Phase 3 studies (GS-US-320-0108/0110) evaluating tenofovir alafenamide (TAF), HBeAg-positive and -negative patients were randomized 2:1 to double-blind treatment with TAF or tenofovir disoproxil fumarate (TDF) up to 144 weeks followed by open-label TAF (i.e., TAF and TDF®TAF groups). Patients were assessed through 384 weeks (8 years). Three blood-based NITs were evaluated: FibroTest (BioPredictive SAS), aspartate aminotransferase–to-platelet ratio index (APRI), and fibrosis index based on 4 factors (FIB-4), all performed at baseline (BL) and annually thereafter.

Results: Overall, 1632 patients were included in this pooled analysis. The mean (SD) absolute values for FibroTest, APRI, and FIB-4 at BL and changes from BL through year 8 were comparable across treatment groups, with the greatest mean declines observed at week 48 (Table). At year 8, 95% of TAF- and 88% of TDF®TAF–treated patients with available FibroTest data with a BL fibrosis category of no or minimal fibrosis remained in that fibrosis category (Table). Similar trends were observed for APRI and FIB-4. For patients with FibroTest values suggestive of cirrhosis at BL, 75% showed improvement at year 8. Similarly, 99% and 83% of patients with advanced fibrosis/cirrhosis at BL by APRI and FIB-4, respectively, improved by year 8.

Conclusions: Improvements in FibroTest, FIB-4, and APRI scores were observed over 8 years of tenofovir-based treatment. Early declines may be due to reduced necroinflammation. The significance of these dynamic long-term changes in fibrosis markers requires further investigation.

Keywords: Fibrosis Markers, Tenofovir, Chronic Hepatitis B

Table. Changes From Baseline in FibroTest, APRI, and FIB-4 Scores by Treatment Group

Mean (SD) Change From Baseline in FibroTest, APRI, and FIB-4									
	FibroTest			APRI			FIB-4		
	TAF (n = 1079)	TDF→TAF (n = 524)		TAF (n = 1085)	TDF→TAF (n = 539)		TAF (n = 1085)	TDF→TAF (n = 539)	
BL, mean (SD)	0.38 (0.23)	0.38 (0.24)		1.22 (1.38)	1.37 (1.87)		1.63 (1.53)	1.76 (1.56)	
W 48, mean (SD)	−0.07 (0.12)	−0.04 (0.13)		−0.77 (1.29)	−0.86 (1.75)		−0.43 (0.99)	−0.43 (0.96)	
W 96, mean (SD)	−0.06 (0.13)	−0.03 (0.14)		−0.83 (1.31)	−0.88 (1.76)		−0.50 (1.05)	−0.48 (1.03)	
W 144, mean (SD)	−0.06 (0.14)	−0.02 (0.15)		−0.82 (1.33)	−0.88 (1.74)		−0.47 (1.08)	−0.40 (1.24)	
W 240, mean (SD)	−0.06 (0.14)	−0.04 (0.16)		−0.87 (1.37)	−0.93 (1.86)		−0.52 (1.17)	−0.47 (1.53)	
W 384, mean (SD)	−0.06 (0.15)	−0.04 (0.17)		−0.87 (1.35)	−0.97 (1.87)		−0.49 (1.19)	−0.46 (1.18)	
Categorical Shift in Fibrosis Stage From Baseline									
	TAF				TDF→TAF				
FibroTest BL	0.00–0.48 (n = 747)	0.49–0.74 (n = 223)	0.75–1.00 (n = 100)	Missing (n = 23)	0.00–0.48 (n = 356)	0.49–0.74 (n = 113)	0.75–1.00 (n = 55)	Missing (n = 15)	
W 384									
0.00–0.48	500 (95%)	98 (59%)	15 (23%)	16	214 (88%)	39 (47%)	8 (20%)	4	
0.49–0.74	26 (5%)	61 (37%)	37 (56%)	1	27 (11%)	36 (43%)	20 (50%)	1	
0.75–1.00	2 (0.4%)	6 (4%)	14 (21%)	1	1 (0.4%)	8 (10%)	12 (30%)	2	
Missing	219	58	34	5	114	30	15	8	
APRI BL	≤0.45 (n = 178)	>0.45–≤2 (n = 757)	>2 (n = 150)	Missing (n = 8)	≤0.45 (n = 89)	>0.45–≤2 (n = 368)	>2 (n = 82)	Missing (n = 0)	
W 384									
≤0.45	118 (96%)	443 (84%)	73 (72%)	6	56 (93%)	200 (81%)	35 (70%)	0	
>0.45–≤2	5 (4%)	85 (16%)	28 (28%)	1	4 (7%)	46 (19%)	13 (26%)	0	
>2	0	1 (0.2%)	0	0	0	2 (1%)	2 (4%)	0	
Missing	55	228	49	1	29	120	32	0	
FIB-4 BL	≤0.7 (n = 208)	>0.7–≤3.25 (n = 785)	>3.25 (n = 92)	Missing (n = 8)	≤0.7 (n = 80)	>0.7–≤3.25 (n = 402)	>3.25 (n = 57)	Missing (n = 0)	
W 384									
≤0.7	85 (71%)	81 (14%)	2 (3%)	1	32 (74%)	37 (13%)	0	0	
>0.7–≤3.25	35 (29%)	481 (85%)	55 (85%)	6	11 (26%)	239 (86%)	27 (75%)	0	
>3.25	0	5 (1%)	8 (12%)	0	0	3 (1%)	9 (25%)	0	
Missing	88	218	27	1	37	123	21	0	

Data are shown as n (%) unless otherwise indicated.
APRI, AST-to-platelet ratio index; **AST**, aspartate aminotransferase; **BL**, baseline; **FIB-4**, fibrosis index based on 4 factors; **TAF**, tenofovir alafenamide; **TDF**, tenofovir disoproxil fumarate; **W**, week.

PE-12

Predictors of Liver Fibrosis Improvement in Patients with HBV-Induced Cirrhosis Treated with Tenofovir Alafenamide

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Aims: Hepatitis B virus (HBV) infection is a leading cause of liver fibrosis and cirrhosis. Antiviral therapy, including tenofovir alafenamide (TAF), effectively suppresses HBV replication and may contribute to fibrosis regression. However, the predictors of fibrosis improvement in patients with HBV-induced cirrhosis receiving TAF remain unclear. Identifying these factors is crucial for optimizing treatment strategies and patient outcomes.

To identify predictors of liver fibrosis improvement in patients with HBV-induced cirrhosis treated with TAF.

Methods: A prospective study was conducted on 63 patients with HBV-induced cirrhosis who received TAF at 103 Cam Khe Clinic from May 2020 to December 2024. Liver fibrosis improvement was assessed using FibroScan.

Results: Liver fibrosis improvement was observed in 11.3% of patients at 6 months, 25.9% at 12 months, and 42.6% at 18 months. Independent predictors of fibrosis improvement at 18 months included: Albumin concentration > 32 g/L (OR 6.19, 95% CI: 1.31–35.11, P<0.01) HBV DNA load > 15,131 IU/mL (OR 8.51, 95% CI: 1.79–36.91, P<0.01).

Conclusions: TAF treatment may improve liver fibrosis in HBV-induced cirrhosis. Higher baseline serum albumin, elevated initial HBV DNA load, and lower baseline liver stiffness were significant predictors of fibrosis improvement.

Keywords: Tenofovir Alafenamide, HBV-Induced Cirrhosis, Liver Fibrosis, Fibroscan

PE-13

Metabolic Dysfunction-Associated Steatotic Liver Disease Increases Hepatocellular Carcinoma Risk in Chronic Hepatitis B: A Systematic Review and Meta-Analysis

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Aims: The recent introduction of the nomenclature "metabolic dysfunction-associated steatotic liver disease (MASLD)" highlights the importance of cardiometabolic risk factors in liver disease. While MASLD is acknowledged as a significant contributor to liver-related morbidity, its impact on hepatocellular carcinoma (HCC) risk in chronic hepatitis B (CHB) remains controversial. This systematic review and meta-analysis aimed to evaluate the association between MASLD and HCC risk in CHB.

Methods: Data from observational studies were collected through PubMed, EMBASE, and the Cochrane Library from inception to March 1, 2025. The primary outcome was the association between MASLD and HCC.

Results: A total of 27 studies involving 329,798 patients with CHB were included. SLD including non-alcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated fatty liver disease (MAFLD), and MASLD, was associated with an increased risk of HCC (OR 1.99, 95% CI 1.40–2.59, I^2=76%). When stratified by disease classification, all SLD subtypes remained associated with an increased HCC risk (MASLD OR 1.85, 95% CI 0.49–3.20; MAFLD OR 1.92, 95% CI 0.38–3.46; NAFLD OR 2.04, 95% CI 1.27-2.82). In subgroup analyses, the association remained consistent in both Asian (OR, 1.90; 95% CI 1.19–2.60; I^2=78%), and non-Asian regions (OR, 2.29; 95% CI 1.16–3.43; I^2=81%), as well as in studies with a median follow - up duration of ≥5 years (OR, 2.32; 95% CI, 1.51–3.13), those excluding alcohol use (OR, 2.57; 95% CI, 1.36–3.78), and those using biopsy - proven steatosis (OR, 3.28; 95% CI, 1.66–4.90). Similar associations were observed in hospital-based (OR 2.0, 95% CI 1.32–2.69) and nationwide datasets (OR 1.22; 95% CI 0.96–1.49). When stratified by antiviral therapy (AVT) use, there was no association between SLD and HCC risk in the non-AVT group (OR 0.95, 95% CI 0.58-1.32), whereas a positive association was observed in the AVT group (OR 1.32, 95% CI 0.93-1.71). Finally, studies that included only steatohepatitis showed the strongest association with an increased HCC risk (OR 3.66, 95% CI 1.83-5.49).

Conclusions: MASLD is associated with an increased risk of HCC in patients with CHB, particularly in those with steatohepatitis, highlighting the importance of identifying concomitant steatosis in CHB.

Keywords: Hepatitis B Virus, Hepatocellular Carcinoma, Metabolic Dysfunction-Associated Steatotic Liver Disease, Meta-Analysis

8. HCV, Basic

PE-1

Burden of Viral Hepatitis and Syphilis Coinfections and Their Association with Virological Status of People Living with HIV in Nepal

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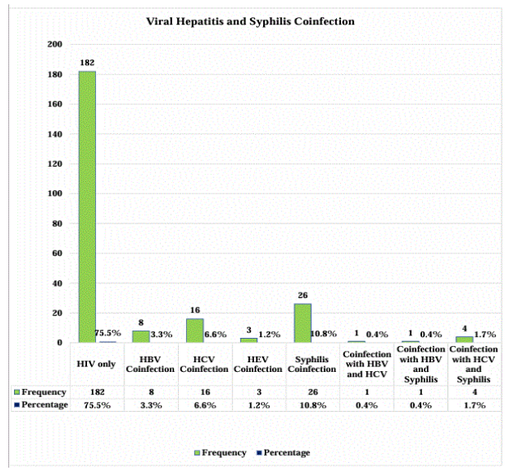
Aims: The burden of viral hepatitis (hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis E virus (HEV)) and syphilis coinfections among people living with HIV (PLHIV) in Nepal.

Methods: This cross-sectional study was conducted at the Sukraraj Tropical and Infectious Disease Hospital, Teku. For this study, 5 ml of blood samples was collected from people living with HIV/AIDS undergoing ART. HIV-1 RNA was quantified by Real-Time PCR. A rapid screening was done for Hepatitis B surface antigen (HBsAg), anti-HCV antibodies, and anti-HEV using immunochromatographic assay and RPR/Syphilis antibody test for syphilis.

Results: Overall, 59 out of 241 participants (24.5%) were co-infected with viral hepatitis and syphilis. Categorically, the seroprevalences of viral hepatitis mono-infections were 3.3% (HBV), 6.6% (HCV), and 1.2% (HEV) among the participants. Syphilis coinfection was observed in 10.8% of participants. Meanwhile, 0.4% of participants were co-infected with HIV-HBV-HCV and HIV-HBV-Syphilis, while 1.7% were co-infected with HIV-HCV-Syphilis. Notably, males, age ≥40 years, and people living with HIV with longer duration were associated with increased HCV coinfection rates. Furthermore, individuals with syphilis coinfections exhibited poorer adherence to ART. Although virological failure rates were relatively low (5%), good adherence (>95%) was associated with better virological outcomes.

Conclusions: The study highlights the substantial burden of viral hepatitis and syphilis coinfections in PLHIV and there was no association with virological status. These findings emphasize the importance of sustained efforts to optimize ART adherence and virological monitoring in PLHIV with coinfections.

Keywords: Coinfections, HBV, HCV, HEV, HIV, SYPHILIS



PE-2

Comparison of Hepatitis C Virus Infection Risk Between Spouses of HCV Patients and Control Group

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Aims: This study compared the risk of Hepatitis C Virus (HCV) infection between spouses of HCV patients and those of the general population (controls), to provide evidence for spouse-focused prevention strategies in meeting the World Health Organization's (WHO) 2030 HCV elimination goal.

Methods: We analyzed National Health Insurance Service data (2002–2023) to identify newly diagnosed HCV patients (2005–2022) and matched them 1:2 with HCV-free individuals by sex and age. The observation period commenced from either the marriage date or HCV diagnosis date (whichever came later) for the patient group, and from the marriage date for the control group. Follow-up continued until the earliest of: spouse's HCV diagnosis, marriage termination (divorce or bereavement), or December 31, 2023. We compared HCV incidence between groups using incidence density per 1,000 person-years, hazard ratios from Cox proportional hazards models, and sex-age adjusted cumulative incidence rates.

Results: The HCV incidence in spouses was significantly higher in the HCV patient group compared to controls (3.05% vs 0.58%, 5.3-fold difference). Incidence density (/1,000 per-

son-years) was 8.4 times higher in the patient group (3.68 vs 0.44). After sex-age adjustment, the hazard ratio for HCV infection was 7.37 (95% CI: 6.96-7.80) in patient spouses, with the highest risk observed in the first year (HR: 65.7). The incidence density (/1,000 person-years) revealed marked gender differences in transmission: male patient to female spouses (17.03), female patients to male spouses (2.89), male controls to female spouses (1.94), and female controls to male spouses (0.23). The sex-age adjusted cumulative incidence reached 2.49% in patient spouses compared to 0.55% in controls.

Conclusions: This study demonstrates that spouses of HCV patients face a substantially higher risk of HCV infection compared to the general population, particularly among female spouses of male patients and during the initial observation period. These findings emphasize the importance of implementing targeted screening programs and preventing measures for spouses of HCV patients.

Keywords: Hepatitis C Virus, Spousal Infection, Prevention Strategies, Big Data

PE-3

Design and Evaluation of siRNA Candidates for Silencing NS3 and NS4 Genes of Hepatitis C Virus: A Bioinformatics Approach

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Aims: Hepatitis C virus (HCV) remains a significant global health challenge, with NS3 and NS4 proteins playing crucial roles in viral replication and pathogenesis. In this study, we aimed to design and evaluate small interfering RNA (siRNA) candidates capable of effectively silencing the NS3 and NS4 genes of HCV.

Methods: Using comprehensive bioinformatics tools, we identified and evaluated siRNA candidates targeting the NS3 (Accession: HQ588345.1) and NS4 (Accession: X78953.1) genes. siPRED was employed to generate siRNA molecules and predict their efficacy, with an inhibition threshold set at ≥ 90%. The siRNA Scales tool was then used to filter potential candidates. These candidates underwent further analysis using MaxExpect and DuplexFold to evaluate the folding free energy of the siRNAs and the binding free energy between the guide strand and the target, respectively.

Results: For NS3, the top siRNA candidate (position 158-176) demonstrated an inhibition rate of 94.43%, with the antisense strand sequence UAUGCUACAGCAUUAAGUC. Similarly, for NS4, the top candidate (position 162-180) showed an inhibition rate of 93.14%, with the antisense strand sequence UAAAAGCCACGAGUGCACC. Additional high-efficacy candidates were identified for both genes, with inhibition rates consistently above 85%.

Conclusions: These findings suggest that the designed siRNAs have strong potential for therapeutic application in HCV treatment by effectively targeting and silencing the NS3 and NS4 genes. Further in vitro and in vivo validation of these siRNA candidates is warranted to confirm their efficacy and therapeutic potential.

Keywords: SIRNA, HCV, NS3/NS4, Bioinformatics

Rank	Antisense strand 5'-3'	Sense strand 5'-3'	Position	Inhibition (%)
1	UAUGCUACAGCAUUAAGUC	GACUUAAUGCUGUAGCAUA	158 - 176	94.43
2	UCAAAGUCGCCGGUGAAGC	GCUUCACCGGCGACUUUGA	254 - 272	92.27
3	UUGCAGUCUAUCACCGAGU	ACUCGGUGAUAGACUGCAA	272 - 290	90.99
4	UCAUUAGAGCGUCUGUUGC	GCAACAGACGCUCUAAUGA	232 - 250	90.47
5	UGCUACAGCAUUAAGUCCG	CGGACUUAAUGCUGUAGCA	156 - 174	90.02
6	UAUCACCGAGUCAAAGUCG	CGACUUUGACUCGGUGAUA	264 - 282	89.97
7	UACAGCAUUAAGUCCGAGG	CCUCGGACUUAAUGCUGUA	153 - 171	89.18
8	UAGAAGGGGAUCUCUCCAG	CUGGAGAGAUCCCCUUCUA	35 - 53	88.94
9	UUUGGAAUGGCAGAAAAUG	CAUUUUCUGCCAUUCCAAA	99 - 117	88.33
10	UGACGGACACAUCAAGACC	GGUCUUGAUGUGUCCGUCA	184 - 202	88.2

Figure 1. NS3 siRNAs.

Rank	Antisense strand 5'-3'	Sense strand 5'-3'	Position	Inhibition (%)
1	UAAAAGCCACGAGUGCACC	GGUGCACUCGUGGCUUUUA	162 - 180	93.14
2	UUAAAAGCCACGAGUGCAC	GUGCACUCGUGGCUUUUAA	163 - 181	90.22
3	AUUGCUGCACACACGACCC	GGGUCGUGUGUGCAGCAAU	265 - 283	89.21
4	UUGAGCAGCCACCCAUCCC	GGGAUGGGUGGCUGCUCAA	21 - 39	89.04
5	UUCAUCCACUGCACAGCCC	GGGCUGUGCAGUGGAUGAA	312 - 330	88.18
6	AUGUCCACAAGCACCUUCC	GGAAGGUGCUUGUGGACAU	115 - 133	87.83
7	UCAUCCACUGCACAGCCCC	GGGGCUGUGCAGUGGAUGA	311 - 329	87.46
8	UUCCCAAGGCCUAUGCUGC	GCAGCAUAGGCCUUGGGAA	100 - 118	86.82
9	UAUGCUGCCAAUGCCGCAC	GUGCGGCAUUGGCAGCAUA	89 - 107	86.78
10	UAUCAGCCGGUUCAUCCAC	GUGGAUGAACCGGCUGAUA	322 - 340	85.97

Figure 2. NS4 siRNA.

PE-4

Exploring Antiviral Peptides as Potential Inhibitors of NS3 in Hepatitis C Virus: A Computational Study

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Aims: Hepatitis C virus (HCV) infection remains a significant global health burden, necessitating the development of novel antiviral agents. Antiviral peptides (AVPs) have emerged as promising therapeutic candidates due to their broad-spectrum activity and low toxicity. This study aimed to identify and evaluate potential AVPs targeting the NS3 protein of HCV using computational approaches.

Methods: Potential AVPs with a length of 21–43 amino acids were retrieved from the CAMPR4 database. The antimicrobial probability of these peptides was assessed using the Antimicrobial Peptide Scanner v2.0, selecting peptides with scores >0.7. Physicochemical properties, including isoelectric point (pI), GRAVY index, instability index, and net charge, were analyzed using the ProtParam server. Peptides with an instability index >40 or negative/zero net charge were excluded. Hydrophobicity/hydrophilicity was assessed using the PEPTIDE 2.0 server, while solubility was evaluated via the Protein-Sol server. Finally, molecular docking between selected peptides and the NS3 protein of HCV was performed using the HDOCK server.

Results: Fifteen potential AVPs were identified, with four peptides (Dermaseptin-4, Rp 71955, antihypertensive protein BDS-1, and LL37) selected for molecular docking. The binding energies for these peptides against NS3 were -156.33, -192.3, -211.68, and -208.15, respectively. Among them, BDS-1 exhibited the lowest binding energy, suggesting its potential as a strong inhibitor of NS3.

Conclusions: In conclusion, this study highlights the potential of antiviral peptides as inhibitors of HCV NS3 protein. The antihypertensive protein BDS-1 demonstrated the highest binding affinity, warranting further experimental validation for its potential therapeutic application against HCV infection.

Keywords: Antiviral Peptides, Hepatitis C Virus, NS3 Protein, Molecular Docking

Table 1. List of potential antiviral peptides

No.	Name	UniProt ID	Source	Amino Acid Sequence	AMP Probability
1	Dermaseptin-4	P80280	*Phyllomedusa sauvagii*	ALWMTLLKKVLKAAAKALNAVLVGANA	AMP (1)
2	Mytilin-B	P81613	*Mytilus edulis*	SCASRCKGHCRARRCGYYVSVLYRGRCYCKCLRC	AMP (1)
3	Human Defensin-5	Q01523	*Homo sapiens*	ATCYCRTGRCATRESLSGVCEISGRLYRLCCR	AMP (1)
4	Rp 71955	P37046	*Actinomycete Sp9440*	CLGIGSCNDFAGCGYAVVCFW	AMP (1)
5	Palicourein	P84645	*Palicourea condensata*	GDPITFCGETCRVIPVCTYSAALGCTCDDRSDGLCKRN	AMP (0.99)
6	Vhl-1	P84522	*Viola hederacea*	CGESCAMISFCFTEVIGCSCKNKVCYLNSIS	AMP (0.97)
7	Kalata-B8	P85175	*Oldenlandia affinis*	OSVLNCQETCLLGTCYTTQCTCNKYRVCTKD	AMP (1)
8	Reptilian Defensin	POCAP0	*Caretta caretta*	EKKCPGRCTLKCGKHERPTLPYNCGKYCCVPVKVK	None
9	Melittin	P01501	*Apis mellifera*	GIGAVLKVLTTGLPALISWIKRKRQQ	AMP (1)
10	Antihypertensive protein BDS-1	P11494	*Anemonia sulcata*	AAPCFCSGKPGRGDLWILRGTCPGGYGYTSNCYKWPNICCYPH	AMP (1)
11	Vhl-1	P84522	*Viola hederacea*	SISCGESCAMISFCFTEVIGCSCKNKVCYLN	AMP (0.94)
12	LL-37	P49913	*Homo sapiens*	LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLVPRTES	AMP (0.99)
13	Human Defensin-5-HD5 [E21R]	Q01523,	Synthetic construct	ATCYCRTGRCATRESLSGVCRISGRLYRLCCR	AMP (1)
14	MBD-4 (11-40) / P9 [H21R,K23R,K28R], P9R	P82019	Synthetic construct	NGAICWGPCPTAFRQIGNCGRFRVRCCRIR	None
15	Alstoside S1	A0A1P7TZ77	*Alstonia scholaris*	CRPYGYRCDGVINQCCDPYHCTPPLIGICL	AMP (0.90)

Table 1. List of potential antiviral peptides.

Table 4. The results of molecular docking between peptides and NS3 of HCV

No.	Name	Binding Energy	Confidence score
1	Dermaseptin-4	-156.33	0.5316
2	Rp 71955	-192.3	0.6997
3	Antihypertensive protein BDS-1	-211.68	0.7744
4	LL-37	-208.15	0.7619

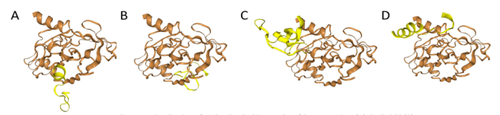

Figure 1. Visualization of molecular docking results of Dermaseptin-4 (A), Rp 71955 (B), Antihypertensive protein BDS-1 (C), and LL-37 (D) against NS3 oh HCV.

Figure 1. The results of molecular docking.

PE-5

Analysis of Demographics and Risk Factors for Liver Disease Mortality in West Asia

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Aims: Liver diseases, including cirrhosis and hepatocellular carcinoma (HCC), are one of the leading causes of death in West Asia. Risk factors such as hepatitis B and C virus infection, obesity, diabetes, and alcohol consumption contribute to the high mortality rate. Data from the Global Burden of Disease (GBD) 2023 shows a 25% increase in cirrhosis and HCC cases in the last two decades, with mortality rates varying across countries. The aim of this study was to analyze trends in liver disease mortality in West Asia based on demographic data, identifying key risk factors.

Methods: This study used a quantitative approach with secondary data analysis from WHO, GBD, and national data of several West Asian countries (2000-2023). Analytical methods included multivariate regression to identify key determinants of mortality and spatial mapping to assess the geographic distribution of cases. Variables analyzed included age, gender, lifestyle factors, hepatitis prevalence, and access to health services.

Results: The analysis showed that the death rate from liver disease in West Asia averaged 30.5 per 100,000 population, with the highest rates in Iraq (38.2/100,000), Iran (32.7/100,000) and Saudi Arabia (28.5/100,000). Mortality is higher in men (male:female ratio = 1.8:1) and increases in individuals aged >50 years. Major risk factors include: Hepatitis infection: HCV has a prevalence of 2.5-5% in some countries, with a significant contribution to HCC. Obesity and Diabetes: The prevalence of obesity reaches 35-40%, increasing the risk of non-alcoholic fatty liver disease (NAFLD). Healthcare Access: Countries with limited healthcare systems show higher mortality rates due to delayed diagnosis and treatment.

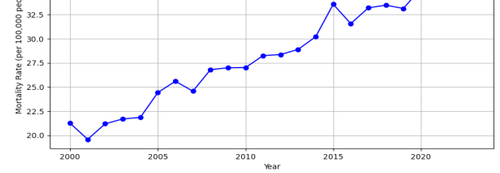

Figure 1. Liver disease mortyality.

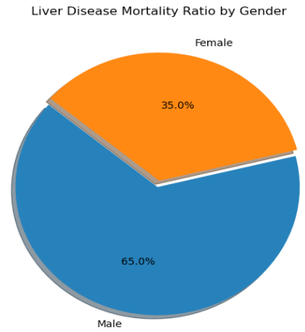

Figure 2. Liver gender.

Conclusions: Mortality from liver disease in West Asia is highest in Iraq with higher mortality in men aged >50 years with risk factors due to HCV.

Keywords: Liver Disease, Mortality, West Asia

PE-6

Molecular Mechanisms of Direct-Acting Antiviral Resistance in Hepatitis C Virus: A Systematic Review

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Aims: Direct-acting antivirals (DAAs) have revolutionized the treatment of hepatitis C virus (HCV) infection, achieving high sustained virological response (SVR) rates. However, the emergence of resistance-associated substitutions (RASs) compromises treatment efficacy, particularly in patients with advanced liver disease or treatment-experienced populations. This systematic review aims to elucidate the molecular mechanisms underlying DAA resistance in HCV and evaluate their impact on therapeutic outcomes.

Methods: A comprehensive search was conducted across PubMed, Web of Science, and Scopus databases from inception through January 2025. The review adhered to PRISMA guidelines. Studies were included if they investigated the molecular basis of DAA resistance in vitro, in vivo, or in clinical cohorts, focusing on NS3/4A protease inhibitors, NS5A inhibitors, and NS5B polymerase inhibitors. Data on resistance-associated substitutions, viral fitness, replication capacity, and treatment outcomes were extracted. Study quality was assessed using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias tool for randomized trials.

Results: 55 studies met the inclusion criteria, encompassing 32 in vitro investigations and 23 clinical cohort studies. Key resistance mutations were identified in the NS3 region (e.g., Q80K, D168A/V), NS5A region (e.g., Y93H, L31M), and NS5B region (e.g., S282T). NS5A inhibitors exhibited the lowest genetic barrier, with persistent RASs leading to cross-resistance among different DAAs. The presence of baseline NS5A RASs reduced SVR rates by up to 30% in genotype 1a-infected individuals. NS5B resistance was less common but conferred by mutations such as S282T, significantly impairing treatment efficacy. Combination regimens and next-generation DAAs demonstrated improved suppression of resistant variants, although long-term management strategies for patients harboring multidrug-resistant HCV remain an unmet need.

Conclusions: DAA resistance in HCV is driven by specific mutations that compromise antiviral efficacy, with the NS5A region being the primary contributor to persistent resistance. Understanding these molecular mechanisms is critical to optimizing treatment strategies, guiding retreatment approaches, and informing the development of next-generation antivirals.

Keywords: Hepatitis C Virus, Direct-Acting Antivirals, Antiviral Resistance, Resistance-Associated Substitutions

9. HCV, Clinical

PE-1

The Characteristics of HCV Related HCC among Mongolian Patients

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Aims: Hepatocellular carcinoma (HCC) due to hepatitis C virus (HCV) infection is one of the major causes of HCC. Eradication of HCV by direct-acting antivirals (DAAs) could reduce the risk of both de novo HCC and recurrent HCC in both cirrhotic and non-cirrhotic patients with chronic HCV infection. Since 2015 when DAAs were first introduced in Mongolia, there has been a lack of studies evaluating the long-term efficacy and an access to DAAs in Mongolia, although the government has announced that most HCV patients have been successfully treated with DAAs. In this study we aimed to investigate the characteristics of HCV-related liver cancer in Mongolian patients.

Methods: Data from 128 HCC participants who were positive for HCV antibodies (HCV-Ab) were analysed from the DETECT-HCC study population. HBsAg positivity was an exclusion criterion. HCC diagnosis and HCV infection were confirmed by Contrast Enhanced-Magnetic Resonance Imaging and other laboratory tests including HCV-Ab detected by the HISCL-5000 chemiluminescence analyser (Sysmex, Japan), and HCV-RNA level measured with the GeneXpert (Cepheid, USA). According to the HCV-RNA status and DAA treatment history, they were divided into three groups (HCV-RNA positive, DAA treated group and spontaneously cleared group) for analysis.

Results: Among Detect HCC study participants, there were a total of 128 HCC participants with positive for HCV-Ab. Mean age was m=67.5 (IQR=13 range between 43 to 91) and 51(39.8%) of them were male. A total of 128 HCC patients with anti-HCV positive, 60 (46.8%) patients are currently HCV-RNA detectable, 68 (53.1%) were HCV-RNA not detectable including 54 (42.1%) were DAA treated and 14 (10.9%) spontaneously cleared. However, there was no significant age difference between these 3 groups. However, most of the DAA-treated group was female (40/74%), while the ratio of males to females was equal in the HCV RNA-positive and spontaneously cleared groups. Regarding the stages of HCC, the majority in all 3 groups fell into BCLC stage B (43.3%), followed by stage C (25%) and stage A (25%). However, in the HCV RNA-positive group, many patients were observed in the advanced fibrosis level of the liver (F4 fibrosis) compared to the other 2 groups. Of the DAA-treated group, 42 (77.8%) were treated between 2016-2018, but only 12 (22.2%) received DAA after 2019.

Conclusions: The overall results highlight the importance of DAAs in the management of cirrhosis and HCC and suggest that a consistent program of treating HCV patients with DAAs may correlate with better outcomes, particularly in earlier stages of the liver diseases including cirrhosis and HCC in Mongolia.

Keywords: HCC, Chronic HCV Infection, DAA

PE-2

Risk Factors for Hepatocellular Carcinoma in Chronic Hepatitis C Patients after Sustained Virologic Response Following Glecaprevir/Pibrentasvir Treatment

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Aims: Hepatitis C virus (HCV) is a leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). Direct-acting antivirals (DAAs) have improved treatment outcomes, achieving high sustained virologic response (SVR) rates, but some patients remain at risk for HCC despite viral eradication. Identifying high-risk individuals is crucial for optimizing post-SVR surveillance and prevention strategies.

Methods: This multicenter, prospective, observational cohort study followed patients with HCV who achieved SVR after treatment with glecaprevir plus pibrentasvir (G/P). We aimed to identify characteristics and risk factors for HCC development after SVR.

Results: A total of 396 patients achieved SVR after G/P treatment, with a mean follow-up duration of 29.9 months. The mean age was 60.5 years, and 44.4% were male. Cirrhosis was present in 23.0% of patients at SVR. Among 14 patients who developed HCC, the cumulative incidence was 2.86%, 2.86%, and 4.29% at 1, 2, and 3 years, respectively. Thirteen of these patients had cirrhosis at the time of SVR. After adjusting for age, sex, alcohol consumption, and BMI, elevated AFP (HR 1.01, *P*=0.001) and APRI (HR 1.78, *P*=0.044) were significant risk factors for HCC in cirrhotic patients.

Conclusions: Elevated AFP and APRI scores increase the risk of HCC in cirrhotic patients after achieving SVR with G/P treatment. These markers provide a simple and cost-effective approach for HCC screening in this population.

Keywords: Chronic Hepatitis C, Glecaprevir/Pibrentasvir, Hepatocellular Carcinoma

PE-3

Awareness and Knowledge of Hepatitis C among People Who Use Drugs (PWUDs) in Korea

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Aims: To eliminate hepatitis C virus (HCV) infection, improving knowledge and awareness of target population is essential. The aim of this study was to evaluate the awareness and knowledge of HCV among people who use drugs (PWUDs) in South Korea.

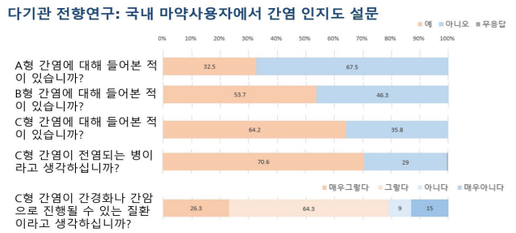
Methods: PWUDs were prospectively enrolled in 4 hospitals from August 2022 to December 2023. For them, blood tests including liver panel and anti-HCV, and questionnaires related to knowledge about hepatitis A, B and C, and awareness on HCV infection were conducted.

Results: Among the 255 PWUDs (median age 43 years, 78% male, and intravenous drug user 89.4%), 23.5%, 53.7%, and 64.2% heard about HAV, HBV, and HCV, respectively,70.6% understood HCV is transmittable, and 82% thought HCV is curable by medication. Testing history for anti-HCV was noticed in 50.2% (n=128) with a positive rate of 53.9% (69/128). Among the 69 self-reported anti-HCV positive PWUDs, 75.4% (52/69) experienced HCV treatment, and 65.4% (34/52) achieved cure.

Anti-HCV positive rate for entire PWUDs was 33.7% (86/255). Anti-HCV positive group was significantly older (53 vs 39 years, *P*<0.001) and showed higher proportion men (86% vs 74%, *P*=0.028) than anti-HCV negative group. Anti-HCV positive group had more knowledge than anti-HCV negative group that HCV can be cured with medication (88.4% vs. 78.7, *P*=0.041). Awareness for HCV among anti-HCV positive group was 75.6% (65/86).

Conclusions: The level of knowledge on HCV is relatively high, and anti-HCV testing rate was suboptimal (50.2%) among PWUDs in South Korea. However, once diagnosed, the treatment rate seems to be high. Strategies need to increase awareness and treatment rates of HCV for PWUDs.

Keywords: Hepatitis C, People Who Inject Drug, Awareness, Elimination



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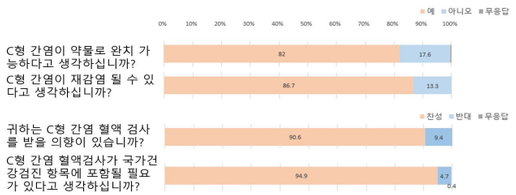

Figure 2.

PE-4

Adverse Events Associated with Vosevi Based on Real-World Data: A Pharmacovigilance Study of the Faers Database

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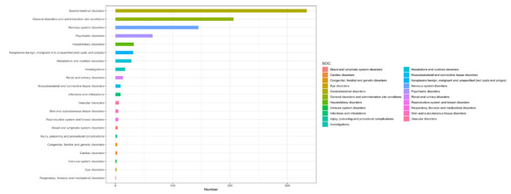
Aims: Vosevi, a combination therapy consisting of sofosbuvir, velpatasvir and voxilaprevir, was approved by the US Food and Drug Administration (FDA) in 2017 for the treatment of patients with chronic Hepatitis C, across genotypes 1-6. Its efficacy in eradicating the virus has been widely recognized, but potential adverse reactions still need to be explored. This study aimed to identify the adverse events associated with Vosevi based on real-world data.

Methods: We collected data form the third quarter (Q3) of 2017 to the fourth quarter (Q4) of 2023 from the FDA Adverse Event Reporting System (FAERS) database. Adverse events were included for disproportionality analysis and bayesian analysis. The signal monitoring results were represented by Reporting Odds Ratio (ROR), Proportion Report Odds Ratio (PRR), Bayesian Confidence Propagation Neural Network (BCPNN) and Multi-Item Gamma Poisson Shrinker (MGPS).

Results: A total of 931 adverse events with Vosevi were identified, with the highest number reported in 2018. Excluding preferred terms (PT) that not drag-related and affected by the primary diseases, 154 PTs and 21 system organ classes (SOCs) were included. Fatigue, headache, nausea, diarrhoea, vomiting, insomnia were the most common adverse drug events and were consistent with the label of the medicine instruction. In addition, there were some unmentioned adverse events involving memory impairment, decreased appetite, oedema peripheral, musculoskeletal pain, dysphagia and dry mouth. The preferred terms with strongest signal strengths were hepatocellular carcinoma (n=17, ROR=58.96, PRR=58.44, EBGM05=58.22, IC025=5.86), hepatic pain (n=3, ROR=24.07, PRR=24.03, EBGM05=23.99, IC025=4.58), hepatic cirrhosis (n=12, ROR=23.17, PRR=23.03, EBGM05=23, IC025=4.52).

Conclusions: Vosevi is an effective treatment for chronic Hepatitis C infection, but it is important to be aware of the potential adverse events, especially those not included in the medicine instruction. This study discovered potential adverse events based on real-world data to promote safer use of Vosevi for chronic Hepatitis C.

Figure 1.



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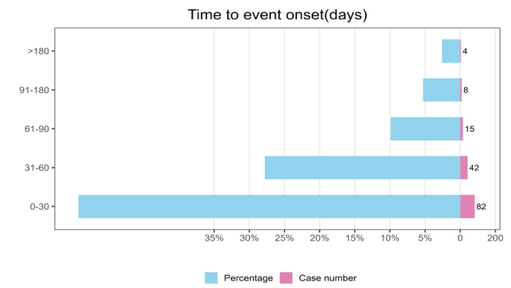

Figure 3.

Keywords: Vosevi, Adverse Events, Hepatitis C, Pharmacovigilance

PE-5

The Association between Hepatitis C Virus Infection and Estimated Glomerular Rate after Direct Acting Antiviral Treatment in Mongolia

Gantogtokh Dashjamts[1], Amin-Erdene Ganzorig[1], Yumchinsuren Tsedendorj[1], Dolgion Daramjav[1], Enkhmend Khayankhyarvaa[1], Bolor Ulziitsogt[1], Otgongerel Nergui[1], Ganchimeg Dondov[1], Tegshjargal Badamjav[1,2], Tulgaa Lonjid[1], Batbold Batsaikhan[1,3]

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Aims: Our objective was to assess renal function in patients with chronic HCV infection in Mongolia after receiving DAA therapy.

Methods: Our study included 4823 patients with HCV infection who were undergoing DAA therapy. Renal function was evaluated by calculating the glomerular filtration rate (eGFR). eGFR assessed at the initiation of the treatment, during treatment, and at 3, months, 6 months, one 1 year, and three 3 years after completion of treatment. The baseline demographic and laboratory parameters of the study participants were evaluated, and the results were analyzed using statistical methods.

Results: The average age of the study participants was 61.35 ± 12.50 years, and 54.5% of were male. The mean of eGFR in baseline and after treatment showed a decrease. Liver fibrosis scores (FIB4, APRI, Fibroscan), and liver function tests were significantly improved after DAA treatment (P=0.001). However, white blood count (5.41 ± 1.7 vs. 5.73 ± 1.9), platelet count (168.04 ± 74.0 vs. 182.11 ± 69.4), and creatinine levels (1.05 ± 1.3 vs. 1.12 ± 1.3) increased after treatment (P=0.001). The number of patients with an eGFR of 60 mL/min/1.73 m^2 decreased both during, and after treatment (P<0.001). Among patients with CKD, eGFR improved after DAA treatment (n = 690, 35.93 ± 19.7 vs. 38.71 ± 23.8; 95% CI −3.56 −1.98; P=0. −01). Logistic regression analysis revealed that renal function improved in patients with CKD who had an eGFR of less than 60 mL/min/1.73 m^2 before DAA treatment (OR 1.62, 95% CI 1.37–1.91, P=0.001).

Conclusions: In individuals with CKD and a baseline eGFR < 60 mL/min per 1.73 m^2, eGFR level was increased during DAA treatment. This suggests that initiating DAA therapy in HCV-infected patients, even those without clinical manifestations, could be a crucial strategy to prevent further decline in renal function.

Keywords: Antiviral Therapy, Hepatitis C, Renal Function, Chronic Kidney Disease

Table 1. Baseline characteristics compared with the characteristics after 3 months of completion DAA treatment.

Parameters	Baseline Characteristics	After 3 Months Characteristics	p Value
Age (mean ± SD)	61.36 ± 12.3	61.82 ± 12.3	0.001
Sex, n (%)			
Male	2395 (46.4)	1990 (45.3)	0.162
Female	2766 (53.6)	2404 (54.7)	
BMI	24.8 ± 3.3	25.2 ± 3.8	0.259
Presence of type 2 diabetes mellitus, n (%)			0.001
Yes	97 (1.9)	14 (0.3)	
No	3872 (75.0)	2011 (39.0)	
Hypertension, n (%)			
Yes	166 (3.2)	21 (0.4)	0.001
No	2935 (56.9)	2003 (38.8)	
Hyperlipidemia, n (%)			
Yes	258 (5.0)	32 (0.6)	0.001
No	4221 (81.8)	1993 (38.6)	
Alcohol drinking, n (%)	655 (12.7)	458 (8.2)	0.001
Smoking history, n (%)	1013 (19.6)	885 (16.5)	0.001
Serum biochemistry			
WBC (mean ± SD)	5.81 ± 1.9	6.01 ± 2.0	0.001
HGB (mean ± SD)	13.49 ± 1.9	13.51 ± 1.9	0.336
PLT (mean ± SD)	186.30 ± 72.0	192.12 ± 71.8	0.001
AST (mean ± SD)	61.62 ± 47.1	28.98 ± 16.7	0.001
ALT (mean ± SD)	70.72 ± 63.3	23.84 ± 20.0	0.001
BII (D) (mean ± SD)	0.20 ± 0.2	0.16 ± 0.1	0.001
AFP (mean ± SD)	16.58 ± 279.2	56.04 ± 2649.7	0.279
eGFR, ml/min per 1.73 m^2	83.92 ± 30.1	83.62 ± 30.6	0.265
CHOL (T) (mean ± SD)	172.77 ± 38.0	187.79 ± 40.4	0.001
TG (mean ± SD)	101.98 ± 56.7	110.91 ± 72.3	0.001
Fibroscan median	12.42 ± 10.9	9.24 ± 8.1	0.001
FIB4	3.23 ± 3.0	2.49 ± 2.1	0.001
APRI	1.11 ± 1.3	0.48 ± 0.5	0.001
Cryoglobulinemia, n(%)	821 (15.9)	70 (1.4)	0.001
CKD, n(%)	4823	3996	
I	2013 (39.0)	1616 (31.3)	0.001
II	2015 (39.1)	1683 (32.6)	
III	517 (10.0)	455 (8.8)	
IV	62 (1.2)	22 (0.8)	
IV	216 (4.2)	200 (3.9)	

Table 3. Univariate and multivariable logistic regression model predicting eGFR improvement after DAA therapy.

	Univariate Model			Multivariate Model		
Baseline Predictors of eGFR Improvement After DAAs	**OR**	**95% CI**	***p* Value**	**OR**	**95% CI**	***p* Value**
Age, per 50 yr	0.90	0.77–1.05	0.20			
Sex (female vs. male)	0.87	0.77–0.99	0.03	0.88	0.78–0.99	0.03
Nondiabetic vs. diabetic	0.83	0.71–0.96	0.01	0.75	0.64–0.87	0.01
Cirrhosis (vs. noncirrhotic)	0.93	0.82–1.06	0.29			
Hypertension (vs. non-hypertensive)	0.95	0.84–1.08	0.48			
Baseline eGFR < 60 mL/min per 1.73 m^2	1.62	1.37–1.91	0.01	1.73	1.46–2.05	0.01

Table 3. Number of patients with and without comorbidities before and after DAA therapy.

Baseline	Post treatment	Participants	p Value
Nondiabetic vs. diabetic patients	Nondiabetic vs. diabetic patients		
-	-	2691	
+	-	159	p < 0.001
-	+	105	
+	+	382	
Non-cryoglobulinemia vs. cryoglobulinemia patients	Non-cryoglobulinemia vs. cryoglobulinemia patients		
-	-	252	p < 0.001
+	-	113	
-	+	11	
+	+	40	
Non-hypertension vs. hypertension patients	Non-hypertension vs. hypertension patients		
-	-	1137	
+	-	84	p < 0.001
-	+	16	
+	+	0	
Non-proteinuria vs. proteinuria patients	Non-proteinuria vs. proteinuria patients		
-	-	144	
+	-	158	p < 0.001
-	+	39	
+	+	176	
Non-other cancer vs. other cancer patients	Non-other cancer vs. other cancer patients		
-	-	1868	
+	-	146	p < 0.001
-	+	10	
+	+	1	

(-): negative; (+): positive

PE-6

Stereotactic Body Radiotherapy for Hepatocellular Carcinoma in a Quaternary Care Centre: A Clinical Experience with an Intention-to-Treat Approach

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Aims: To analyse the efficacy of Stereotactic Body Radiotherapy and its outcomes in advanced Hepatocellular carcinoma

Methods: All patients with HCC who underwent SBRT from January 2022 to December 2024 were enrolled retrospectively and toxicity, clinical, radiological outcomes and overall survival analysed along with demographics. Liver Imaging, Recording and Data Systems (LI-RADS) treatment response algorithm (LR-TRA) v2024 was used for radiological outcomes.

Results: 134 patients (93.3% males) with HCC underwent SBRT. Mean age 61.19 (± 9.777) yrs. Common aetiology was NASH in 48 %. ALBI grade 1, 2, 3 in 26.3%, 66.2%, 7.5% respectively. Mean CTP score = 6.46 (±1.375), mean MELD=9.62 (±2.859). 109 patients (82.7 %) had vascular invasion . 48.2 % had main portal vein invasion . 14.9 % had hepatic vein/ IVC involvement, 16.4 % had extra-hepatic metastasis. 100 (74.62%) had tumour >5 cm; 92% were in BCLC Stage C followed by 8 % and 1% stage B & A respectively. SBRT was the initial therapy in 72 (53.7 %) of patients. The median dose was 35.597 Gy (± 8.18) in five fractions. Classical RILD-worsening of Ascites, hepatomegaly seen in 18 (13.7%) & 2 (1.5%) respectively. Non-classical RILD-Transaminase elevation & increase in CTP ≥ 2 was seen in 5 (3.8%) and 22 (16.4%) respectively. Median follow-up duration was 3.92 (IQR-1.93-9.83) months. Radiological response is given in the Table 1. Median overall survival (OS) is 10.13 months (95 % CI : 11.65-17.88 M) . 3M, 6M, 12M, 2Yr survival was seen in 81%, 58.9%, 48.9 %, 26.1%. Freedom from local progression was achieved in 97.9 %. 5 (3.8 %) patients underwent Liver transplant after SBRT .

Conclusions: SBRT is an effective, well-tolerated loco-regional therapy for HCC for tumours with vascular invasion with good local control.

Keywords: Hepatocellular Carcinoma, Stereotactic Body Radiotherapy, Locoregional Therapy, Down Staging

Table 1: Radiological response assessment at 12 weeks post therapy.

Response assessment using LIRADS-treatment assessment algorithm v2024	LT-TRA at around 12 weeks	
	Tumour	Tumour thrombus
LR-TR Non-viable	41(30.6%)	45(33.6%)
LR-TR Non-progressing	54 (40.3%)	16(11.9%)
LR-TR viable	0	0
Total response assessed	95	61

PE-7

Clinical Significance of Low HCV RNA Levels in Korean Patients with Chronic Hepatitis C Infection: A Multicenter Prospective Cohort Study

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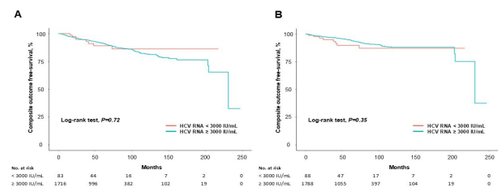
Aims: The clinical significance of low HCV RNA levels in chronic hepatitis C infection remains unclear, particularly in relation to treatment response and long-term outcomes. This study aimed to estimate the proportion of low viral titer patients, and to evaluate the sustained virologic response (SVR) and clinical outcomes, including hepatocellular carcinoma (HCC) incidence and composite liver-related events, in patients with low (<3000 IU/mL) versus high (≥3000 IU/mL) HCV RNA levels.

Methods: We analyzed data from a multicenter prospective cohort collected from nine tertiary centers in Korea between 2007 and 2024. Patients with chronic HCV infection were classified into low RNA titer (HCV RNA <3000 IU/mL) and high RNA titer (HCV RNA ≥3000 IU/mL) groups. Baseline cirrhosis status and SVR rates after interferon (IFN) or direct-acting antiviral (DAA) treatment were compared. Clinical outcomes were assessed by analyzing HCC incidence and composite liver-related events, which included decompensated liver cirrhosis, liver transplantation, HCC, and death. Statistical analyses included odds ratios (ORs) for baseline characteristics, while Kaplan-Meier survival analysis and Cox proportional hazards regression were used to evaluate clinical outcomes.

Results: A total of 2,298 patients were included. The median age was 60.0 years (IQR: 51.0–69.0), and 51.1% were male. Among them, 105 (4.6%) were in the low RNA titer group, while 2,193 (95.4%) were in the high RNA titer group. Baseline characteristics, including age (*P*=0.86) and sex distribution (*P*=0.74), did not significantly differ between groups. Cirrhosis prevalence was also similar (OR: 0.80, 95% CI: 0.53–1.20, *P*=0.28). SVR rates among IFN-treated patients were 62.5% (5/8) in the low RNA titer group and 70.2% (193/275) in the high RNA titer group (*P*=0.70). In the DAA-treated group, SVR rates were 93.5% (29/31) and 95.2% (1075/1129), respectively (*P*=0.66). For the composite event analysis, 1,799 patients were analyzed over a median follow-up of 60 months (IQR: 31–95), with 191 events occurring. The high RNA titer group had an HR of 1.14 (95% CI: 0.56–2.31, *P*=0.72), showing no significant difference between the groups (Figure 1A). For HCC incidence, 1,876 patients were analyzed over a median follow-up of 60 months (IQR: 31.75–95), during which 124 patients developed HCC. The high RNA titer group showed a hazard ratio (HR) of 0.71 (95% CI: 0.35–1.45, *P*=0.35) compared to the low RNA titer group (Figure 1B).



Conclusions: In Korean HCV patients, the proportion of low HCV RNA levels was less than 5%, and they had comparable SVR rates and clinical outcomes to those with high RNA levels following IFN or DAA treatment. Although these patients are minor, they include cases with decompensated cirrhosis and HCC, underscoring the need for careful clinical assessment and active treatment.

Keywords: Hepatitis C, Low Viral Load, Sustained Virologic Response, Survival, Hepatocellular Carcinoma

PE-8

Hepatitis C Virus Genotypes and Their Clinical Outcomes in South Korea: A Prospective Multicenter Cohort from 2007 to 2024

Seungteak Lee[1], Sangmi Jang[1], Gwang Hyeon Choi[1], Min Kyung Park[1], Eun Sun Jang[1], Young Seok Kim[2], Youn Jae Lee[3], In Hee Kim[4], Sung-Bum Cho[5], Kyung-Ah Kim[6], Byung Seok Lee[7], Han Chu Lee[8], Jeong Won Jang[9], Moran Ki[10], Da hye Paik[10], Sook-Hyang Jeong[1]

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Aims: The aim of this study is to investigate the clinical characteristics and outcomes of chronic hepatitis C virus (HCV) infected patients according to genotype (GT) in Korea from 2007 to 2024.

Methods: We analyzed data from the prospective multicenter "Korea HCV cohort study" including 2,903 patients with GT testing result at 9 tertiary centers. Baseline clinical information with questionnaire survey results on the risk factors for HCV infection were collected, and liver-related and overall survival were analyzed according to HCV GTs.

Results: Among the 2,687 HCV RNA-positive patients, the proportions of each GT of 1, 2, 3, 4 and 6 were 51.2% (n=1,485), 47.5% (n=1,378), 0.8% (n=22), 0.2% (n=5) and 0.4% (n=13), respectively. The mean ages were 56.6, 60, 49.5, 59.6, and 45.9 years, respectively (*P*<0.001). The male proportions were 54.5%, 47.0%, 54.5%, 80.0%, and 46.2%, respectively (*P*<0.001). Tattooing (69.2%) and intravenous drug use (23.1%) were more frequent in patients with GT6. The overall treatment rate, including both interferon-based therapy and direct-acting antivirals, was 72.1%, with no significant difference across HCV genotypes. The overall sustained virological response (SVR) rate was 87.91%, showing a lower SVR rate in GT 3 (60.0%) and 4 (66.7%) (*P*<0.001). During a median follow-up of 69 months (interquartile range: 38–108 months), a total of 177 HCC cases and 294 composite outcome events occurred. Survival analysis showed that GT3 had the poorest prognosis in both composite outcome-free survival (hazard ratio [HR] = 3.18, 95% confidence interval [CI]: 1.17–8.63, *P*=0.023, figure 1A) and HCC-

free survival (HR= 4.79, 95% CI: 1.57–14.63, *P*=0.008, figure 1B), followed by GT1 (composite outcome-free: HR = 1.54, 95% CI: 1.21–1.96, *P*<0.001, figure 1A; HCC-free: HR = 2.09, 95% CI: 1.57–2.79, *P*<0.001, figure 1B).

Conclusions: About 99% of HCV infection in Korea were attributed to GT 1 and 2, showing stable proportion during 17 years. Different epidemiological profiles and long-term outcomes were noticed according to GT, suggesting HCV genotyping is still considered in the era of pangenotypic therapeutics in Korea.

Keywords: Genotype, Epidemiology, Sustained Virologic Response, Hepatocellular Carcinoma

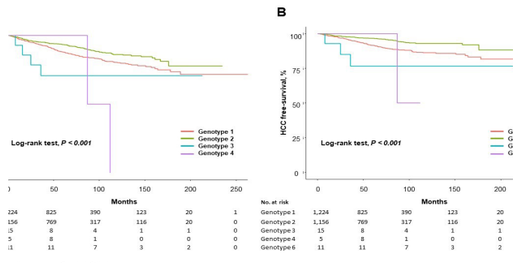

Figure 1. HCV genotype.

10. Liver Cancer, Basic

PE-1

AI-Driven Hepatic Splicing Dysregulation Mapping Using a Deep Quantum Graph Learning Model to Predict Cryptic Exon Activation in Non Alcoholic Steatohepatitis Driven Fibrosis and Hepatocellular Carcinoma Progression

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Aims: Non Alcoholic Steatohepatitis (NASH) is a major driver of hepatic fibrosis and hepatocellular carcinoma (HCC), but existing risk models lack precision. Cryptic exon activation in fibrosis-associated genes may promote pro-fibrotic signaling and malignant transformation, but its role in clinical progression remains unclear. This study develops an AI-driven deep learning model to predict fibrosis-to-HCC transition at the patient level, enabling improved risk stratification and early detection of high-risk patients.

Methods: Single-cell long-read RNA sequencing data were obtained from the Human Liver Cell Atlas (HLCA), The Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA-LIHC), and the Gene Expression Omnibus (GEO) database (GSE115469, GSE185477), comprising 38,724 hepatic cells. Splicing-specific Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq) and Cleavage Under Targets and Release Using Nuclease (CUT&RUN) datasets (4,923 profiles) mapped cryptic exon accessibility and splicing factor binding. Methylated RNA Immunoprecipitation sequencing (MeRIP-seq) profiled N6-methyladenosine (m6A) modifications. Ribosome footprinting (2,312 samples) captured translation efficiency of aberrant splicing events. A deep learning model integrating a quantum variational encoder and splicing dysregulation networks was trained on 4,218 fibrosis-to-HCC transition trajectories, optimized using AdamW (LR=2e-4, batch=256, 400 epochs), and evaluated against Model for End-Stage Liver Disease (MELD), Liver Imaging Reporting and Data System (LI-RADS), and NASH Clinical Research Network (NASH CRN) classifications.

Results: The model outperformed fibrosis-HCC predictors (AUROC: 0.87, 95% CI: 0.857–0.878; Concordance Index (C-index): 0.81, *P*<0.001). Cryptic exon inclusion score (CEIS >3.1) predicted 69% fibrosis-to-HCC transition risk (*P*<0.0001). Dysregulated splicing factor activation (DSFA >2.3) correlated with a 4.7-fold increased HCC risk (*P*<0.001). AI reclassified 26% of "low-risk" fibrosis patients into high-risk HCC categories, indicating improved early detection of high-risk fibrosis patients who require closer surveillance or preventive interventions. Shapley Additive Explanations (SHAP) analysis showed splicing features contributed 58% more predictive value than standard biomarkers.

Conclusions: This study develops an AI-driven cryptic exon activation model that improves risk stratification and early detection of high-risk fibrosis patients progressing to HCC. By integrating quantum-enhanced AI with hepatic transcriptomics, this work enhances fibrosis and HCC prediction models, supporting biomarker-based precision medicine for MASLD-related HCC prevention.

Keywords: Splicing Dysregulation, Cryptic Exon Activation, Hepatic Fibrosis to Hepatocellular Carcinoma Transition, Ai In Transcriptomics

PE-2

Differential Gene Expression between Early and Advanced Stages of Hepatocellular Carcinoma as Potential Biomarkers for Early Detection and Therapeutic Targeting

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Aims: Hepatocellular carcinoma (HCC) is one of the most prevalent and aggressive cancers worldwide, often diagnosed at an advanced stage. The molecular mechanisms underlying HCC progression remain poorly understood, and identifying biomarkers for early detection and targeted therapy is crucial. This study aims to compare gene expression profiles between early stage and advanced stage HCC to identify differentially expressed genes (DEGs) that could serve as potential biomarkers and therapeutic targets.

Methods: We analyzed gene expression data from the Gene Expression Omnibus (GEO) dataset, focusing on major (advanced stage) and minor (early stage) resected liver samples. The expression levels of genes were compared between these groups using bioinformatics tools. Differentially expressed genes (DEGs) were identified, and their roles in HCC progression were explored. Cytoscape was used to build protein-protein interaction (PPI) networks, and enrichment analysis was performed using DAVID to identify pathways implicated in tumor progression.

Results: Our analysis identified several genes with significant differential expression between major HCC and minor HCC. TNFAIP8L1 and ITGA1 were upregulated in major HCC resected liver tissues, suggesting a role in proliferation, invasion, and metastasis associated with advanced-stage tumors. Conversely, GPR84 was found to be upregulated in minor HCC, which may indicate its involvement in immune modulation and inflammatory responses in early-stage tumors. These genes are implicated in critical pathways that drive HCC progression and might be used as biomarkers for early detection or therapeutic targets.

Conclusions: Our study highlights the potential of TNFAIP8L1, ITGA1, and GPR84 as biomarkers for different stages of HCC. While TNFAIP8L1 and ITGA1 are associated with advanced tumor stages and could serve as therapeutic targets, GPR84 may act as an early marker for immune responses in minor HCC. Further research is needed to validate these findings in clinical settings and explore their utility in improving early detection and treatment strategies for HCC.

Keywords: Advanced Stages, Biomarkers, Early Stages, Hepatocellular Carcinoma

PE-3

Identification and Functional Analysis of Differentially Expressed Genes in Hepatocellular Carcinoma

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Aims: Hepatocellular Carcinoma (HCC) is one of the leading causes of cancer-related deaths worldwide. Understanding the gene expression changes associated with HCC progression can provide valuable insights into its diagnosis and therapy. This study aims to identify differentially expressed genes (DEGs) in HCC and explore their roles in disease progression, focusing on gene expression profiles, functional interactions, and genetic mutations that may influence treatment outcomes.

Methods: Gene expression datasets from the Gene Expression Omnibus (GEO) were analyzed to identify differentially expressed genes (DEGs) between HCC patients and healthy controls. Protein-protein interaction (PPI) networks were constructed using Cytoscape to explore functional relationships among DEGs. Enrichment analyses using DAVID and Enrichr were performed to identify biological pathways associated with these genes. Functional domains and deleterious mutations were examined using Prosite, SIFT, and PolyPhen.

Results: Our analysis identified several DEGs in HCC, including MIR4738, SMC4, and VTI1A, which were downregulated, and SLC35B4, CD58, and SYNCRIP, which were upregulated. Enrichment analyses revealed the involvement of these genes in critical pathways such as cell cycle regulation, apoptosis, immune signaling, metabolic processes, and inflammatory responses. Mutational analysis highlighted functional domains and deleterious variants in key genes, offering insights into their roles in HCC pathogenesis and progression.

Conclusions: These findings provide important insights into the roles of genes in the pathogenesis of HCC and highlight how mutations and protein interactions may contribute to liver cancer progression. This study suggests the potential use of these genes as diagnostic and prognostic biomarkers for HCC, as well as potential therapeutic targets.

Keywords: Biomarkers, Differentially Expressed Genes, Hepatocellular Carcinoma, Therapeutic

PE-4

Association between Family History of Cancer and Liver Cancer: Statistical Analysis of Viral and Non-Viral Etiologies

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Aims: Mongolia has the highest prevalence and mortality rate of liver cancer worldwide. However, the role of genetic factors in liver cancer risk remains unclear. This study aims to evaluate the association between family history of liver cancer and its occurrence, as well as the role of viral and non-viral etiologies in a Mongolian population.

Methods: We analyzed data from 1,243 participants in the DETECT-HCC study, collected between September 23, 2023, and February 5, 2025. Participants included 457 hepatocellular carcinoma (HCC) cases and 786 non-HCC controls, categorized into viral (n = 923) and non-viral (n = 320) groups based on liver cancer etiology. Family cancer history was recorded using the NEVIOM electronic data capture system. We used Chi-square tests and odds ratios (ORs) to assess associations between family history of cancer and liver cancer occurrence.

Results: Among 1,243 participants, 42.0% (522 participants) reported a family history of cancer, with liver cancer being the most frequently reported cancer (499 family members). Chi-square analysis revealed no significant association between the participant's family history of liver cancer and the participant's liver cancer occurrence ($\chi^2 = 5.23$, P=0.156). A weak correlation was observed between family history of liver cancer and hepatitis virus infection status ($\chi^2 = 3.21$, P=0.360).

Conclusions: In Mongolia, the fact that multiple members of a single family suffer from liver cancer is more likely due to the high rate of hepatitis virus infection within the family rather than hereditary factors. Therefore, it is important to incorporate a family history-based element into liver cancer screening programs to better address the liver cancer burden in Mongolia.

Keywords: Liver Cancer, Hepatocellular Carcinoma, Heritability, Mongolia

Table 1: Comparison of Family Cancer History Between group with Liver Cancer and Non-Cancer Groups

	Total	Liver cancer first degree relatives	% out of all participants	Liver cancer second degree relatives	% out of all participants	Other cancer first degree relatives	% out of all participants	Other cancer second degree relatives	% out of all participants
	1243	*292*	*23%*	*92*	*7%*	*207*	*17%*	*54*	*4%*
Liver cancer group	457	110	24%	25	5%	71	16%	14	3%
Non-cancer group	786	182	23%	67	9%	136	17%	40	5%

Table 2: Comparison of Family Cancer History Between Participants with Viral Etiology and Non-Viral Etiology Groups

	Total	Liver cancer first degree relatives	% out of all participants	Liver cancer second degree relatives	% out of all participants	Other cancer first degree relatives	% out of all participants	Other cancer second degree relatives	% out of all participants
	1243	*292*	*23%*	*92*	*7%*	*207*	*17%*	*54*	*4%*
Viral	923	227	25%	68	7%	157	17%	36	4%
Non-viral	320	65	20%	24	8%	50	16%	18	6%

PE-5

A Novel Flavonoid Galangin Modulates Hepatic Ischemia–Reperfusion Injury and Regulates TLR-4/NF-κB/NLRP3 Inflammatory Pathway Following Orthotopic Liver Tranplants in Rat Models

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CSVTU, SHUATS, HMFA-MIET, India

Aims: Hepatic ischemia can result in metabolic issues and an inflammatory milieu inside the liver, which may produce early graft malfunction, hepatic pathological damage, apoptosis, or rejection of the graft. In this study, we used orthotopic liver transplant rat models to examine the possibility of flavonoid Galangin in alleviating hepatic IRI and its underlying causes.

Methods: We performed orthotopic liver transplantation using a novel magnetic anastomosis approach. Following liver transplantation, hepatic IRI rat models were treated with intraperitoneally 10–20 and 30 mg b.w. of Galangin while using the RAW 264 hypoxia/reoxygenation (H/R) model. Western blotting, qRT-PCR, terminal deoxynucleotidyl transferase dUTP nick-end labeling staining, hematoxylin–eosin staining, immunosorbent assay, qRT-PCR, and hepatic and non-hepatic parameters were used to analyze the impact of Galangin on hepatic IRI. Oxidative stress profile and proinflammatory cytokines were also evaluated.

Results: In vitro research showed that Galangin inhibits the production of proteins associated to the TLR-4/NF-κB/NLRP3 inflammatory pathway in RAW264.7 cells treated with H/R. Galangin significantly reduces liver function levels (AST, ALP, ALT, and AFP) and serum levels of proinflammatory cytokines (IL-1, IL-18, and TNF-α) in rats following liver transplantation. It also attenuates hepatocyte apoptosis and reduces histopathological changes (degree of coagulation necrosis, architectural anomalies, and hepatocyte vacuolization), according to our in vivo assays. Furthermore, Galangin attenuates the inflammatory response and neutrophil infiltration (IL-1β, IL-18, IL-6, TNF-α, Ly6G and CD11b, and macrophage M2 polarization) caused by hepatic IRI and And decreased the expression of TLR-4/NF-κB/NLRP3 inflammatory pathway related proteins in rats following liver transplantation (TLR-4, MyD88, p-IKKα, p-IKKβ, p-IKK, p-IκBα, p-P65, NLRP3, ASC, Cleaved caspase-1, IL-1β, IL-18, TNF-α and IL-6).

Conclusions: our research demonstrated that Galangin suppresses hepatic inflammatory response after liver transplantation via modifying the TLR-4/NF-κB/NLRP3 inflammatory pathway.

Keywords: Galangin, Hepatic Ischemia–Reperfusion Injury, Orthotopic Liver Tranplants

PE-6

A Study on Factors Related to the Efficacy of Triple Therapy in Patients with Advanced Hepatocellular Carcinoma

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Aims: Liver cancer is one of the most common cancers worldwide and its incidence is rising in Western countries. Globally, it has a mortality to incidence ratio of 0.91, occurs 2.3 times more frequently in men than in women, and 72% of new cases are diagnosed in Asia. Hepatocellular carcinoma (HCC) is often detected in later stages and is the second deadliest cancer. The aim of this study was clinical and pathological data and survival analysis of triple therapy (intervention therapy + anti PD1 + lenvatinib) to identify the important factors that influence OS and PFS.

Methods: 216 patients with diagnosis aHCC Barcelona Clinic Liver Cancer (BCLC-B/C) China Liver Cancer (CNLC IIb-III) staging, either that had whom received Transarterial chemoembolization (TACE), Hepatic artery infusion therapy (HAIC), Lenvatinib and anti-PD1 combination therapy at ** hospital in China (this is a multicenter study of China), as well as in Tianjin Medical University Cancer Institute & Hospital, Tianjin, China, between May 2018 and September 2022.OS and PFS are the primary endpoints and clinicopathological factors including gender, age, etiology (HBV/Others), tumor stage (CNLC), liver cirrhosis, liver function (ALT/AST/GGT/TB/ALB, Child-Pugh, ALBI score), systemic inflammation factors (NLR, PLR) were analyzed to explore the association between important factors with triple therapy.

Results: The mean OS for the entire patient population was 48.2 months. Univariate analysis showed that Status of hepatitis (HR=4.448; 95% CI:16.783-34.217 P=0.035), Hepatic vein thrombosis (HR=4.988; 95% CI:20.290-40.543 P=0.029), Number of TACE/HAIC (HR=4.988; 95% CI:20.990-40.543 P=0.004), and ECOG PS (HR=4.989; 95% CI:20.989-40.546 P=0.045) meanwhile Status of hepatitis (P=0.049) CNLC staging (HR=2.765; 95% CI:42.843-53.681 P=0.039) and AFP level (P=0.002) were found to be important risk factors for PFS and OS, respectively. In multivariate Cox regression analysis, Hepatic vein thrombosis (HR:1.913; 95% CI: 1.057-3.463; P=0.032), number of TACE/HAIC (HR: 2.121; 95% CI: 1.252-3.593; P=0.005) and ECOG PS (HR:0.517; 95% CI: 0.268-0.998; P=0.049) were independent risk factors for PFS and CNLC staging (HR:4.061; 95% CI: 0.959-17.193; P=0.009) and AFP level (HR:33.084; 95% CI: 0.818-1338.27; P=<.001) were independent risk factors for OS. Status of hepatitis was only independent factor for both PFS (HR:0.247; 95% CI: 0.060-1.013; P=0.014) and OS (HR:0.040; 95% CI: 0.000-6.033; P=0.009).

Conclusions: The result of our study triple combination therapy showed that status of hepatitis is only independent factor for both OS and PFS with patients with advanced stage HCC.

Keywords: HCC, ANTI-PD1, Interventional Therapy, Lenvatinib, Survival

PE-7

Unraveling HCC Immunotherapy Outcomes: A Radiomics-Enabled Framework for Precision Medicine

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Aims: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality, with immunotherapy revolutionizing treatment paradigms. However, the heterogeneous response to immune checkpoint inhibitors (ICIs) necessitates robust predictive biomarkers. Radiomics, an advanced quantitative imaging technique, offers non-invasive insights into tumor heterogeneity, microenvironment, and treatment response. This systematic review aims to critically evaluate radiomics-based predictive models for assessing HCC response to immunotherapy, integrating imaging biomarkers with clinical and molecular correlates.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and Embase, adhering to PRISMA guidelines. Studies published between 2015 and 2024 evaluating radiomics-based approaches for predicting HCC response to immunotherapy were included. Data extraction focused on study design, imaging modalities (contrast-enhanced CT, MRI, PET), radiomic feature selection, machine learning algorithms, validation strategies, and integration with clinical and molecular biomarkers. Risk of bias was assessed using QUADAS-2 criteria, and study heterogeneity was evaluated through meta-analytical techniques.

Results: From 58 eligible studies, radiomics-based models demonstrated consistent predictive power (AUC 0.80–0.95) in differentiating responders from non-responders. Tumor heterogeneity, shape descriptors, and vascularization patterns emerged as dominant radiomic biomarkers. Studies integrating radiomics with clinical parameters (AFP, liver function) and molecular markers (PD-L1, TMB, immune infiltrates) exhibited enhanced predictive accuracy. However, methodological heterogeneity, lack of external validation, and inconsistent feature standardization remain significant challenges.

Conclusions: Radiomics represents a promising, non-invasive tool for predicting HCC response to immunotherapy, offering superior predictive capabilities compared to conventional biomarkers. However, standardization of radiomic feature extraction, multi-center validation, and AI-driven feature optimization are crucial for clinical translation. Future studies should focus on integrating multi-omics data with radiomics to advance precision oncology in HCC management.

Keywords: QUADAS-2, Radiomics, Immune Checkpoint Inhibitors (ICIS), Multi-OMICS

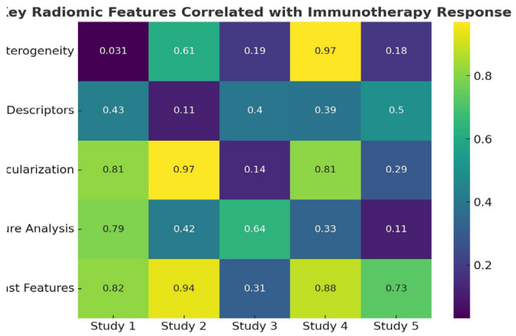

Figure 1.

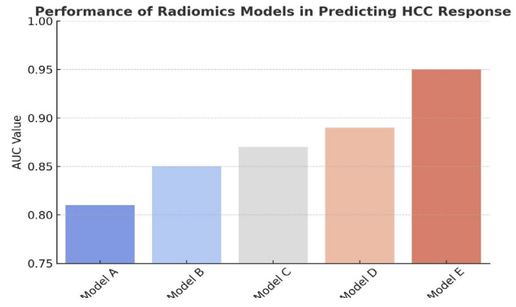

Figure 2.

PE-8

Impact Evaluation of Policy Interventions on Liver Disease Prevalence: Assessing the Smoking and Alcohol Regulation

Rosinta Hotmaida Pebrianti Purba[1], Helen Try Juniasti[2,1], Lintong Hottua Simbolon[1]

[1]The Pranala Institute, Indonesia, [2]Cendrawasih University, Indonesia

Aims: Liver disease, encompassing conditions such as cirrhosis, alcoholic hepatitis, and hepatocellular carcinoma, poses a global public health challenge. Cigarette smoking and excessive alcohol consumption are leading modifiable risk factors. Governments worldwide have implemented policies such as excise taxes, advertising bans, and public health campaigns to reduce consumption. However, the effectiveness of these policies in reducing liver disease prevalence remains underexplored, especially when accounting for socioeconomic disparities.

Methods: Using multi-country panel data from WHO, World Bank, and national health surveys (2000-2023), the variables includes cigarette and alcohol consumption (annual per capita measures packs/liters), liver disease prevalence (ICD-10 codes for liver conditions per 100,000 population), and policy indicators (excise taxes, advertising restrictions, and public health campaigns). Control variables includes GDP per capita, urbanization rate, and healthcare access. Fixed-effects regression analyzed individual and combined policy impacts on consumption and liver disease prevalence.

Results: Higher excise taxes significantly reduced cigarette (-5.4 packs) and alcohol consumption (-0.7 liters), leading to a 10.5-case decrease in liver disease prevalence per 100,000 population (P<0.001). Advertising restrictions (-6.8 cases) and public health campaigns (-4.2 cases) also contributed, though less substantially. Combined consumption of cigarettes and alcohol increased liver disease prevalence by 20.8 cases per 100,000, with excise taxes mitigating the largest portion (-9.6 cases). Interaction analysis revealed that excise taxes were most effective in low-income regions, while high GDP per capita reduced policy effectiveness due to higher baseline consumption.

Conclusions: Public policies targeting smoking and alcohol significantly reduce liver disease prevalence, with excise taxes emerging as the most effective intervention. Synergistic effects among policies amplify impact, emphasizing the need for comprehensive approaches tailored to socioeconomic contexts. Policymakers should address regional disparities to enhance health outcomes.

Keywords: Policy Evaluation, Cigarette Consumption, Alcohol Consumption, Liver Disease

PE-9

Biomarkers Identification to Predict Inflammatory and Immune Outcomes in Liver Cancer Surgery Patients

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Aims: Liver cancer, particularly hepatocellular carcinoma (HCC), is a leading cause of cancer-related mortality. Surgical resection is a primary treatment, but postoperative inflammatory and immune responses significantly impact outcomes. Identifying predictive biomarkers for these responses is critical for personalized treatment and improved survival. This study aims to identify and validate biomarkers associated with inflammatory and immune outcomes in liver cancer surgery patients.

Methods: A systematic review and meta-analysis were conducted following PRISMA guidelines, analyzing studies from PubMed, Scopus, and Web of Science. Open-source transcriptomic and proteomic datasets (e.g., GEO, TCGA) were used for validation. Key variables included inflammatory biomarkers (CRP, IL-6, TNF-α), immune biomarkers (PD-L1, CD8+ T-cells, IFN-γ), and outcomes (SIRS, sepsis, tumor recurrence, overall survival). Control variables included demographics, tumor stage, and liver function. Statistical analyses included descriptive statistics, random-effects meta-analysis, and multivariate Cox regression.

Results: Descriptive statistics shows that mean pre-surgery CRP levels were 12.5 mg/L, indicating systemic inflammation, while PD-L1 expression was 15%, reflecting moderate immune checkpoint activity. The 1-year tumor recurrence rate was 30%, and 1-year overall survival was 75%. Meta-analysis shows that CRP was strongly associated with SIRS (OR = 2.5, 95% CI: 2.0–3.0), with a stronger effect in advanced-stage disease (OR = 3.0). IL-6 predicted sepsis (OR = 3.0, 95% CI: 2.5–3.5), particularly in patients with decompensated liver function (OR = 3.5). PD-L1 was associated with tumor recurrence (HR = 1.8, 95% CI: 1.5–2.1), while CD8+ T-cell infiltration predicted improved survival (HR = 0.6, 95% CI: 0.5–0.7). Further, regression analysis shows that CRP (β = 2.2, P<0.001) and PD-L1 (β = 1.7, P<0.01) were significant predictors of SIRS and tumor recurrence, respectively. CD8+ T-cells were protective (β = 0.5, P<0.001), with stronger effects in patients with preserved liver function. Interaction effects revealed that tumor stage and liver function significantly modified biomarker-outcome relationships.

Conclusions: This study identifies CRP, IL-6, PD-L1, and CD8+ T-cell infiltration as robust biomarkers for predicting inflammatory and immune outcomes in liver cancer surgery patients. These findings support personalized biomarker-driven strategies to improve postoperative outcomes and survival.

Keywords: Liver Cancer Surgery, Inflammatory Biomarkers, Immune Biomarkers, Postoperative Outcomes

PE-10

The Role of Radiogenomics in Early-Stage Liver Cancer Screening

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Aims: Liver cancer often presents at advanced stages, reducing survival rates. Early detection is critical, and radiogenomics offers a promising approach by integrating imaging and genomic data to improve diagnostic accuracy and enable personalized screening. This study evaluates the diagnostic performance, cost-effectiveness, and key variables influencing the success of radiogenomic models in early-stage liver cancer screening.

Methods: A cross-sectional study utilized systematic review data from peer-reviewed journals published between 2015 and 2024. Key metrics included sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC). Independent variables were radiogenomic features (e.g., tumor heterogeneity, vascular patterns) and genomic alterations (e.g., TP53 mutations). Control variables included age, gender, hepatitis B/C status, and tracer pricing. Multivariate regression and cost-effectiveness analyses assessed diagnostic accuracy and economic viability.

Results: Radiogenomic models achieved an AUC of 0.92, outperforming traditional methods (0.78). Sensitivity and specificity were 85% and 80%, respectively. Tumor heterogeneity had the highest predictive value (AUC +0.12, P<0.01), followed by vascular patterns (+0.08, P<0.05). Hepatitis B/C status significantly enhanced accuracy (+0.15, P<0.01). Cost-effectiveness analysis showed radiogenomics was highly cost-effective in high-income countries (ICER: $15,000/QALY) but marginally cost-effective in LMICs (ICER: $20,000/QALY), where tracer costs posed barriers.

Conclusions: Radiogenomics is a highly accurate and cost-effective tool for early-stage liver cancer screening, particularly in high-income settings. Tumor heterogeneity and vascular patterns are key contributors to its success, while reducing tracer costs could enhance its feasibility in LMICs. Radiogenomics represents a transformative approach to improving early detection and patient outcomes.

Keywords: Radiogenomics, Early Detection, Genomic Biomarkers, Liver Cancer

Table 1. Analysis of The Role of Radiogenomics in Early-Stage Liver Cancer Screening

Metric	Radiogenomic Models	Traditional Screening	
Sensitivity (%)	85	70	
Specificity (%)	80	65	
AUC	0.92	0.78	
Region	**ICER ($/QALY)**	**Threshold ($/QALY)**	**Cost-Effectiveness**
High-Income Countries	15000	50000	Highly Cost-Effective
Low- and Middle-Income Countries (LMICs)	20000	20000	Marginally Cost-Effective
Variable	**Impact on Early Detection (AUC)**	**P-Value**	
Tumor Heterogeneity	0.12	<0.01	
Vascular Patterns	0.08	<0.05	
Hepatitis B/C Status	0.15	<0.01	
Tracer Pricing	-0.05	<0.05	

11. Liver Cancer, Clinical

PE-1

Values of AFP-L3% and PIVKA-II in Diagnosing in Hepatocellular Carcinoma

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Aims: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. Early diagnosis is crucial for improving patient outcomes. Traditional biomarkers like AFP have limitations in sensitivity and specificity. AFP-L3% and PIVKA-II have emerged as promising biomarkers, offering better diagnostic accuracy and prognostic value in HCC detection and management.

This study aims to evaluate the diagnostic value of AFP-L3% and PIVKA-II in hepatocellular carcinoma (HCC).

Methods: A cross-sectional, prospective study was conducted on 63 patients diagnosed with HCC who presented at Clinic 103 Cam Khe for examination between June 2022 and September 2024. Serum levels of AFP, AFP-L3%, and PIVKA-II were measured, and their diagnostic performance was analyzed. The associations between AFP-L3% and PIVKA-II with tumor characteristics were also assessed.

Results: At an AFP threshold of 10 ng/mL, the sensitivity of AFP-L3% at cut-off values of 10% and 15% (49.6% and 45.8%, respectively) was lower than that of AFP (65.3%). However, at a cut-off of 5%, the sensitivity of AFP-L3% was comparable to that of AFP.

At an AFP threshold of 20 ng/mL, the sensitivity of AFP-L3% at all evaluated cut-offs (5%, 10%, 15%) was nearly equivalent to the sensitivity of AFP.

PIVKA-II (cut-off: 40 mAU/mL) exhibited significantly higher sensitivity (97%) than AFP and AFP-L3% alone. The combined use of PIVKA-II and AFP-L3% further improved diagnostic accuracy.

AFP-L3% was significantly associated with tumor encapsulation but showed no correlation with other tumor characteristics.

PIVKA-II was significantly associated with tumor size and microvascular invasion but not with other tumor features.

Conclusions: AFP-L3% and PIVKA-II are valuable biomarkers for diagnosing HCC. PIVKA-II, in particular, demonstrated superior sensitivity compared to AFP. These biomarkers play a crucial role in supporting early diagnosis, monitoring treatment response, detecting recurrence, and assessing prognosis in HCC patients.

Keywords: AFP-L3, PIVKA-II, Hepatocellular Carcinoma

PE-2

Understanding the Differences in Acute Kidney Injury in Acute-on-Chronic Liver Failure and Decompensated Cirrhosis

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Aims: To compare the occurrence of acute kidney injury (AKI) in patients with acute-on-chronic liver failure (ACLF) versus those with decompensated cirrhosis (DC).

Methods: Between December 2022 and July 2024, 280 patients with hepatitis B virus (HBV)-related acute-on-chronic liver failure (HBV-ACLF) and 132 patients with HBV-related decompensated cirrhosis (HBV-DC) who were admitted to our center were consecutively enrolled in an observational study. Urine samples were collected from all participants, and levels of five urinary tubular injury biomarkers neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), liver-type fatty acid binding protein (L-FABP), cystatin C (CysC), and kidney injury molecule-1 (KIM-1) were measured. Additionally, patient demographics, the onset and progression of acute kidney injury (AKI), and responses to terlipressin therapy were documented. All patients were followed up for three months or until death after enrollment.

Results: Acute kidney injury (AKI) occurred in 71 HBV-ACLF patients and 28 HBV-DC patients (25.4% vs 21.2%, *P*=0.358). Among all patients, the levels of four urinary biomarkers NGAL, CysC, L-FABP, and IL-18 were significantly higher in HBV-ACLF patients with AKI (ACLF-AKI) compared to those with HBV-DC and AKI (DC-AKI), or those without AKI. A higher proportion of ACLF-AKI patients experienced AKI progression compared to DC-AKI patients (49.3% vs 17.9%, *P*=0.013). Forty-three ACLF-AKI patients and 19 DC-AKI patients were treated with terlipressin. The response rate was significantly lower in ACLF-AKI patients than in DC-AKI patients (32.6% vs 57.9%, *P*=0.018). Additionally, ACLF-AKI patients had the lowest 90-day survival rates among all groups (*P*<0.001).

Conclusions: AKI in ACLF patients is more closely linked to structural kidney injury, tends to be more progressive, and is associated with a poorer response to terlipressin treatment and worse prognosis compared to DC patients.

Keywords: Decompensated Cirrhosis, Acute-on-Chronic Liver Failure, Acute Kidney Injury, Biomarker, Prognosis

PE-3

Diagnostic Performance of Tumor Marker DCP and AFP with HCC in Mongolia

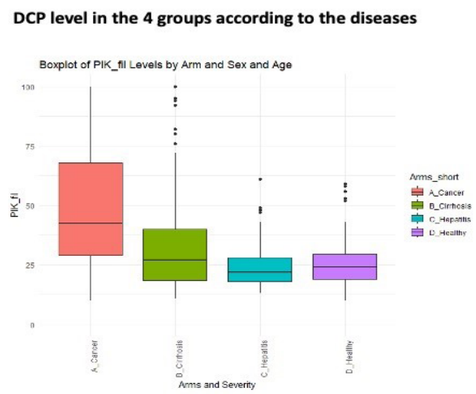
Purevjargal Bat-Ulzii, Ganbolor Jargalsaikhan, Sumiya Byambabaatar, Barkhas Batkhuu, Byambasuren Ochirsum, Munguntsetseg Batkhuu, Tuvshinjargal Ulziibadrakh, Oyungerel Lkhagva-Ochir, Bekhbold Dashtseren, Baigal Narantuya, Uurtsaikh Baatarsuren, Nomuunaa Bayarbat, Enkhnomin Ochirbat, Orkhonselenge Davaadamdain, Erdenechuluun Sainbayar, Sharawdorj Gur, Zolzaya Doljoo, Munkhzaya Munkhbaatar, Badamsuren Mend-Amar, Altankhuu Mordorjyn, Dahgwahdorj Yagaanbuyant, Naranbaatar Dashdorj, Naranjargal Dashdorj

Liver Center, Ulaanbaatar, Mongolia

Aims: Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and the second most common cause of cancer death. Mongolia has the world's highest liver cancer mortality rate, and HCC is the main cause of mortality. The poor survival rate is, in part, related to the diagnosis of HCC at advanced stages where effective therapies have been lacking. This study aimed to investigate the diagnostic significance of des-gamma-carboxy prothrombin (DCP) alone or in combination with alpha-fetoprotein (AFP) in patients with chronic hepatitis, liver cirrhosis, HCC, and healthy control.

Methods: The study was approved by the Ethics Committee of Ministry of Health of Mongolia. Participants were enrolled at the Liver Center between September 2023 and December 2024 (n = 940) in four groups: Healthy controls (159), Chronic hepatitis (264), Liver cirrhosis (LC) (151) and HCC (366). HCC was confirmed by CE-MRI. Serum levels of DCP and AFP were assessed by HISCL 5000 (Sysmex Tokyo, Japan) and fibrosis was performed using Fibroscan Expert 630 (Echosens, France). Participants of the HCC group were classified by BCLC stages. Statistical analyses were performed using SPSS software version 30. Sensitivity, specificity were determined by ROC analysis.

Results: Elevated DCP was observed in 5.6% (n = 9) of healthy individuals, 3.04% (n = 8) with chronic hepatitis, 31.5% (n = 47) with liver LC, and 84.8% (n = 308) with HCC. Similarly, elevated AFP levels were found in 1.88% (n = 3) of healthy controls, 5.32% (n = 14) with chronic hepatitis, 53.3% (n = 80) with LC, and 68.6% (n = 249) with HCC. For a DCP cut-off at 44.5 mAU/mL (AUC 0.924), sensitivity, specificity, PPV, and NPV were 85.4%, 88.6%, 82.0%, and 90.0%, respectively. For AFP at a cut-off of 5.85 ng/mL, these values were 80.9%, 74.3%, 66.0%, and 85.0%, respectively. When AFP and DCP were combined, there was a sensitivity of 85.4%, a specificity of 80.2%, and an AUROC of 0.930. The ROC curve analysis illustrated that the AUCs of AFP and DCP for distinguishing early-stage HCC from LC were 0.517 (95% CI=0.445 to 0.590) and 0.738 (95% CI=0.678 to 0.798), respectively.



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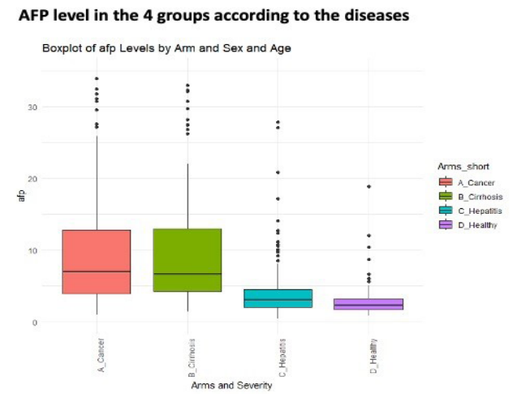

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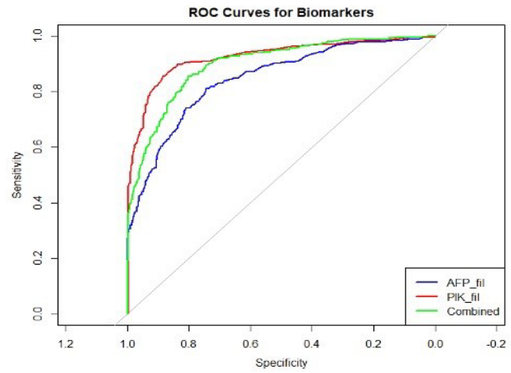

Figure 3.

Conclusions: In summary, elevated DCP and AFP levels were observed in increasing frequencies with disease severity, particularly in hepatocellular carcinoma (HCC), where 84.8% of patients exhibited elevated DCP and 68.6% had elevated AFP. For distinguishing HCC from liver cirrhosis (LC), DCP demonstrated higher diagnostic performance (AUC 0.924) compared to AFP (AUC 0.517). Combined, DCP and AFP offered improved diagnostic accuracy with a sensitivity of 85.4% and an AUROC of 0.930. These findings suggest that DCP, particularly in combination with AFP, may be a valuable tool for differentiating HCC from LC, with potential for clinical application in early detection and disease monitoring.

Keywords: PIVKA II, DCP, AFP, HCC

PE-4

Prognostic Effect and Potential Therapeutic Implication of Mitotic Index in Very Early Hepatocellular Carcinoma

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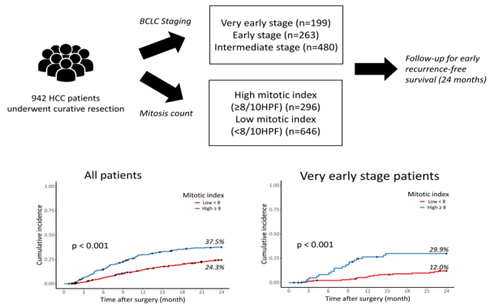
Aims: Surgical resection and ablation therapy are both primary treatment options for very early stage hepatocellular carcinoma (HCC). Patients with a high risk of recurrence may benefit from curative resection, rather than ablation. We investigated whether the mitotic index is associated with the early recurrence rate in HCC and can be used as a histologic criterion for the determination of primary treatment in very early stage HCC.

Methods: The number of mitoses was counted in representative tumor slides from 942 cases of surgically resected HCC from Samsung Medical Center. A high mitotic index was defined as more than eight mitoses in 10 high-power fields. The relationship between mitotic index, clinicopathological characteristics, and prognosis were analyzed. External validation was performed using 112 HCC cases obtained from Hallym University Sacred Hospital.



Results: High mitotic index was identified in 296 patients and was significantly associated with aggressive clinicopathological features including higher Edmondson grade, advanced American Joint Committee on Cancer T stage, and early tumor recurrence. Patients with a high mitotic index displayed a significantly shorter early recurrence-free survival (e-RFS). In subgroup analysis of patients with very early stage, the high mitotic index group showed unfavorable influences on e-RFS.

Conclusions: High mitotic index is a strong predictor of early recurrence in HCC patients and may have practical utility as a histologic criterion for primary treatment selection in very early stage HCC.

Keywords: Hepatocellular Carcinoma, Prognosis, Recurrence, Mitotic Index

PE-5

S100A14 as a Diagnostic Marker for Hepatocellular Carcinoma among Sudanese Patients at Ibn Sina Hospital

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Aims: This study aimed to study the sensitivity/ specificity /PPV and NPV of the tumor marker S100A14 as a diagnostic marker for HCC among Sudanese patients.This study aimed to study the sensitivity/ specificity /PPV and NPV of the tumor marker S100A14 as a diagnostic marker for HCC among Sudanese patients.

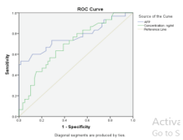
Methods: Descriptive case control study, hospital based. Was Conducted on two groups of patients. Serum alpha fetoprotein & S100A14 blood samples were collected then was investigated by using ELISA technique. Data analyzed using SPSS version 2. Chi-square test was used in the comparison between two groups with qualitative data. The comparison between more than two groups with quantitative data and parametric distribution was done by using one-way analysis of variance (ANOVA) test. The (ROC) was used to assess the best cut-off point between two groups with its sensitivity, specificity, positive predictive value(PPV),negative predictive value (NPV) and area under the curve (AUC).

Table 1 Demographic data of all studied groups

		Control group (No. = 29)		Cirrhosis group (No. = 30)		HCC group (No. = 30)		Chi-squared test	
		No.	%	No.	%	No.	%		p value
Sex	Female	7	24.1%	6	20.0%	8	26.7%	0.337	0.828
	Male	22	75.9%	24	80.0%	22	73.3%		
Age	Mean ± SD	32.03 ± 6.332		44.60 ± 13.286		57.07 ± 13.916		116.853	0.001
	Range	25 – 60		19 – 80		28 – 85			

Table 2 ANOVA table for S100A14 in all studied groups

S100A14(ng/ml)	Groups		
	Control group (No. = 29)	Cirrhosis group (No. = 30)	HCC group (No. = 30)
Mean ± SD	3.740072 ± 2.5124718	9.958994 ± 7.002447 4	11.075249 ± 7.2096020
Min - max	.3322 - 10.0512	.3294 - 21.1812	2.5000 - 24.6471
One-way ANOVA	F 12.689		
	p value <0.001		
Post hoc test			
Cirrhosis group vs control group	p value <0.001		
HCC group vs control group	p value <0.001		
Cirrhosis group vs HCC group	p value 0.753 (NS)		



Results: The total number of patients enrolled in the study were 89 patients. The S100A14 was significantly elevated in the HCC group. A cut-off value for serum S100A14 between HCC and control group is ≥5.012 with a sensitivity of 83% and specificity of 49.6%. S100A14 level was a significant diagnostic factor for HCC.

Conclusions: The results considered that S100A14 is a useful diagnostic marker for HCC.

Keywords: Hepatocellular Carcinoma, S100A14, Cirrhosis

PE-6

Resurrecting Oncogenic Relics: Endogenous Retrovirus Reactivation as an Impetus for Hepatocellular Carcinoma - A Trailblazing for Precision Therapeutics

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ACS Medical College and Hospital, Dr. M.G.R. Educational and Research Institute, India

Aims: 8% of the human genome is made up of Endogenous Retroviruses (ERVs), which are leftovers from previous viral infections. Despite being largely dormant, ERVs can be reactivated by chronic inflammation, epigenetic dysregulation, and viral co-infections (such as the Hepatitis B and C viruses) and may contribute to the development of hepatocellular carcinoma (HCC). The function of ERVs in liver oncogenesis, their relationship to HBV/HCV, and their potential as therapeutic targets and diagnostic indicators are all examined in this study.

Methods: The following topics were the subject of a systematic evaluation of the literature from around 24 articles of PubMed, Scopus, Google Scholar and Web of Science (2013–2025):

1. Using RNA sequencing and epigenetic profiling to identify ERRV expression in liver cancer.

2. ERV activation by HBV/HCV via viral integration and inflammation.

3. ERV-associated oncogenic pathways, including as interferon signalling, NF- κ B, and Wnt/ β -catenin.

4. Possible treatment approaches, such as immunotherapies that target ERV-derived antigens and epigenetic inhibitors.

Results: According to the results, some ERVs (such as HERV-K and HERV-H) are increased in HCC tissues and are associated with immunological evasion and a poor prognosis. Infections with HBV and HCV cause ERV reactivation, which intensifies immune suppression, genomic instability, and pro-inflammatory cytokines. Long non-coding RNAs (lncRNAs) and viral-like proteins produced from ERVs aid in the development of tumors. Preclinical research indicates potential for ERV-based cancer vaccines and epigenetic modulators (DNMT and HDAC inhibitors, for example).

Conclusions: Influenced by immunological dysregulation and viral hepatitis co-infection, ERVs constitute a new carcinogenic pathway in HCC. New treatment approaches for liver cancer may be possible by focusing on oncogenic pathways and ERV-derived antigens. Future research should concentrate on precision medicine strategies that combine immunomodulation and epigenetic treatment.

Keywords: Endogenous Retroviruses (ERV), HBV/HCV Co-Infection, Hepatocellular Carcinoma, Long Non-Coding RnaS (LNCRNAS)

PE-7

Advanced Hepatocellular Carcinoma Was Treated Radically with Multimodality Treatment: A Case Report

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Aims: Advanced hepatocellular carcinoma (HCC) includes patients with portal vein thrombosis or extrahepatic metastases, palliative systemic therapy is the main method at this stage.

Methods: Here, we report a case of HCC with portal vein thrombosis that was cured with a combination of methods.

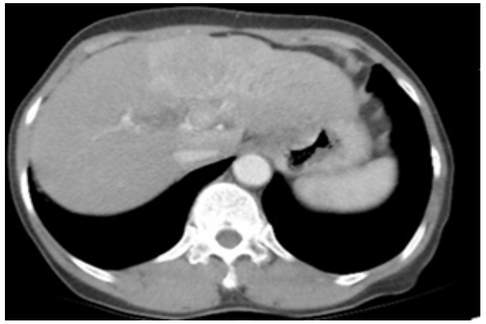
Results: A 70-year-old female, without comorbidities, presented with epigastric pain, examination found an enlarged liver 3cm below the sternum. The patient was tested and showed the α-fetoprotein (AFP) level of 3000 ng/ml and viral hepatitis B infection, an abdominal computed tomography (CT) scan showed a left liver tumor with the characteristics of hepatocellular carcinoma, a size of 56x74 mm. The tumor causes dilation of some peripheral biliary braches and thrombosis of the left brach of the portal vein (Vp3). Chest computed tomography was normal, liver function was good. The patient was diagnosed with hepatocellular carcinoma – BCLC C – viral hepatitis B – Child Pugh 5.

Lenvatinib was orally administrated at 8mg/day. After 2 months, the patient had no abdominal pain, AFP decreased to 20 ng/ml, and CT showed a decrease in size of the liver tumor. However, the patient developed hypertension (the highest was 220/100 mmHg), hand-foot syndrome grade 2, the patient was treated with a combination of two antihypertensive drugs, the blood pressure decreased to 150/80 mmHg. Because the blood pressure was difficult to control, the patient stopped Lenvatinib and was switched to the transarterial chemoembolization (TACE). After TACE, the patient underwent surgery to remove the left liver lobe, and specimen analysis showed liver tumor and portal vein thrombosis with no tumor cell left. After surgery, the tumor marker returned to normal, and CT scan showed no abnormalities. The patient was discharged from the hospital, took hepatitis B antiviral drugs and had surveillance.

Conclusions: For this advanced HCC patient with left portal vein thrombosis, after treatment with Lenvatinib, TACE and surgery, curative treatment was achieved. Thus, it is necessary to individualize, coordinate methods, and multidisciplinary team consultations for hepatocellular carcinoma patients to achieve

optimal results.

Keywords: Advanced Hepatocellular Carcinoma, Multimodality Treatment, Curative Treatment



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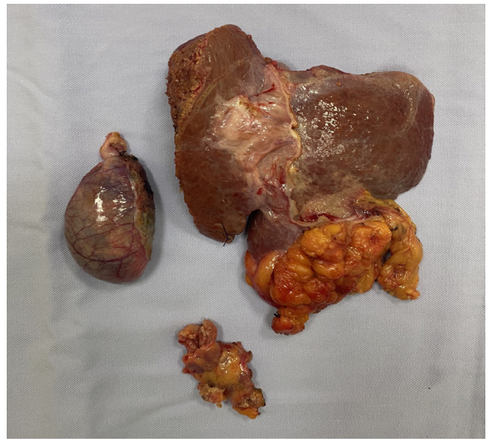

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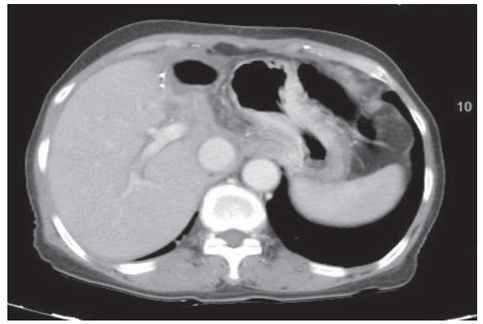

Figure 3.

PE-8

Ion Channel Genes as Predictive Biomarkers: Implications for Personalized Prognosis in Hepatocellular Carcinoma

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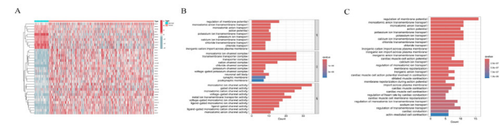
Aims: The primary aim of this study is to construct a robust risk assessment model based on ion channel-related genes (ICRGs) to predict the prognosis of hepatocellular carcinoma (HCC) patients. By identifying differentially expressed ICRGs and exploring their biological functions, we seek to uncover their potential roles in HCC progression and therapeutic response. Additionally, this study aims to evaluate the prognostic value of the identified ICRGs in relation to clinical outcomes, tumor microenvironment (TME) characteristics, immune cell infiltration, and drug sensitivity. Ultimately, this research aims to provide new insights into the molecular mechanisms of HCC and offer a foundation for personalized treatment strategies targeting ion channel-related pathways.

Methods: We obtained transcriptomic and clinical data for HCC patients from the Cancer Genome Atlas (TCGA) cohort as a training set and the International Cancer Genome Consortium (ICGC) cohort for validation. Differentially expressed ion channel-related genes (DE-ICRGs) were identified by comparing HCC tissues with normal controls. Enrichment analysis was performed using clusterProfiler. Prognostic genes were selected via univariate Cox regression, and a prognostic signature was constructed using LASSO Cox regression. The signature's prognostic value was assessed using Kaplan-Meier and ROC curve analyses. Further evaluations included clinical characteristics, tumor microenvironment (TME), drug sensitivity, and immunotherapy response.

Results: A total of 35 differentially expressed DE-ICRGs were identified, primarily involved in ion transport and channel activity. Among these, three biomarkers-CLCN2, CLIC1, and KCNJ11-were selected to construct a risk model for HCC. The model demonstrated robust predictive performance, with AUC values exceeding 0.7. Kaplan-Meier (KM) analysis revealed significantly shorter overall survival (OS) in the high-risk group compared to the low-risk group, a trend consistently observed across age and gender subgroups. Additionally, significant differences were noted between the high- and low-risk groups in terms of immune cell infiltration, immune checkpoint expression, and drug sensitivity. These findings underscore the prognostic value of the risk model and its potential implications for immune microenvironment modulation and therapeutic strategies in HCC.

Conclusions: This study identified three ICRGs as biomarkers and developed a novel risk prediction model based on these to assess the prognosis of HCC patients. This finding not only provides new insights into the relationship between ICRGs and HCC but also offers support for the personalized treatment of HCC.

Keywords: Ion channel genes, Hepatocellular carcinoma, Biomarkers, Prognostic model



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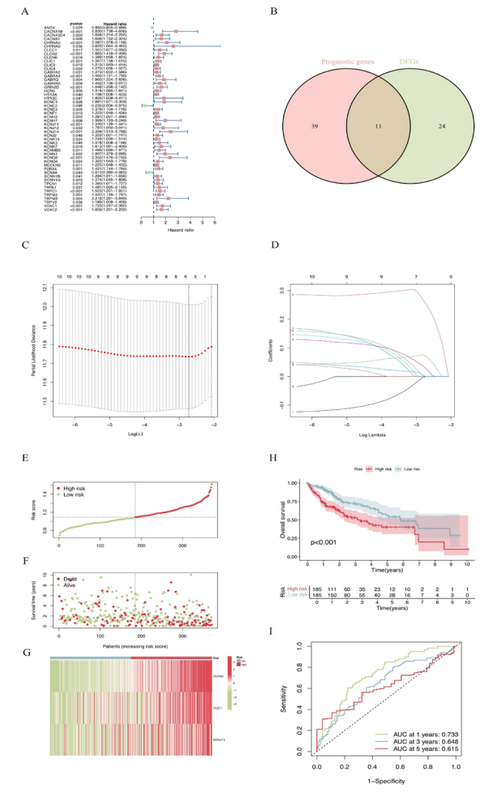

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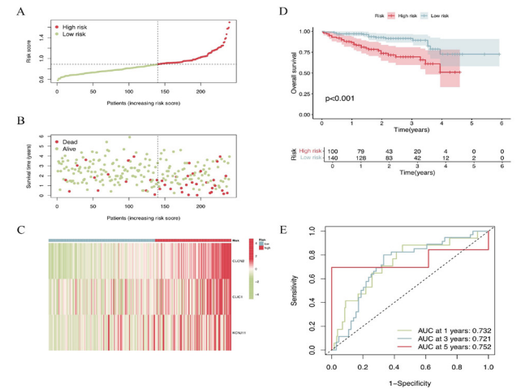


Figure 3.

PE-9

Disparities and Trends in Hepato-Biliary-Pancreatic Cancer Incidence and Mortality in the United States

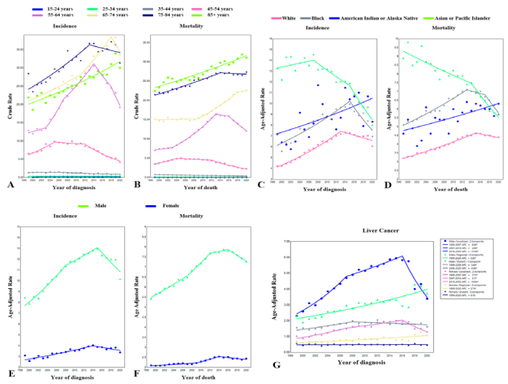
Jia Xu, Jingyuan Liao, Qiong Yan, Mingming Deng, Xiaowei Tang

The Affiliated Hospital of Southwest Medical University, China

Aims: Previous studies have only focused on incidence and mortality in individual cancer type of hepato-biliary-pancreatic system. To fill this gap, we tried to comprehensively elucidate disparities and trends in incidence and mortality of four major hepato-biliary-pancreatic cancers (liver, gallbladder, bile duct and pancreas) in the United States from 1999 to 2020.

Methods: Incidence data was extracted from the National Cancer Institute Surveillance, Epidemiology and End Result (SEER) database and mortality data from the Centers for Disease Control and Prevention (CDC) WONDER online database. Rates were calculated by age, state, race, gender and stage. Temporal trends were analyzed by Joinpoint regression.

Results: Age-adjusted incidence rates (AAIRs) in all the four cancers decreased, while age-adjusted mortality rates (AAMRs) of cholangiocarcinoma and pancreatic cancer increased in the latest follow-up period. Overall AAIRs and AAMRs increased except for cancer of gallbladder, whose incidence and death rates had been steadily declining but increased in Black and distant-stage group. AAMRs decreased in American Indian or Alaska Native (AIAN) individuals with cancer of bile duct and pancreas. Distant-stage was most common in pancreatic cancer patients and increased fastest in cholangiocarcinoma, while localized cancer ranked first in liver. Crude rates for mortality presented positive correlation with age, and overall death rate increased in 55+ years old cohort in cancer of liver, bile duct and pancreas.



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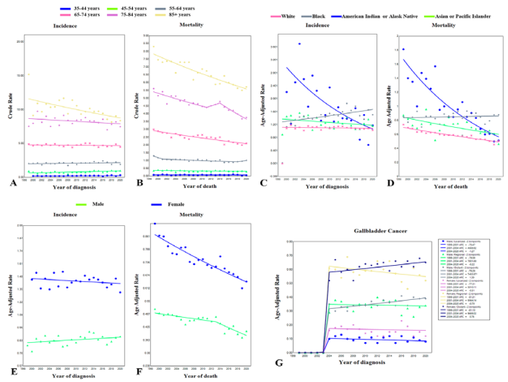

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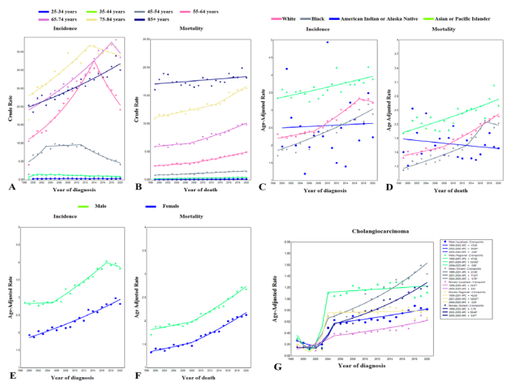


Figure 3.

Conclusions: We found both favorable and unfavorable trends in incidence and mortality of cancers in hepato-biliary-pancreatic system. Further studies are supposed to elucidate the reasons behind these findings.

Keywords: Liver Cancer, Gallbladder Cancer, Cholangiocarcinoma, Pancreatic Cancer

PE-10

Subset of Child-Pugh Score 7 Shows Comparable Survival Outcomes to Child-Pugh Score 6 in Hepatocellular Carcinoma Patients Treated with Atezolizumab and Bevacizumab

Jaejun Lee, Keungmo Yang, Ji Won Han, Pil Soo Sung, Jeong Won Jang, Seung Kew Yoon, Hee Sun Cho, Hyun Yang, Si Hyun Bae, Ji Hoon Kim, Heechul Nam, Chang Wook Kim, Hae Lim Lee, Hee Yeon Kim, Sung Won Lee, Ahlim Lee, Do Seon Song, Myung Jun Song, Soon Woo Nam, Jung Hyun Kwon, Soon Kyu Lee

Division of Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

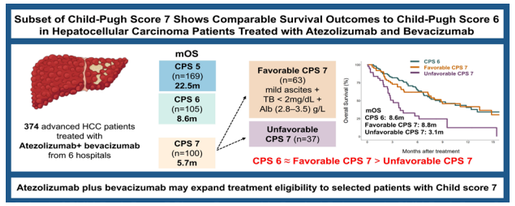
Aims: Given the limited data on the effectiveness of Atezolizumab plus Bevacizumab (Ate/Bev) in hepatocellular carcinoma (HCC) patients with a Child-Pugh score (CPS) of 7, this study aims to evaluate the treatment's efficacy in this population and identify specific CPS 7 subgroups that may benefit from it.

Methods: This study included patients with advanced HCC who received Ate/Bev as first-line therapy between September 2020 and December 2023 at six university hospitals. The primary outcome was overall survival (OS), while secondary outcomes included progression-free survival (PFS) and treatment response.

Results: Among the 374 included patients, those with CPS 5 (n=169) demonstrated the highest OS and PFS, followed by patients with CPS 6 (n=105) and CPS 7 (n=100) (P<0.05). For the variables comprising CPS, the hazard ratio (HR) for OS increased with elevated total bilirubin (TB) levels and was lower in patients with mild ascites (P<0.05). The HR for OS tended to increase as albumin levels dropped to 2.8 g/dL. Based on these findings, CPS 7 patients were further classified into two subgroups: favorable (TB <2 mg/dL, 3.5 ≥ Alb ≥ 2.8 g/dL, mild ascites, and absence of hepatic encephalopathy) and unfavorable (other CPS 7). Compared to patients with CPS 6, those in the favorable CPS 7 group exhibited comparable OS and PFS, while unfavorable CPS 7 patients had significantly lower OS and PFS (P<0.05). These findings were consistently observed in the multivariate analysis.

Conclusions: This study suggests that Ate/Bev treatment can be effective in subset of CPS 7 patients, highlighting the potential to broaden treatment eligibility for this population.

Keywords: Atezolizumab, Bevacizumab, Hepatocellular Carcinoma, Child-Pugh Score



PE-11

MRI with Gadoxetate Disodisum Using Conventional Portal Venous Phase and Late Portal Venous Phase for the Noninvasive Diagnosis of Hepatocellular Carcinoma: Intraindividual Comparison of MRI with Extracellular Agent

Sunyoung Lee, Boryeong Jeong

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Aims: To investigate the diagnostic performance of MRI with gadoxetate disodisum (EOB-MRI) using conventional portal venous phase (CPVP) and late portal venous phase (LPVP) for the noninvasive diagnosis of hepatocellular carcinoma (HCC), with intraindividual comparison of MRI with extracellular agent (ECA-MRI).

Methods: The present study included 108 prospectively enrolled at-risk patients (mean age, 59.4 years; 89 men) with 143 lesions (including 118 HCCs) who underwent both ECA-MRI and EOB-MRI including CPVP and LPVP. Two radiologists independently reviewed and assigned all lesions according to the Liver Imaging Reporting and Data System v2018, and per-lesion sensitivity and specificity were compared intraindividually.

Results: In HCCs, nonperipheral washout appearance was less frequently observed on EOB-MRI using CPVP than on ECA-MRI (R1: 69.5% vs. 79.7%, P=0.02; R2: 66.9% vs. 76.3%, P=0.02), whereas it was more frequently observed on EOB-MRI using LPVP than on ECA-MRI (R1: 94.1% vs. 79.7%, P<0.001; R2: 92.4% vs. 76.3%, P<0.001). In LR-5, EOB-MRI using LPVP showed a significantly higher sensitivity for diagnosing HCC than ECA-MRI (R1, 80.5% vs. 72.0%, P=0.03; R2: 79.7% vs. 71.2%, P=0.01), while EOB-MRI using CPVP showed a significantly lower sensitivity than ECA-MRI (R1: 64.4% vs. 72.0%, P=0.03; R2: 64.4% vs. 71.2%, P=0.03). The specificity of EOB-MRI using LPVP (both R1 and R2: 88.0%) was not significantly different from ECA-MRI (both R1 and R2: 92.0%, P=0.31) or EOB-MRI using CPVP (both R1 and R2: 92.0%, P=0.31).

Conclusions: In direct individual comparisons, EOB-MRI using LPVP provided better sensitivity than ECA-MRI or EOB-MRI using CPVP for the diagnosis of HCC, without significant difference in specificity.

Keywords: Hepatocellular Carcinoma, Diagnosis, Magnetic Resonance Imaging, Contrast Media

PE-12

Liver Stiffness by VCTE Predicts Hepatic Decompensation and Differential Efficacy of Atezolizumab-Bevacizumab versus TKIs in Advanced Hepatocellular Carcinoma

Jaejun Lee, Hyun Yang, Si Hyun Bae, Hee Sun Cho, Keungmo Yang, Pil Soo Sung, Jeong Won Jang, Seung Kew Yoon, Heechul Nam, Chang Wook Kim, Hae Lim Lee, Hee Yeon Kim, Sung Won Lee, Ahlim Lee, Do Seon Song, Myung Jun Song, Soon Woo Nam, Soon Kyu Lee, Jung Hyun Kwon, Ji Won Han

Division of Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: Hepatic decompensation following systemic treatment, including atezolizumab plus bevacizumab (Ate/Bev), is a critical prognostic event in advanced hepatocellular carcinoma (HCC). This study evaluates the predictive utility of liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) for decompensation incidence post-treatment.

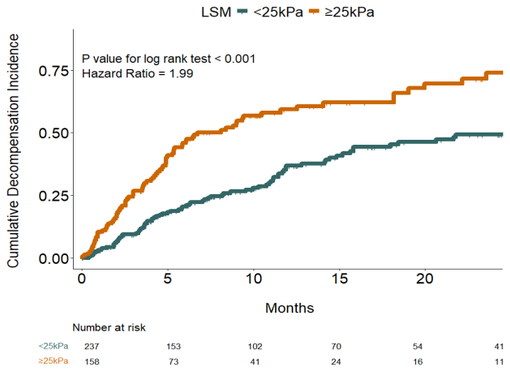
Methods: We analyzed 396 HCC patients treated with systemic therapy (Ate/Bev, lenvatinib, or sorafenib) who underwent VCTE prior to treatment. Hepatic decompensation, overall survival (OS), and progression-free survival (PFS) were assessed. Decompensation was defined as new or worsening ascites, variceal bleeding, or hepatic encephalopathy. A 25 kPa LSM threshold, based on Baveno criteria for significant portal hypertension, stratified patients into high and low LSM groups.

Results: Of the 396 patients, 176 received Ate/Bev, while 45 and 175 received lenvatinib and sorafenib, respectively. Ate/Bev improved OS (HR 0.72, P<0.05) and PFS (HR 0.75, P<0.05) but was associated with higher risks of decompensation (HR 1.81, P<0.05) and variceal bleeding (HR 4.6, P<0.05) compared to TKIs. Treatment distribution was similar between high and low LSM groups (P=0.546). High LSM was associated with increased decompensation risk (HR 1.99, P<0.001) and a trend toward worse OS (HR 1.27, P=0.065) and PFS (HR 1.10, P=0.417). In the low LSM group, Ate/Bev outperformed TKIs in OS and PFS (P<0.05) without increasing decompensation risk. In contrast, in the high LSM group, Ate/Bev and TKIs showed no OS or PFS differences, but Ate/Bev significantly increased decompensation and variceal bleeding risk (P<0.05). Patients with both high LSM and high-grade portal vein thrombosis (HGPVT) had the highest decompensation, varix bleeding, and mortality risk (HR 3.96, P<0.05).

Conclusions: LSM by VCTE predicts hepatic decompensation following systemic therapy in advanced HCC. In patients with

high LSM, Ate/Bev increases decompensation and mortality risk, warranting careful treatment selection.

Keywords: Vibration Controlled Transient Elastography, Hepatic Decompensation, Atezolizumab Plus Bevacizumab, Varix Bleeding



PE-13

Prognostic Impact of Cytokeratin 19 Expression in Advanced Hepatocellular Carcinoma Treated with Hepatic Arterial Infusion Chemotherapy

Keungmo Yang[1], Jaejun Lee[1], Ji Won Han[1], Jeong Won Jang[1], Seung Kew Yoon[1], Suho Kim[2], Jung Suk Oh[2], Ho Jong Chun[2], Eun Ji Jang[3], Pil Soo Sung[1,3]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul; [2]Department of Radiology, Seoul St Mary's Hospital, The Catholic University of Korea, 222, Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea; [3]The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Korea

Aims: Cytokeratin 19 (CK19) is a well-known biomarker associated with poor prognosis in cholangiocarcinoma. However, its clinical implications in advanced hepatocellular carcinoma (HCC) remain unclear. This study aimed to investigate the impact of CK19 expression on survival outcomes in patients with advanced HCC treated with hepatic arterial infusion chemotherapy (HAIC).

Methods: A retrospective analysis was conducted on 68 patients with pathologically confirmed advanced HCC who received HAIC. Patients were categorized into two groups based on CK19 expression: CK19-negative (n = 46) and CK19-positive (n = 22). Baseline clinical characteristics, treatment responses, overall survival (OS), and progression-free survival (PFS) were compared between the two groups. Univariate and multivariate Cox regression analyses were performed to identify independent prognostic factors for survival outcomes.

Results: The CK19-positive group showed the better OS compared to the CK19-negative group (HR = 0.42, 95% CI: 0.18-1.01, *P*=0.046). Univariate and multivariate analyses confirmed CK19 expression as an independent prognostic factor for OS (HR = 0.38, 95% CI: 0.15-0.98, *P*=0.045), while it was not significantly associated with PFS (*P*=0.222). Other clinical factors, including tumor size, portal vein tumor thrombosis, and extrahepatic metastasis, did not show significant associations with OS in multivariate analysis.

Conclusions: Our study highlights the importance of pathological analysis through tissue biopsy in patients with advanced HCC. The findings suggest that CK19-positive HCC patients may benefit from HAIC, supporting its potential as an effective treatment option for this subgroup. Further prospective studies are needed to validate these findings and optimize therapeutic strategies for CK19-positive HCC patients.

Keywords: Advanced Hepatocellular Carcinoma, Cytokeratin 19, Hepatic Arterial Infusion Chemotherapy, Survival Analysis

PE-14

Metastatic Patterns and Their Clinical Implications in Hepatocellular Carcinoma: Analysis of a Nationwide Korean Cancer Registry

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Aims: Although the staging classification of advanced hepatocellular carcinoma (HCC) is well established, there is a paucity of studies investigating the metastatic patterns. This study aims to analyze patterns of metastasis in advanced HCC and their clinical implications.

Methods: The study population consisted of 7,014 individuals aged 20 years or older, identified from the Korea Primary Liver Cancer Registry between 2014 and 2017. We analyzed metastatic patterns concerning tumor size, multiplicity, presence of cirrhosis, vascular invasion, and lymph node metastasis.

Results: Tumors larger than 10 cm were associated with a higher incidence (>50%) of tumor multiplicity and vascular invasion. However, this was not proportionally correlated with an increased rate of lymph node metastasis or overall distant metastasis. In the subgroup analysis, tumor size and vascular invasion showed a significant association in both single and multiple tumors but were not correlated with lymph node metastasis. This trend was also observed in the cirrhosis with multiple tumor groups. For HCC cases without vascular invasion or lymph node metastasis, tumor size was correlated with metastasis regardless of the metastatic site. However, in cases with vascular invasion but without lymph node metastasis, lung metastasis was the only site significantly associated with tumor size. Conversely, in patients with lymph node metastasis but without vascular invasion, metastases to the bone, adrenal gland, or non-regional lymph nodes were more prominent than lung metastases. Notably, in cases where both vascular invasion and lymph node metastasis were present at the time of diagnosis, metastases were observed in >40% of tumors measuring ≤2 cm.

Conclusions: Hematogenous-dominant and lymphangitic-dominant metastatic patterns may need to be classified separately. Additional transcriptomic analyses are currently in progress to gain insights into the differences between hematogenous and lymphangitic metastatic patterns.

Keywords: Hepatocellular Carcinoma, Patterns, Metastasis

PE-15

Adjuvant CIK Cell Therapy Following Curative Treatment of Hepatocellular Carcinoma Prolongs Recurrence-Free Survival in the Real-World Setting: A Large Two-Center Cohort Study

Hyunjae Shin[1], Youngsu Park[1,2], Byeong Geun Song[3], Jae Woong Yoon[1], Gyung Sun Lim[1], Juyeon Kim[1], Yunmi Ko[1], Jeayeon Park[1], Moon Haeng Hur[1], Yun Bin Lee[1], Eun Ju Cho[1], Su Jong Yu[1], Dong Hyun Sinn[3], Yoon Jun Kim[1], Joon Hyeok Lee[3], Jung-Hwan Yoon[1], Jeong-Hoon Lee[1]

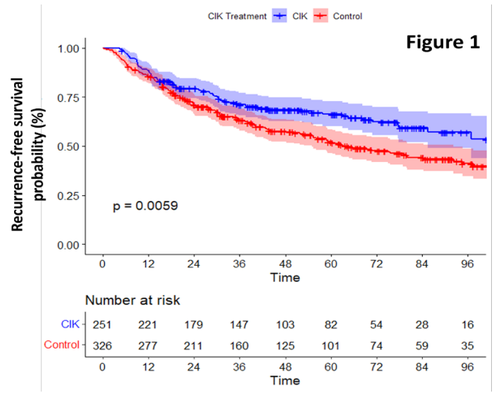
[1]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [2]Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Goyang, Republic of Korea; [3]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

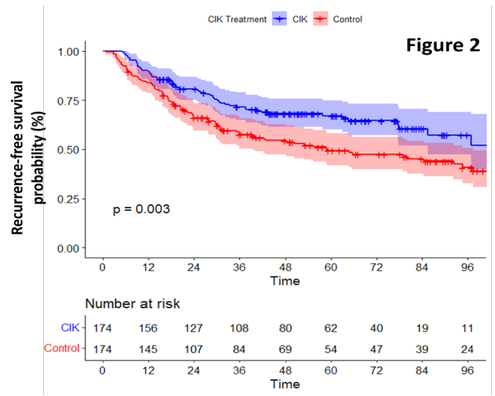
Aims: Despite the need for effective adjuvant therapies for hepatocellular carcinoma (HCC), most strategies, including sorafenib and atezolizumab/bevacizumab combination therapy, have failed to prolong recurrence-free survival (RFS). Meanwhile, cytokine-induced killer (CIK) cell therapy has demonstrated potential in improving RFS in previous clinical studies. This study aimed to evaluate the clinical outcomes of CIK cell therapy in patients with HCC who underwent curative treatment, emphasizing its effectiveness in real-world practice.

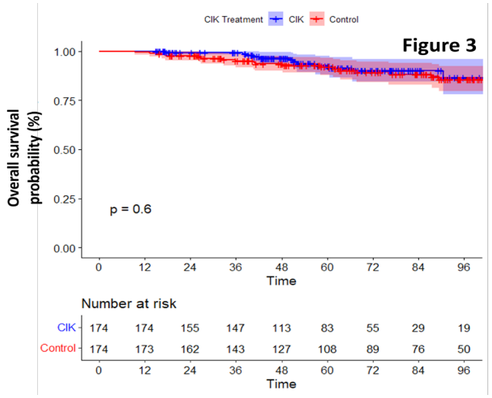
Methods: This retrospective cohort study analyzed 577 patients who received curative treatment for HCC at two tertiary hospitals in Korea. Patients were categorized into either CIK (*n*=251) or control group (*n*=326). Propensity score matching (PSM) was applied to balance baseline characteristics. Primary and secondary endpoints were RFS and overall survival (OS), respectively.

Results: The median follow-up duration was 57.2 (interquartile range, 35.9–82.5) months. Before PSM, the CIK group had a higher proportion of multiple tumors (26.3% vs. 6.1%) and larger tumor size (median, 2.5 cm vs. 2.0 cm) (both *P*<0.001), suggesting a worse natural course. However, the CIK group exhibited significantly prolonged RFS compared to the control group (median=101.2 vs. 64.7 months; HR=0.69, 95% CI=0.53–0.90, *P*=0.006; Figure 1). No significant difference was observed in OS between the groups (median=not reached in both groups; HR=0.96, 95% CI=0.55–1.68, *P*=0.88), possibly due to the small number of events. After PSM, key variables were well balanced (all SMD<0.1) in 174 matched pairs (*n*=348). The CIK group maintained significantly prolonged RFS compared to the control group (median=not reached vs. 58.9 months; HR=0.61, 95% CI=0.44–0.85, *P*=0.003; Figure 2), however, OS did not differ between the groups (HR=0.83, 95% CI=0.41–1.67, *P*=0.60; Figure 3).

Conclusions: Our real-world clinical data on adjuvant autologous CIK cell therapy following curative treatment of HCC showed an association with improved RFS, but no improvement in OS. These findings suggest that CIK therapy may be effective in reducing tumor recurrence in real-world practice, which is consistent with previous randomized controlled trial results.







Keywords: Hepatocellular Carcinoma, Adjuvant Immunotherapy, Cytokine-Induced Killer Cells, Recurrence-Free Survival

PE-16

Assessment of Focal Liver Observations Using the Ultrasound LI-RADS Algorithm: Experience from the Detect-HCC Study in Mongolia

Sharavdorj Gur[1], Barkhas Batkhuu[1], Erdenechuluun Sainbayar[1], Orhon Gombosuren[2], Javzandolgor Nyamsambuu[3], Regzedmaa Tsognemekh[2], Munguntsetseg Batkhuu[1], Nomuunaa Bayarbat[1], Tuvshinzaya Purevdorj[1], Oyungerel Lkhagva-Ochir[1], Tuvshinjargal Ulziibadrakh[1], Ganbolor Jargalsaikhan[1], Naranbaatar Dashdorj[1], Dahgwahdorj Yagaanbuyant[1], Naranjargal Dashdorj[1]

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Aims: Mongolia has the highest prevalence and mortality rate of liver cancer worldwide, yet a risk-targeted liver cancer surveillance program is lacking. This study aimed to evaluate the suitability of the LI-RADS US Surveillance 2024 algorithm for liver cancer detection in the Mongolian population.

Methods: We analyzed data from 1,243 participants (male: 638; female: 605) in the DETECT-HCC study. Among them, 459 were diagnosed with HCC. A total of 953 participants underwent contrast-enhanced MRI or CT, with the majority (82%) receiving Primovist-enhanced MRI. Ultrasound examinations were performed on 939 participants, including 588 individuals meeting AASLD criteria for HCC surveillance. Two radiologists with over three years of experience conducted ultrasound evaluations using the LI-RADS US Surveillance 2024 algorithm, while MRI/CT diagnoses followed the LI-RADS CE-CT/MRI 2018 algorithm by three radiologists with over ten years of experience.

Results: Among the 588 AASLD target population, LI-RADS US Surveillance 2024 showed:

- Sensitivity 94%, specificity 87%, PPV 90%, NPV 93.7% (oncologist-diagnosed HCC).

- Sensitivity 95%, specificity 70%, PPV 68.4%, NPV 96.1% (HCC diagnosed by LI-RADS LR-5 criteria).

For 351 non-target participants:

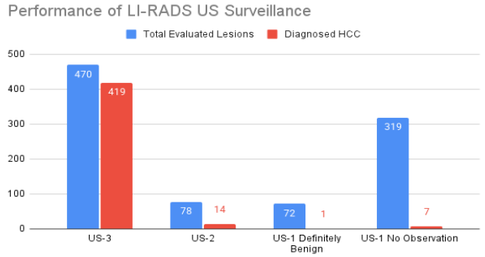
- Sensitivity 96%, specificity 92%, PPV 87%, NPV 97.5% (oncologist-diagnosed HCC).

- Sensitivity 95%, specificity 89%, PPV 81%, NPV 96% (HCC diagnosed by LI-RADS LR-5 criteria).

Of all ultrasound evaluations, 25% were VIS-A, 73% VIS-B, and 2% VIS-C. Ultrasound missed 115 observations, mainly in segments S8 (24%), S5 (23%), and S7 (20%).

Conclusions: LI-RADS US Surveillance 2024 demonstrated high sensitivity and specificity for HCC detection in both target and non-target populations. While most missed lesions were in challenging liver segments, the algorithm proved effective for detection, supporting its potential implementation in Mongolia. But we should remember that ultrasound was conducted by highly experienced radiologist so it may be biased and given Mongolian high prevalence and late-stage diagnosis the results can be biased.

Keywords: LI-RADS Algorithm, Ultrasound, Liver Cancer, Mongolia



PE-17

Validation for the Efficacy of AI Platforms on Liver Cancer Treatment Strategies

Keungmo Yang, Jaejun Lee, Jeong Won Jang, Seung Kew Yoon, Pil Soo Sung, Ji Won Han

Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

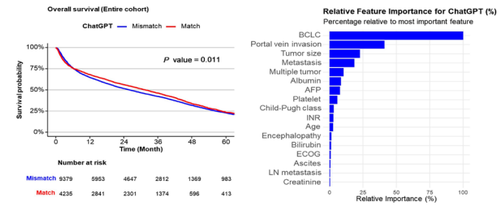
Aims: Decisions regarding hepatocellular carcinoma (HCC) treatments are highly individualized, depending on tumor burden, liver function, or performance status. Recent advancements in artificial intelligence (AI) and large language models (LLMs) have facilitated access to extensive clinical information. However, their applicability in treatment planning remains uncertain. This study evaluates the efficacy of LLM-generated treatment strategies by comparing them with real-world physician decisions and assessing survival outcomes.

Methods: A total of 19,774 HCC patients from the Korean Primary Liver Cancer Registry were analyzed, with 13,614 included after exclusions. Three LLMs (ChatGPT, Gemini, and Claude) were trained on clinical guidelines to generate treatment plans. Patients were categorized into matched and mismatched groups based on agreement with LLM-generated plans. Survival analysis assessed differences between these groups to evaluate AI-driven treatment efficacy. Additionally, survival outcomes among the three LLMs were compared using inverse probability of treatment weighting (IPTW).

Results: Among 13,614 patients, treatment plans recommended by ChatGPT, Gemini, and Claude matched those of physicians in 4,235 (31.1%), 4,446 (32.7%), and 3,641 (26.8%) cases, respectively. Overall survival was significantly better in patients who received AI-recommended treatments from ChatGPT (P=0.011), with the survival advantage being most pronounced in BCLC stage A patients across all three LLM models (P<0.001). Major discrepancies in treatment decisions between LLM models and clinicians were most notable in the management of early-stage HCC. Both AI models and human clinicians prioritized BCLC staging as the most critical factor in treatment decision-making; however, while clinicians placed greater emphasis on liver function, AI models focused more on tumor characteristics. Survival analyses comparing the three LLMs after IPTW adjustment showed no significant differences in treatment efficacy among AI models (P=0.879).

Conclusions: These findings highlight the potential of AI-assisted treatment planning in early-stage HCC while emphasizing its limitations in more advanced cases. Further refinement of AI models and their integration with clinical expertise will be essential to improving decision-making accuracy and ensuring their reliable application in real-world practice.

Keywords: Hepatocellular Carcinoma, Large Language Model, Artificial Intelligence, Survival Analysis



PE-18

Comparison of the Pathological Features among HBV, HCV and Fatty Liver Disease-Related Hepatocellular Carcinoma on the Post Liver Resection Patients

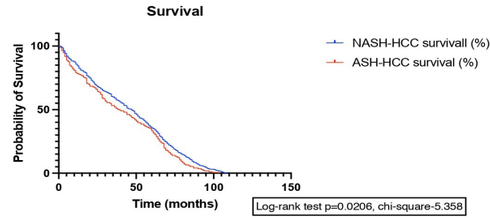
Enkhtsatsral Batmunkh[1], Bayart-Uils Bayar[1], Unenbat Gurbadam[2], Ariyabilig Otgongerel[2], Tserendorj Demchig[2], Amgalantuul Batgerel[2], Batsaikhan Bayartugs[2], Munkhdelger Byambaragchaa[2], Yerbolat Amankeldi[2], Munkhzaya Chogsom[2], Lkham Nyam-Osor[2], Chinburen Jigjidsuren[2], Gantuya Dorj[3]

[1]Department of Pathology, National Cancer Center of Mongolia; 2Hepatobiliary and Pancreatic Transplantation Centre, National Cancer Center of Mongolia; [3]School of Public Health, Mongolian National University of Medical Sciences, Mongolia

Aims: Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer-related deaths globally, with over 900,000 new cases and 830,000 deaths reported in 2020. The incidence of HCC is projected to increase by 55% by 2040. Mongolia has the highest HCC incidence worldwide, driven by hepatitis B and C infections and alcohol consumption.

Methods: This study compared the clinical, biochemical, and tumor characteristics of HCC caused by non-alcoholic steatohepatitis (NASH-HCC) and alcoholic steatohepatitis (ASH-HCC) in 980 patients who underwent liver resection between 2015 and 2018 at the National Cancer Center of Mongolia.

Results: ASH-HCC patients were predominantly younger males (mean age 52) with heavy alcohol consumption, while NASH-HCC patients were older (mean age 64) and more likely to have metabolic syndrome. NASH-HCC tumors were larger (>5 cm; P=0.0045), poorly differentiated (G4; P=0.0248), and associated with severe fibrosis (ISHAK stages 5–6; P=0.0285). Despite higher recurrence rates (48.1% vs. 33.5%; P=0.0001), NASH-HCC patients had better median survival (92.6 vs. 80 months; P=0.0206) compared to ASH-HCC. HBV/HCV co-infection was more prevalent in NASH-HCC (P=0.0148), highlighting the interplay between viral and metabolic factors in HCC pathogenesis.



Conclusions: This study underscores the distinct clinicopathological profiles of NASH-HCC and ASH-HCC, emphasizing the need for tailored surveillance and early detection strategies,

particularly for non-cirrhotic NASH-HCC cases. Advanced imaging and biomarkers may improve outcomes, while alcohol reduction remains critical for ASH-HCC prevention.

Keywords: HCC, NASH, ASH

PE-19

Role of Erastin in Intestinal Injury Following Perioperative Liver Transplantation via Ferroptosis in Animals

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Aims: Apart from liver injury, perioperative liver transplantation (LT) can result in heart, brain, renal, lung, and particularly intestine damage. Research on ferroptosis in intestinal epithelial cells reveals that the pathophysiological process of intestinal I/R damage is related with it. This work aimed to investigate the function of ferroptosis activator Erastin in perioperative LT intestinal damage in rats and thus elucidate the putative mechanism.

Methods: All the rats were randomly divided into different groups following I/R. Collected from the portal vein (PV), inferior vena cava blood specimens were six hours and twenty-four hours respectively. We have evaluated measures of liver and intestinal damage, inflammatory and death signals (enzyme-linked immunosorbent assay (ELISA)).Determined were the amounts of serum interleukin 6 (IL-6) and serum malondialdehyde (MDA). Each group's PV opening yielded ileal tissue from rats at both six and twenty-four hours; these sections were thereafter under light microscopy

Results: We found alteration in serum transaminase (AFP, AST, ALP and AST) and the levels of intestinal MDA, and antioxidant parameter such as superoxide dismutase (SOD), glutathione (GSH), glutathione peroxidase 4 (GPX4), and tissue iron by Erastin. Western blot helped to ascertain the expression of xCT (cysteine glutamate reverse transporter light chain protein) and GPX4. It also mitigates the inflammatory cytokines and apoptosis (P53, Bax, B-actin and Bcl). Damaged intestinal by liver hepatic ischemia-reperfusion in rats showed ferroptosis-mediated and supported by experimental data of ERASTIN. Further aggravate the intestinal damage is corrected by Erastin which may block the cystine/glutamate antiporters /GSH/GPX4 signal axis in intestinal damage induced by I/R in rat LT liver, or iron overload after reperfusion, causing a significant accumulation of L-ROS and activating cellular ferroptosis.

Conclusions: Our studies suggest that Erastin will be beneficial drug in the management of IR following LT with underlying mechanism.

Keywords: Eratin, Ferroptosis, Liver Transpalntation

PE-20

Single-Cell Omics in Hepatocellular Carcinoma: Dissecting the Immune Microenvironment to Unlock Novel Therapeutic Paradigms

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Aims: Hepatocellular carcinoma (HCC) is a major contributor to cancer-related deaths, with its immune microenvironment playing a crucial role in tumor progression and resistance to treatment. Single-cell omics, particularly single-cell RNA sequencing (scRNA-seq), allows for an in-depth analysis of immune cell diversity in HCC. This systematic review and meta-analysis assess the immune landscape of HCC to identify potential therapeutic targets.

Methods: A systematic search of PubMed, EBSCO, and Embase was conducted according to PRISMA guidelines. Studies analyzing scRNA-seq data from human HCC tissues, focusing on immune cell composition and function, were included. A random-effects model was used to perform meta-analysis, with effect sizes reported as Hedges' g and odds ratios (OR) with 95% confidence intervals (CI).

Results: A total of 13 studies were analyzed. The meta-analysis revealed a significantly higher proportion of exhausted CD8+ T cells in tumors compared to adjacent tissues (38.4% vs. 15.7%, OR: 3.12, 95% CI: 2.21–4.23, P<0.001). Tumor-associated macrophages (TAMs) predominantly exhibited an immunosuppressive M2 phenotype (Hedges' g: 1.75, P<0.001), while Tregs were significantly enriched (12.6%, OR: 2.87, P<0.001). Immune checkpoint markers LAG-3, TIGIT, and CTLA-4 were upregulated, with TGF-β and IL-10 pathways driving immune suppression.

Conclusions: Single-cell omics highlight significant immune dysfunction in HCC, characterized by T-cell exhaustion, immunosuppressive macrophages, and increased Treg activity, contributing to tumor immune escape. Targeting LAG-3, TIGIT, and TGF-β may enhance anti-tumor immunity. Future research integrating multi-omics and clinical data is essential for developing precision immunotherapies for HCC.

Keywords: Hepatocellular Carcinoma, Single-Cell Omics, Immune Microenvironment, Immune Landscape

PE-21

Hepatocellular Carcinoma in Korea: An Analysis of the 2016–2018 Korean Nationwide Cancer Registry

Jihyun An[1,2], Young Chang[1,3], Gwang Hyeon Choi[1,4], Won Sohn[1,5], Jeong Eun Song[1,6], Hyunjae Shin[1,7], Jae Hyun Yoon[1,8], Jun Sik Yoon[1,9], Hye Young Jang[1,10], Eun Ju Cho[1,7], Ji Won Han[1,11], Suk Kyun Hong[1,12], Ju-Yeon Cho[1,13], Kyu-Won Jung[14], Eun Hye Park[14], Eunyang Kim[14], Bo Hyun Kim[1,15]

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Aims: Hepatocellular carcinoma (HCC) is the sixth most common cancer and second leading cause of cancer-related deaths in South Korea. This study evaluated the characteristics of Korean patients newly diagnosed with HCC in 2016–2018.

Methods: Data from the Korean Primary Liver Cancer Registry (KPLCR), a representative database of patients newly diagnosed with HCC in South Korea, were analyzed. This study investigated 4,462 patients with HCC registered in the KPLCR in 2016–2018.

Results: The median patient age was 63 (interquartile range, 55–72) years; 79.7% of patients were male. Hepatitis B infection was the most common underlying liver disease (54.5%). The Barcelona Clinic Liver Cancer (BCLC) staging system classified patients as follows: stage 0 (14.9%), A (28.8%), B (7.5%), C (39.0%), and D (9.8%). The median overall survival was 3.72 years (95% CI: 3.47–4.14), with 1-, 3-, and 5-year overall survival rates of 71.3%, 54.1%, and 44.3%, respectively. In 2016–2018, there was a significant shift toward BCLC stage 0–A and Child–Turcotte–Pugh liver function class A (Ps<0.05), although survival rates did not differ by diagnosis year. In the treatment group (n=4,389), the most common initial treatments were transarterial therapy (31.7%), surgical resection (24.9%), best supportive care (18.9%), and local ablation therapy (10.5%).

Conclusions: Between 2016 and 2018, HCC tended to be diagnosed at earlier stages, with better liver function in later years. However, since approximately half of the patients remained diagnosed at an advanced stage, more rigorous and optimized HCC screening strategies should be implemented.

Keywords: Epidemiology, Hepatocellular Carcinoma, Hepatitis B, Survival

PE-22

Association between Early Changes in Tumor Markers and Treatment Efficacy in Combination Therapy of Durvalumab and Tremelimumab for Unresectable Hepatocellular Carcinoma

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Aims: Since early 2023, the combination therapy of Durvalumab and Tremelimumab (Dur+Tre) has been approved for unresectable hepatocellular carcinoma (HCC) and is widely used nationwide. In this study, we report the association between aarly changes in tumor markers and treatment efficacy in Dur+Tre for unresectable hepatocellular carcinoma.

Methods: The study included 26 patients with unresectable HCC who received Dur+Tre therapy at our institution (mean age: 74 years, male-to-female ratio: 21:5, HCV: alcohol: non-B non-C = 7:3:16, BCLC stage B:C = 13:13, Child-Pugh score 5:6:7 = 13:11:2, modified ALBI grade 1:2a:2b = 8:8:10). Imaging studies were performed every 4 to 6 weeks after initiation of treatment, and treatment efficacy was evaluated using RECIST v1.1. Tumor markers were measured at weeks 2 and 4 after initiation to examine their correlation with early treatment response. Adverse events were also evaluated using CTCAE v5.0.

Results: Regarding treatment efficacy, 1 patient achieved complete response (CR), 4 had partial response (PR), 3 had stable disease (SD), and 18 had progressive disease (PD), with an objective response rate (ORR) of 20% and a disease control rate (DCR) of 32%. Among the 20 patients who received Dur+Tre as up to second-line therapy, the ORR improved to 26.3%, and the DCR increased to 42.1%. In terms of correlation with tumor markers, DCP levels increased as early as week 2 in PD cases (except for three cases) and showed a further increase by week 4. Conversely, all four PR cases showed a decrease in DCP levels at week 2. No significant changes in tumor markers were observed in SD cases. Treatment discontinuation due to adverse events occurred in eight cases: diarrhea (4 cases), loss of appetite (1 case), rash (2 cases), and neutropenia (1 case). The neutropenic patient was admitted to the emergency department on day 23 after Dur+Tre administration due to generalized pain and fever. Upon admission, the white blood cell (WBC) count was 1,300, and the neutrophil count was 970. Despite antibiotic treatment, by day 26, the WBC count had dropped to 300 and the neutrophil count to 30. G-CSF and steroid pulse therapy were immediately initiated, but by day 29, WBC had declined to 100 and neutrophils to 0. Despite continued G-CSF and steroid administration, the patient did not recover and had a fatal outcome.

Conclusions: Early treatment efficacy of Durvalumab + Tremeli-

mumab combination therapy may be associated with changes in tumor markers at weeks 2 and 4 after administration, potentially serving as a predictor of treatment response. Additionally, severe immune-related adverse events (irAEs) can occur, necessitating careful monitoring.

Keywords: HCC, Durvalumab and Tremelimumab

PE-23

Impact of Routine Screening on Early Detection and Clinical Outcomes of Primary Liver Cancer: A Randomized Controlled Study in a High-Risk Population

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Aims: Primary liver cancer (PLC) is a significant health concern in India, associated with hepatitis B virus (HBV) infection, alcohol abuse, and non-alcoholic fatty liver disease (NAFLD). This study investigates whether routine screening enhances early PLC detection and improves clinical outcomes.

Methods: Residents of Delhi aged 35 to 55 with blood evidence of chronic liver disease or HBV infection were eligible for recruitment in this randomized controlled study. Participants were assigned to one of two groups using cluster sampling: the screening group (8109 participants) or the control group (9711 participants). Subjects in the screening group underwent real-time ultrasonography and serum Alpha-Fetoprotein (AFP) testing every six months, with one to four screening rounds conducted. Liver cancer treatment was determined based on the stage of diagnosis.

Results: At the conclusion of the study, patients were categorized into four outcomes: alive with liver cancer, alive without liver cancer, deceased from liver cancer, or deceased from another cause. The screening group and control group had total follow-ups of 12,038 person-years and 9,573 person-years, respectively, with an average follow-up of 1.2 years.A total of 38 PLC cases were identified in the screening group compared to 18 cases in the control group. In the screening group, the 1-year and 2-year survival rates were 88.1% and 77.5%, respectively. Additionally, 70.6% of patients in the screening group underwent resection, and 76.8% were diagnosed at a subclinical stage.Conversely, none of the patients in the control group were diagnosed at a subclinical stage, none underwent resection, and no patient survived beyond one year. The estimated lead time was 0.45 years.

Conclusions: The study showed that combining serum AFP testing with ultrasonography screening enables early PLC detection, improves resection rates, and enhances survival. Therefore, PLC screening is recommended for high-risk regions.

Keywords: Serum Alpha-Fetoprotein, Liver Cancer

PE-24

A Comparative Analysis of Prognosis Through Propensity Score Matching Following Surgical Resection of Combined Hepatocellular Carcinoma and Cholangiocarcinoma in Patients with BCLC 0 or a Stage versus Those with Hepatocellular Carcinoma

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Aims: Combined hepatocellular and cholangiocarcinoma (cHCC-CCA) is accounting for less than 5% of all primary liver cancers. Continuous evolvement of its definition and rarity hampered prognostic evaluation; previous studies reported conflicting results on prognosis. This study aimed to analyze the prognosis of cHCC-CCA and hepatocellular carcinoma (HCC) after surgical resection in BCLC 0 or A stage adjusting other confounding factors.

Methods: This retrospective analysis included 3,637 patients with HCC and 148 patients with cHCC-CCA, diagnosed at BCLC 0 or A stage pathologically, who underwent surgical resection between 2010 and 2018. Primary outcome was recurrence-free survival (RFS) and overall survival (OS) was secondary outcome. Uni- and multi-variate analysis were performed for RFS and OS. Propensity score (PS) matching (1:4 ratio of combined HCC-CCA to HCC) was subsequently performed to adjust for potential confounding variables. Kaplan-Meier analysis and hazard ratios (HR) with 95% confidence interval (CI) were then calculated. Subgroup analysis was performed between PS matched groups to analyze potential factors in prognosis other than cancer type.

Results: In multivariate analysis, cHCC-CCA demonstrated significantly worse RFS (HR, 1.51; 95% confidence interval [CI], 1.22–1.88; P<0.001) and OS (HR, 2.48; 95% CI, 1.88–3.26; P<0.001). In the PS-matched cohort, cHCC-CCA patients still exhibited inferior RFS (HR, 1.45; 95% CI, 1.14–1.84; P=0.003) and OS (HR, 2.21; 95% CI, 1.61–3.03; P<0.001) compared to HCC. The 5-year RFS rate following surgical resection was 47.9% for cHCC-CCA, compared to 58.5% for HCC (P<0.001). The 5-year OS rate for cHCC-CCA was 70.9%, significantly lower than the 87.8% observed in HCC (P<0.001). Subgroup analysis confirmed that cHCC-CCA was associated with worse RFS and OS, independent of other clinical and pathological factors.

Conclusions: cHCC-CCA is an independent poor prognostic entity after surgical resection in very early and early stage of disease compared with HCC even after adjusting confounding factors.

Keywords: Combined HCC-CCA, HCC, Surgery

PE-25

Success Story: Introducing Stereotactic Body Radiation Therapy for Patients with Liver Cancer at the National Cancer Center of Mongolia

Byambasuren Magsar[1], Uranchimeg Tsegmed[1], Undrakh Unenbat[1], Bilegsaikhan Batsuuri[1], Enkhtsetseg Vanchinbazar[1], Unurjargal Bayasgalan[1], Oyundari Bayarsaikhan[1], Mi-Sook Kim[2], Minjmaa Minjgee[1]

[1]Department of Radiation Oncology, National Cancer Center of Mongolia (NCCM), Mongolia; [2]Department of Radiation Oncology, KIRAMS, Mongolia

Aims: Background: In Mongolia, liver cancer remains a major health concern, with an incidence rate of 108.2 per 100,000 people. Notably, 70% of cases are diagnosed at an advanced stage, and hepatocellular carcinoma (HCC) accounts for 43.9% of cancer-related deaths.

Within the framework of the International Atomic Energy Agency project MON6021: "Improving the Quality of Radiotherapy Services for Common Cancers through the Implementation of Stereotactic Body Radiation Therapy" and the National project by the Government of Mongolia "Establishing Navigation and Stereotactic Treatment Center", the NCCM installed and completed commissioning the Truebeam and our multi-disciplinary team was trained at Hiroshima University Hospital (HUH), Japan which allowed us to successfully introduced SBRT for liver cancer in June 2024.

Methods: Materials/Methods: A total of 4 patients with Child-Pugh class A and greatest tumor dimensions of ≤5 cm were treated with SBRT. Two patients were female and two patients were male with inoperable HCC, recurrent HCC after the operation, post-TACE, and metastatic liver cancer from tracheal cancer, respectively. SBRT was given 40 Gy in four fractions by VMAT technique using 10X Flattening Filter Free beam on Acuros Algorithm with normalization to 95[A1] [A2] %. We used Deep Expiration Breath Hold technique with the Abches system to control respiratory motion. The plan quality of SBRT was assessed using the Conformity Index and the Gradient Index.

Results: Results: We organized a workshop on SBRT in NCCM on June 17, 2024, with the HUH team, and during that time, we treated 2 patients with HCC. Since then, we have performed SBRT independently on 2 patients with HCC. There were no acute and subacute toxicities during follow-up, and no tumor progressions were observed.

Conclusions: Conclusion: The NCCM has successfully implemented SBRT for liver cancer. Initial findings suggest that SBRT is a safe and effective treatment option for both primary and metastatic liver cancers.

Keywords: SBRT, HCC, DEBH, ABCHES

PE-26

AI-Driven Multi-Omics Integration for Early Hepatocellular Carcinoma Detection: A Breakthrough in Precision Oncology

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Aims: Hepatocellular carcinoma (HCC) remains a major global health challenge, with survival largely dependent on early detection. Traditional diagnostic modalities, including serum biomarkers and imaging, often lack accuracy, leading to delayed diagnoses. This review aims to explore the latest advancements in artificial intelligence (AI)-driven diagnostic strategies, emphasizing their integration with multi-omics and imaging technologies for early and precise HCC detection.

Methods: A comprehensive review of recent literature was conducted, examining AI-based models for HCC detection, including deep learning in radiology, machine learning for biomarker discovery, and liquid biopsy advancements. The role of multi-omics integration (genomics, transcriptomics, proteomics, and metabolomics) in improving diagnostic accuracy was assessed. Key challenges in clinical application, such as data standardization, model interpretability, and ethical concerns, were also analyzed.

Results: Emerging evidence suggests that AI-enhanced radiomics can significantly improve lesion characterization, achieving accuracy rates exceeding 90% in differentiating benign from malignant liver nodules. Machine-learning models analyzing circulating exosomal RNA and cfDNA have demonstrated superior sensitivity for early HCC detection compared to AFP-based screening. AI-driven multi-omics integration has identified novel biomarker panels linked to early oncogenic pathways, providing a non-invasive diagnostic alternative. However, real-world clinical adoption is hindered by heterogeneous data quality, regulatory barriers, and integration complexities in clinical workflows.

Conclusions: AI-powered diagnostic tools represent a paradigm shift in HCC detection, offering high precision, non-invasiveness, and scalability for early screening. Future efforts should focus on large-scale validation, regulatory frameworks, and real-time AI monitoring systems to facilitate clinical adoption. The integration of AI with multi-omics holds transformative potential in liver oncology, paving the way for personalized and data-driven hepatology practices.

Keywords: AI in Liver Surgery, OMICS

PE-27

CRISPR-Based Gene Editing in Liver Cancer

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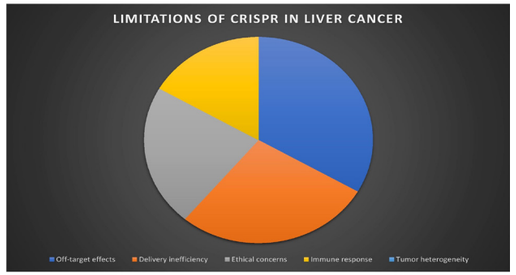
Aims: This review explores the potential of CRISPR-based gene editing in hepatocellular carcinoma (HCC) treatment, analyzing recent advancements and identifying key challenges that hinder clinical application.

Methods: A comprehensive literature review was conducted using PubMed, Scopus, and Web of Science to analyze studies on CRISPR applications in liver cancer. The focus was on oncogene targeting, immune modulation, gene therapy, and delivery methods, alongside an evaluation of associated risks and limitations.

Results: CRISPR has demonstrated significant potential in liver cancer therapy. Studies show that CRISPR can knock out oncogenes (*MYC*, *CTNNB1*) and restore tumor suppressor genes (*p53*, *PTEN*), leading to reduced tumor proliferation. Additionally, CRISPR enhances immunotherapies by modifying T cells for improved tumor targeting. Gene therapy applications, including chemotherapy sensitization and RNA-based editing, offer promising avenues for personalized treatment. However, critical challenges persist: (1) Off-target effects may lead to unintended mutations and secondary malignancies. (2) Efficient delivery methods remain a hurdle, with viral vectors posing toxicity risks and non-viral methods having limited efficacy. (3) Ethical and regulatory barriers complicate clinical translation due to concerns over germline modifications. (4) Tumor heterogeneity presents difficulties in designing a universal CRISPR-based therapy. (5) Immune responses against CRISPR components may reduce efficiency.

CRISPR Approach	Target Gene/Cell	Outcome	Challenges
Oncogene Knockout	MYC, CTNNB1	Reduced tumor growth	Off-target effects
Tumor Suppressor Restoration	p53, PTEN	Enhanced tumor suppression	Delivery issues
Immunotherapy Enhancement	T cells	Improved tumor targeting	Immune rejection
Chemotherapy Sensitization	ABC transporters	Increased drug efficacy	Tumor heterogeneity



Conclusions: CRISPR-based gene editing holds immense promise in liver cancer treatment by enabling targeted oncogene disruption and enhancing immune responses. However, unresolved challenges such as precision, safety, and delivery limitations must be addressed before clinical implementation. Future research should focus on optimizing CRISPR specificity, developing safe delivery mechanisms, and integrating CRISPR with existing cancer therapies. Addressing these concerns will pave the way for CRISPR to revolutionize liver cancer treatment and contribute to personalized medicine.

Keywords: CRISPR, Gene Editing

PE-28

The Declining Trend of Hepatocellular Carcinoma-Related Mortality during the COVID-19 Pandemic

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Aims: The COVID-19 pandemic may have affected hepatocellular carcinoma (HCC)-related mortality. This study investigated mortality trends for HCC and impact of COVID-19 on them.

Methods: We analyzed data from the National Vital Statistics System and CDC WONDER database (2006–2023) in U.S. adults ≥25. We investigated age-standardized all-cause mortality (ASACM) rates for HCC and measured annual percentage changes. We quantified the percentage of COVID-19 related deaths.

Results: We identified 137,887 HCC-related deaths in U.S. adults aged ≥25 (2018–2023). The ASACM for HCC showed a consistent decline from 2018 to 2022 (9.05 to 8.63/100,000 persons), and increased in 2023 (8.66/100,000 persons) (2018-2023 APC, -1.01%). Subgroup analysis revealed similar decreasing ASACM trends in in men, middle age group (45-64 years), and the Black/Asian-Pacific Islander/Hispanic populations, whereas the increasing ASACM trends was noted in women, old age group (≥65 years), and the White populations. The proportion of COVID-19-related deaths in HCC increased from 2020 to 2022 (1.7%-> 2.0%-> 2.2%) and decreased in 2023(0.8%). The proportion of COVID-19-related deaths was higher in women than in men. The young age group and AI/AN and Hispanic individuals showed the highest proportion for COVID-19 related death.

Conclusions: The decreasing trend of HCC-related mortality was maintained during COVID-19 pandemic. Although there must be indirect impacts of COVID-19 on the healthcare environment, percentage of COVID-19 related death was minimal. The observed disparities in mortality warrants the targeted management for vulnerable groups.

Keywords: HCC, Mortality, COVID-19, Trends

PE-29

Mongolian Experience in Hepatocellular Carcinoma Assessment Using the CT/MRI LI-RADS: Preliminary Results

Barkhas Batkhuu[1], Orkhon Gombosuren[3], Regzedmaa Tsogmemekh[3], Javzandolgor Nyamsambuu[4], Nomuunaa Bayarbat[2], Munguntsetseg Batkhuu[2], Tuvshinjargal Ulziibadrakh[2], Ganbolor Jargalsaikhan[2], Oyungerel Lkhagva-Ochir[2], Baigal Narantuya[2], Erdenechuluun Khorolgarav[2], Sharawdorj Gur[2], Tuvshinzaya Purevdorj[1], Naranbaatar Dashdorj[1], Naranjargal Dashdorj[2]

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Aims: Hepatocellular carcinoma (HCC) is the most common cancer in Mongolia and the leading cause of cancer-related mortality. In our country, the prevalence of viral infections is high among patients with HCC. Imaging-based non-invasive diagnosis and early detection are essential for treatment and management of HCC. Imaging diagnostic standard guideline is currently demanded in our country. The study aimed to assess implementation of CT/MRI LI-RADS in detection of HCC among high-risk patients.

Methods: We analyzed data from 1,243 participants (male: 638; female: 605) in the DETECT-HCC study between October 2023 and February 2024. A total of 921 participants underwent contrast-enhanced MRI (CE-MRI) and CT (CE-CT), of which 75.6% underwent MRI with Primovist. Among them, 434 HCCs were diagnosed clinically, and 67 participants are reported with pathology diagnosis. Three radiologists with over ten years of experience assessed liver observations using the LI-RADS CT/MRI v2018.

Results: Out of 921 participants 193 (21%) had no observations, whereas 424 (46%), 62 (6.7%), and 242 (26.3%) were reported having observations individually, in aggregate, and as in a combination of both, respectively. Among 434 participants who had HCCs, 58 (13%) were classified as LR-4, 292 (67%) as LR-5, 33 (7.6%) as LR-M, 36 (8.3%) as LR-TIV and 15 (3.5%) as LR-M and LR-5. Among pathologically diagnosed 67 participants, only 1 case of LR-M and 1 case of LR-4 were not HCC.

Conclusions: Using CT/MRI LI-RADS in a country with a high prevalence of HCC is crucial for preventing cancer-related mortality. Correspondence between pathology and imaging shows the high efficiency of implementing non-invasive imaging diagnostic method according to CT/MRI LI-RADS v2018 guideline in Mongolia.

Keywords: HCC, LI-RADS V2018, CT, MRI

Table 1. Characteristics of all observed participants

Variable*	Target[1] N = 706	Non-Target[1] N = 215	p-value[2]	Overall[1] N = 921
Age	54 (11)	61 (13)	<0.001	56 (12)
Sex			0.091	
Female	341 (48.3%)	118 (54.9%)		459 (49.8%)
Male	365 (51.7%)	97 (45.1%)		462 (50.2%)
Imaging contrast			<0.001	
Iodinated Contrast	43 (6.1%)	25 (11.6%)		68 (7.4%)
Gadovist	105 (14.9%)	49 (22.8%)		154 (16.7%)
Primovist	558 (79.0%)	141 (65.6%)		699 (75.9%)
Cohort			<0.001	
HCC	323 (45.8%)	111 (51.6%)		434 (47.1%)
Cirrhosis	197 (27.9%)	-		197 (21.4%)
Chronic Hepatitis	186 (26.3%)	50 (23.3%)		236 (25.6%)
Other	-	54 (25.1%)		54 (5.9%)
Observation type			<0.001	
No Observation	139 (19.7%)	54 (25.1%)		193 (21.0%)
Individually	301 (42.6%)	123 (57.2%)		424 (46.0%)
In aggregate	54 (7.6%)	8 (3.7%)		62 (6.7%)
Individually and in aggregate at the same time	212 (30.0%)	30 (14.0%)		242 (26.3%)
Final LI-RADS				
LR-1	48 (8.5%)	26 (16.3%)		74 (10.2%)
LR-2	102 (18.0%)	14 (8.8%)		116 (16.0%)
LR-3	74 (13.1%)	8 (5.0%)		82 (11.3%)
LR-4	67 (11.8%)	9 (5.6%)		76 (10.5%)
LR-5	211 (37.2%)	81 (50.6%)		292 (40.2%)
LR-M	26 (4.6%)	10 (6.3%)		36 (5.0%)
LR-M,5	11 (1.9%)	4 (2.5%)		15 (2.1%)
LR-TIV	28 (4.9%)	8 (5.0%)		36 (5.0%)

[1] Mean (SD); n (%)
[2] Wilcoxon rank sum test; Pearson's Chi-squared test

Table 2. Characteristics of individual Lesions by Etiology

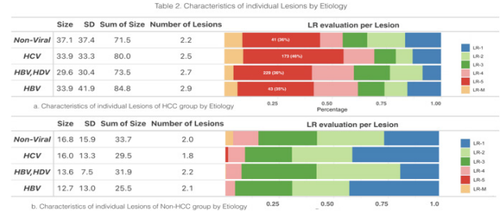

Table 3. LI-RADS report confirmed by Pathology diagnosis

Variable*	Target N = 39[1]	Non-Target N = 27[1]
Final LI-RADS		
LR-4	6	4
LR-5	***29***	***21***
LR-M	3	1
LR-M,5	1	1

[1] n

LR-M,5 stands for multiple lesions that had individual reports of LR-5 and LR-M

PE-30

Preoperative ASAP Score for Prognostic Prediction among Patients Undergoing Hepatectomy for HBV-Associated Hepatocellular Carcinoma: A Multicenter Analysis

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Aims: Despite advances in surgical techniques, tumor recurrence remains a significant challenge after hepatectomy for hepatocellular carcinoma (HCC). This prospective study evaluated the utility of the ASAP score, which incorporates age, sex, alpha-fetoprotein, and PIVKA-II for early detection of HCC among patient with chronic HBV infection, as a preoperative tool for predicting recurrence and survival after resection for HBV-related HCC.

Methods: We prospectively enrolled 752 patients undergoing curative hepatectomy for HBV-related HCC across multiple tertiary centers (2018-2023). Preoperative ASAP scores were calculated and optimal stratification thresholds were determined through X-tile analysis. Cumulative recurrence and overall survival were assessed using Kaplan-Meier survival analysis and competing risk models. Multivariate Cox regression analysis evaluated the score's independent prognostic value while accounting for established surgical-pathological factors.

Results: X-tile analysis identified 4.8 as the optimal ASAP score threshold. High-score patients (≥4.8, n=291) exhibited significantly poorer surgical outcomes compared to low-score patients (<4.8, n=461), with markedly higher 5-year recurrence rates (73.4% vs. 52.1%, *P*<0.001) and lower overall survival rates (30.7% vs. 58.1%, *P*<0.001). Multivariate analysis confirmed the score's independent prognostic value for both recurrence (HR=1.264, 95%CI:1.010-1.582) and overall survival (HR=1.266, 95%CI:1.097-1.608), maintaining significance after adjusting for other liver-, virus-, and tumor-related factors.

Conclusions: The ASAP scoring system demonstrates robust capability in stratifying recurrence and survival after resection for HBV-related HCC. This readily applicable preoperative tool could enhance surgical decision-making, guide resection strategies, and optimize postoperative surveillance protocols. Its integration into surgical practice may facilitate more personalized management approaches for HBV-related HCC patients undergoing hepatectomy.

Keywords: Hepatocellular Carcinoma, Hbv-Associated, Prognostic Prediction

PE-31

Statistical Cure Analysis Following Hepatic Resection in HBV-Associated Hepatocellular Carcinoma: A Novel Risk-Stratified Approach

Yifan Li[2], Lanqing Yao[1], Ren Hong[3], Yingjian Liang[4], Han Liu[5], Kongying Lin[6], Ziqiang Li[7], Lei Cai[8], Tinghao Chen[9], Yahao Zhou[10], Hong Wang[11], Hongwei Guo[12], Qixuan Zheng[13], Zhong Chen[2], Tian Yang[1]

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Aims: Statistical cure, defined as achieving life expectancy comparable to disease-free individuals, represents an important outcome metric in oncologic surgery. This study aimed to establish a cure probability model for hepatitis B virus (HBV)-associated hepatocellular carcinoma (HCC) following curative hepatic resection.

Methods: A retrospective analysis was performed on 740 patients who underwent curative hepatic resection for HBV-HCC (2011-2022) across multiple institutions. Risk factors for disease-free survival were identified through Cox-regression analyses. Patient stratification was accomplished using X-tile analysis. A spline-based cure model compared survival outcomes against matched HBV carriers (Shanghai CDC data) and the general Chinese population (National Bureau of Statistics data).

Results: Eight independent risk factors for decreased disease-free survival were identified: elevated viral load, compromised liver function, tumor multiplicity, size >5cm, satellite lesions, macro/microvascular invasion, perioperative transfusion, and HBV reactivation. Overall cure probability was 21.2% versus matched HBV carriers and 11.1% versus the general population. Risk stratification revealed distinct prognostic groups: low-risk patients (63.2%) achieved 30.1% initial cure probability versus HBV carriers, reaching 95% cure certainty at 8.6 years, while high-risk patients (15.2%) showed minimal cure probability.

Conclusions: This novel analysis demonstrates that statistical cure is achievable in selected patients following hepatic resection for HBV-HCC. The risk-stratified model provides quantitative prognostic information, potentially optimizing surgical candidate selection and surveillance strategies. These findings may facilitate more informed surgical decision-making and patient counseling regarding long-term outcomes.

Keywords: Hepatocellular Carcinoma, Risk-Stratified, Statistical Cure Analysis

PE-32

The Application of Contrast-Enhanced Ultrasound with Sonazoid in the Diagnosis of Small Liver Cancer

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Aims: Primary liver cancer is a common clinical malignant tumor of digestive system . Hepatocellular carcinoma (HCC) is the sixth most common tumor and the fourth leading cause of cancer-related death worldwide.

Methods: In this paper, the application experience of Sonazoid-CEUS in the diagnosis of small liver cancer was shared, and the future development prospect of Sonazoid-CEUS was prospected.

Results: Hepatocellular carcinoma (SHCC) is called small hepatocellular carcinoma (SHCC) if the diameter of a single nodule is less than 2cm or the total diameter of adjacent nodules is less than 2cm. Most patients are diagnosed with the disease at an advanced stage, thus unable to grasp the optimal opportunity for surgical treatment. Therefore, early diagnosis of SHCC and reasonable medical intervention are conducive to delaying the disease process.Contrast-enhanced ultrasound (CEUS) is a new ultrasound imaging technology. It has been widely used in the diagnosis and differential diagnosis of diseases because of its non-invasive, non-radiative, real-time and repeatable advantages. Sonazoid is a new second-generation ultrasound contrast agent, and multiple clinical application guidelines have shown that Sonazoid can be used in the diagnosis of liver diseases .

Conclusions: In the future, with the continuous development and improvement of technology, Sonazoid-CEUS technology will bring more breakthroughs and progress for the diagnosis and treatment of small liver cancer, and the technology is expected to achieve wider application and promotion in the treatment of liver cancer, bringing greater survival benefits to patients.

Keywords: Sonazoid, Contrast Ultrasound, Small Liver Cancer

12. Liver Cirrhosis, Portal Hypertension with Cx. Basic

PE-1

From Injury to Recovery: Single-Cell RNA Sequencing Sheds Light on Liver Fibrosis and Regeneration Pathways

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Aims: Liver fibrosis and regeneration are pivotal in chronic liver disease progression and treatment. Despite extensive research, underlying cellular and molecular mechanisms remain incompletely understood. Single-cell RNA sequencing (scRNA-seq) has revolutionized liver research by revealing cellular heterogeneity and novel disease pathways. This review consolidates recent scRNA-seq findings on liver fibrosis and regeneration, emphasizing hepatic stellate cells (HSCs), liver sinusoidal endothelial cells (LSECs), and hepatocytes, while identifying therapeutic targets.

Methods: A systematic search of PubMed, Scopus, and Web of Science (2010–2024) included studies employing scRNA-seq to investigate liver fibrosis and regeneration. Keywords included "single-cell RNA sequencing," "liver fibrosis," "liver regeneration," and "hepatic stellate cells." Extracted data covered study design, methodologies, key findings, and therapeutic implications.

Results: **Hepatic Stellate Cells (HSCs):** scRNA-seq revealed functional heterogeneity, identifying portal vein-associated HSCs (PaHSCs) and central vein-associated HSCs (CaHSCs). CaHSCs were dominant in centrilobular fibrosis. Additional subpopulations, including GPC3+ (glycosaminoglycan metabolism) and DBH+ (antigen-presenting) HSCs, highlight diverse roles in fibrosis and immunity.

Liver Sinusoidal Endothelial Cells (LSECs): Distinct LSEC subpopulations in cystic fibrosis-associated liver disease (CFLD) upregulated complement and coagulation genes, implicating endothelial dysfunction in fibrosis.

Hepatocytes: scRNA-seq revealed hepatocyte metabolic zonation and plasticity post-injury, with distinct regeneration-associated populations balancing repair and metabolic function.

Molecular Pathways & Therapeutic Targets: Key pathways

include NF-κB, cGAS/STING, and LPAR1 signaling, which drive inflammation and fibrosis. Inhibiting STING or LPAR1 showed promise in reducing fibrosis in experimental models.

Conclusions: scRNA-seq has unveiled the cellular complexity of liver fibrosis and regeneration, identifying novel cell populations and therapeutic targets. Future research should translate these findings into clinical applications, enhancing targeted antifibrotic and regenerative therapies.

Keywords: Single-Cell Rna Sequencing, Liver Fibrosis, Liver Regeneration, Hepatic Stellate Cells

PE-2

Assessing the Diagnostic Accuracy of APRI and FIB-4 Scores for Liver Fibrosis in Patients with Chronic Liver Disease

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Aims: The APRI and FIB-4 scores are widely studied non-invasive tools for diagnosing and staging liver fibrosis in chronic liver disease (CLD). In Mongolia, limited access to FibroScan and liver biopsy poses significant challenges, particularly for rural populations. This study aimed to evaluate the accuracy of APRI and FIB-4 scores against FibroScan, the gold standard for assessing liver fibrosis severity in CLD patients.

Methods: We enrolled 396 patients who underwent FibroScan examinations between October 2023 and February 2025 as part of the DETECT-HCC study. Demographic data, including sex, age, and nationality, were collected. Clinical characteristics were evaluated using BX-3010 and XN-550 analyzers (Sysmex, Japan). Fibrosis stages (F0-1: without fibrosis; F2-F4: with fibrosis) were defined by FibroScan Expert 630 (Echosens, France) using kPa thresholds. The predictive accuracy of APRI and FIB-4 scores in distinguishing "without fibrosis" from "with fibrosis" was assessed using receiver operating characteristic (ROC) curve analysis. Statistical analyses were performed using SPSS version 26.

Results: A total of 396 patients were analyzed, comprising 56.8% females (n = 225) with a mean age of 54.1 ± 12.1 years; males had a mean age of 51.8 ± 11.5 years. Fibrosis prevalence by FibroScan was highest in HBV+HDV patients (68.8%, n = 104), followed by HCV (55.2%, n = 42), HBV (30.4%, n = 14), and non-viral causes (20.4%, n = 27). The mean ± standard deviation (SD) for APRI and FIB-4 scores were 1.0 ± 1.5 and 2.4 ± 3.2, respectively. Significant correlations were observed between FibroScan scores and FIB-4 (r = 0.690), APRI (r = 0.754), and AST/ALT ratio (r = 0.166) (P<0.001). ROC analysis identified an APRI cut-off >0.637 (72% sensitivity, 87% specificity) and a FIB-4 cut-off >1.814 (66% sensitivity, 86% specificity) for distinguishing fibrosis stages. Both scores effectively identified fibrosis across HBV, HDV, and HCV groups, with APRI prevalence rates highest in HBV+HDV patients (61.7%, n = 92) and HCV patients (47.9%, n = 35). Similarly, FIB-4 was predictive in HBV+HDV (50.3%, n = 75) and HCV (52.0%, n = 38) groups. The APRI score (AUC = 0.876) outperformed the FIB-4 score (AUC = 0.841) in identifying advanced fibrosis. The likelihood ratios for the APRI cut-off (5.5) were relatively higher than for FIB-4 (4.71), highlighting its superior diagnostic utility for liver fibrosis in HBV, HDV, and HCV patients.

Conclusions: APRI and FIB-4 scores demonstrate reliable diagnostic accuracy for assessing liver fibrosis in patients with chronic liver disease, including those with HCV, HBV, and HDV. APRI showed slightly superior performance, making these scores practical alternatives to FibroScan, particularly in resource-limited settings like rural Mongolia.

Keywords: APRI, FIB-4, Liver Fibrosis, Chronic Liver Disease

PE-3

Hyodeoxycholic Acid Ameliorates Cholestatic Liver Fibrosis by Facilitating m6A-Regulated Expression of a Novel Anti-Fibrotic Target ETV4

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Aims: Cholestatic liver fibrosis is a common pathological feature of various biliary tract diseases. the underlying pathological mechanisms are not fully elucidated, posing significant obstacles to the discovery of new drug targets. The current study aims to evaluate protective effects of hyodeoxycholic acid (HDCA) against cholestatic liver fibrosis and to ascertain whether ETV4 is a novel anti-fibrotic target involving in the therapeutic effects of HDCA.

Methods: The therapeutic effect of HDCA was verified using bile duct ligation (BDL) and *Abcb4*$^{-/-}$ mouse models. *Etv4*$^{-/-}$ mice were subjected to BDL to investigate the role of ETV4 in liver fibrogenesis and the therapeutic effects of HDCA. The N^6-methyladenosine (m^6A) modification was investigated using MeRIP-qPCR and IF/FISH techniques.

Results: HDCA levels were decreased in both cholestatic patients and mice, while HDCA supplementation significantly ameliorated cholestatic liver fibrosis. By inducing ETV4 expression in cholangiocytes, HDCA induced MMP9 secretion, facilitating extracellular matrix (ECM) degradation. Findings in cholestatic fibrosis patients and *Etv4*$^{-/-}$ mice further revealed a promising role of ETV4 in improving liver fibrosis and in therapeutic effects of HDCA. Mechanistically, HDCA promoted m^6A modification of *ETV4* mRNA, promotes IGF2BP1 recognition and PABPC1 recruitment to inhibit the deadenylation of *ETV4* mRNA, leading to increased mRNA stability, storage in P-bodies, and prolonged translation. The mutation of m^6A site on *ETV4* mRNA or knocking down critical genes involved in m^6A modification significantly abolished the regulative effects of HDCA.

Conclusions: The present study underscores ETV4 as a novel anti-fibrotic target and demonstrates that HDCA remodels ECM by facilitating m^6A-regulated ETV4 expression, offering potential therapeutic approaches for cholestatic liver fibrosis.

Keywords: Cholestasis, ECM, ETV4, Cholangiocyte, IGF2BP1, Mrna Stability

PE-4

Deep Learning-Driven Integration of Spatial Transcriptomics and Circulating Epitranscriptomics Identifies Endothelial RNA Modifications as Predictors of Hepatic Decompensation in Cirrhotic Portal Hypertension

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Aims: Hepatic decompensation in cirrhotic portal hypertension (PH) remains unpredictable despite existing clinical risk scores. Current tools, such as MELD-Na and HVPG, fail to capture endothelial dysfunction, a key driver of PH progression. This study employs deep learning-integrated spatial epitranscriptomics and circulating RNA methylation analysis to identify endothelial RNA modifications as predictive biomarkers for early decompensation risk stratification.

Methods: We analyzed spatial transcriptomics and epitranscriptomics of liver sinusoidal endothelial cells (LSECs) using data from the Human Cell Atlas (HCA, n=3,846), Human Liver Single-Cell Transcriptomic Atlas (n=2,127), and NIH HuBMAP project (n=1,176). Exosomal RNA methylation data were obtained from GEO (GSE136103, n=1,038) and the Liver Cirrhosis Biomarker Study (LCBS, n=1,092). Deep learning models were trained using multi-modal graph neural networks (MM-GNNs) to integrate spatial RNA modifications, exosomal m6A/pseudouridine signatures, and liver microvascular proteomics from the Human Protein Atlas (HPA, n=687). Biomarkers were validated through self-supervised contrastive learning, with benchmarking against MELD-Na and HVPG scores. The primary endpoint was hepatic decompensation (ascites, variceal bleeding, hepatic encephalopathy) within 18 months.

Results: Our AI model achieved AUROC 0.83 (95% CI: 0.82–0.84), comparable to MELD-Na (0.81) and HVPG (0.83, P=0.05). Key predictors included LSEC m6A hypermethylation of KLF2 (HR: 1.98, P<0.05), exosomal pseudouridylated VEGFA (>1.5-fold, HR: 1.71, P<0.05), and gut microbiome-derived lactate loss (HR: 1.89, P<0.05). 29.4% of stable PH patients with low MELD-Na were reclassified as high-risk, enabling early intervention. Sensitivity and specificity reached 87.6% and 85.4%, respectively. m6A hypermethylation significantly correlated with endothelial dysfunction severity and fibrosis progression rates.

Conclusions: This AI-driven model integrates spatial and circulating epitranscriptomics, substantially improving decompensation risk prediction, surpassing clinical scores, and enabling precision medicine in hepatology.

Keywords: Epitranscriptomics, Deep Learning, Hepatic Decompensation, Spatial Transcriptomics

PE-5

Target Validation of CYP8B1 and Establishment of Small Molecule Screening in Non-Alcoholic Fatty Liver Disease

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Aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects millions of patients worldwide, with liver fibrosis being a major cause of mortality. Currently, there are no approved medications for liver fibrosis treatment. This study aims to validate CYP8B1, an enzyme involved in the classic pathway of bile acid synthesis, as a potential therapeutic target for liver fibrosis and establish a screening platform for CYP8B1 inhibitors.

Methods: We analyzed mRNA sequencing data from liver tissue samples of 164 clinical patients to evaluate CYP8B1 expression according to fibrosis severity. We introduced siCYP8B1 in hepatic stellate cells (LX-2) treated with TGF β1 to assess fibrosis markers. Known CYP8B1 inhibitors (Clotrimazole, Econazole,

Miconazole) were tested for cytotoxicity and lipid-reducing effects. CYP8B1 expression was compared across various mouse models of fatty liver disease. A spectroscopic analysis platform based on hydroxylation at position 12 was established for CYP8B1 inhibitor screening.

Results: CYP8B1 gene expression significantly increased with fibrosis severity in patient liver tissues, showing a positive correlation with fibrosis scores. In siCYP8B1-transfected hepatic stellate cells, TGF β1 treatment led to decreased expression of fibrosis markers (TGF β1, FN-1, Collagen1) and reduced cell migration. CYP8B1 inhibitor treatment decreased lipid accumulation in hepatocytes. Hepatic Cyp8b1 expression was significantly higher in mouse models with fibrosis compared to simple steatosis models. A spectroscopic analysis method was established for CYP8B1 inhibitor screening based on hydroxylation at position 12.

Conclusions: This study demonstrates that CYP8B1 expression is closely associated with liver fibrosis progression in MASLD, and CYP8B1 inhibition may alleviate liver fibrosis and lipid accumulation. The established target validation and small molecule screening platform for CYP8B1 may contribute to the development of novel therapeutics for liver fibrosis.

Keywords: CYP8B1, Metabolic Dysfunction-Associated Steatotic Liver Disease, Liver Fibrosis, Drug Screening

PE-6

Low Shear Stress Activates Hepatic Kallikrein-Kinin Signaling, Enhancing Vascular Adhesion and Thrombosis in the Liver

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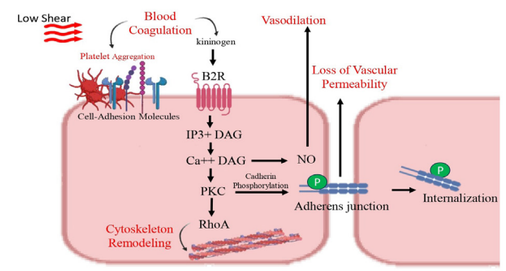
Aims: This study aims to investigate how intrahepatic low shear stress and associated hydrostatic pressure activate specific mechanosensors in LSECs and to elucidate the downstream signaling mechanisms involved in the regulation of intrahepatic vascular tone.

Methods: Experimentally, intra-hepatic low shear was induced by 60% pre- hepatic portal vein obstruction. Shear flow was evaluated by transonic flow system and intra-vital imaging with Rhodamine-6G-fluorophore-stained platelet at 24 and 48hrs post PVL. Hepatic hemodynamic was monitored followed by Molecular, cellular and histological analysis. Hepatic tissue Proteomics analysis was performed. Electron microscopy was to identify endothelial cell's phenotypic changes.

Results: Hemodynamic studies revealed that portal blood flow index was markedly decrease 44.44% and 55.55% at 24hrs and 48hrs respectively post PPVL and PP was raised (13.01±2.51 +104.5% and 14.71±1.18 +131%) at 24h and 48h and Portal blood flow also decrease in liver by 50% and 56.2% at 24h and 48h respectively in comparison to controls. 50% reduction in Shear was observed in portal vein. Histologically, intrahepatic sinusoidal dilatation was observed. Proteomic analysis revealed significant upregulation of S100A8 and S100A9 (also known as MRP8 and MRP14, respectively) a neutrophil secreted protein, adhesion protein like- integrins, ICMA1, VCAM1, Cadherinswhich promotes inflammatory cell chemotaxis, adhesion and trans-endothelial migration. Coagulations factor like- XII and IX, high and low weight kininogen is also upregulated in low shear. Interestingly, plasma protease C1 inhibitor, an antagonist of the kallikrein-kinin system, is upregulated, acting as a negative feedback loop. The G(s) and (q) subunit alpha, downstream messengers of B1/B2 (bradykinin) receptor expression, also exhibit a significant increase in low shear, indicating the activation of the Bradykinin-Receptor. Other mechanosensors like VEGFR2, PIEZO1, NOTCH1, CD-31 and α-SMA, vWF, eNOS genes upregulation was observed by RT-PCR. Scanning electron microscopy reveals intra- sinosoidal mesh like structure of blood clot formed by fibrin protein and bllod cells like- RBC, neutrophils and platelets trapped in them.



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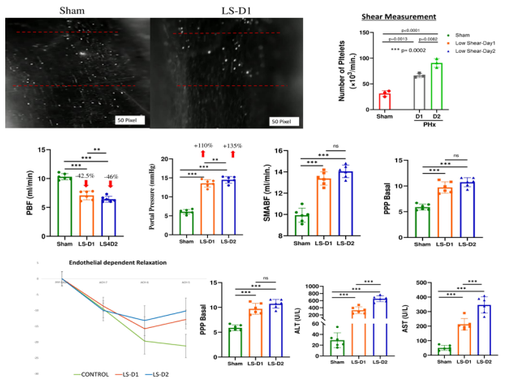

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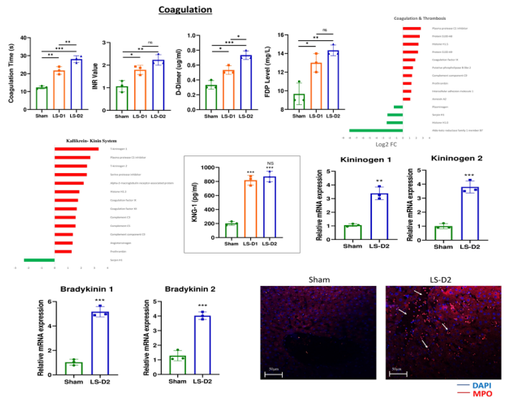

Figure 3.

Conclusions: trahepatic low shear induces the activation of kallikrein-kinin system which promotes vascular adhesion and activates coagulation cascade, resulting in trans-endothelial migration.

Keywords: Intra-Hepatic Low-Shear, Portal Hypertension, Endothelial Dysfunction, Bradykinin- 2 Receptor (B2R)

13. Liver Cirrhosis, Portal Hypertension with Cx. Clinical

PE-1

Do Systemic Inflammation, Severity and Treatment Modalities of Hepatic Encephalopathy Determine Prognosis in Patients with Acute Overt HE in Liver Cirrhosis?

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Aims: The study aimed to evaluate the clinical spectrum, systemic inflammation, treatment outcomes, prognostic significance, and survival probability of hepatic encephalopathy (HE) in patients with liver cirrhosis.

Methods: Over five years, consecutive patients with HE were evaluated for symptoms, signs, aetiology, inflammatory markers, prognostic index, and response to treatment. Primary outcomes included reversal of HE up to 10 days of admission and mortality at 28 days. Secondary outcomes included length of hospital stay, time taken for resolution of HE, adverse events, and recurrence of HE over 28 days

Results: 539 patients were included. The mean age was 46 ± 11 years, with 84.4% males. Hyponatremia (65.4 %) was the most common precipitating factor. Complete reversal of HE occurred in 62.8%. Mean hospital stay of 7.91±3.97 days, and overall mortality during the study period was 26.1%. The survival probability was higher in grade 2 HE than in grade 3 and grade 4 (79.79 vs 74.31 vs 60.22%, P=0.0020). Arterial ammonia, serum IL-6, and albumin were independent prognostic factors. Patients with resolution of HE had better survival {H.R 0.271 [95%C. I (0.187 – 0.394)], P<0.005}.

Conclusions: Approximately one-third of patients with liver cirrhosis with acute episodes of HE have non-reversal of HE and poor survival. The development of HE and its resolution is a crucial prognostic event in liver cirrhosis patients.

Keywords: Ammonia, Prognostic Index, Interleukins, Lactulose

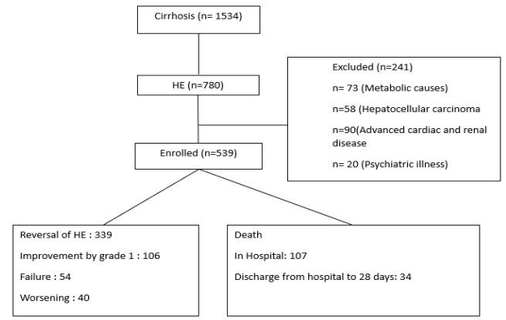
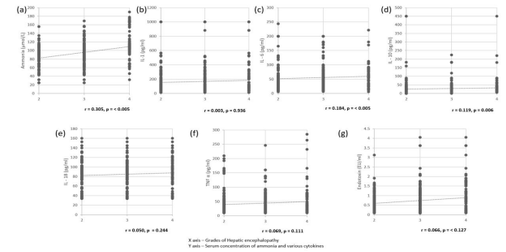


Figure 1.



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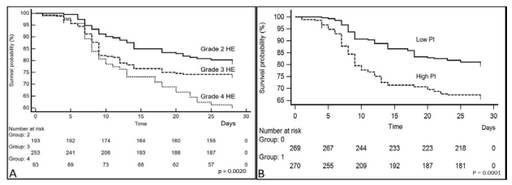

Figure 3.

PE-2

Growth Differentiation Factor-15 is Associated with Adverse Outcome, Malnutrition Risk and Health Deficit in Decompensated Cirrhosis

Chao Sun

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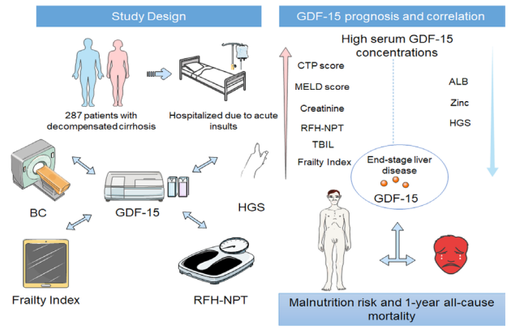
Aims: Growth differentiation factor (GDF)-15 represents diverse pathophysiological roles and is linked to anorexia, wasting conditions and adverse outcomes. However, its clinical implication as a biomarker amongst cirrhosis remains enigmatic, thus we explored the relationships between serum GDF-15 and multiple endpoints including nutritional status, all-cause mortality and health deficit.

Methods: This observational study analyzed 287 patients hospitalized due to acute decompensating insults (median age 64 years, 55.8% male). Malnutrition risk, multiple body composition, health deficit and underlying disease severity were assessed by RFH-NPT scale, CT scans, handgrip strength/frailty index and CTP/MELD-Na score, respectively.

Results: The median concentrations of GDF-15 were 4.75 (Q1, Q3: 3.25, 7.54) ng/mL. Higher GDF-15 levels were related to more prevalent malnutrition risk and more detrimental disease severity. Patients with increased GDF-15 had more impairment to renal/hepatic function, lower zinc levels and marked hypoalbuminemia, pinpointing metabolic imbalance. Moreover, patients with higher GDF-15 also exhibited more significant health deficit like multidimensional frailty. Multivariate Cox analysis indicated that elevated GDF-15 was an independent predictor of 1-year mortality, adjusted for coexisting nutritional status and underpinning disease burden (CTP: HR: 1.07, 95%CI: 1.01, 1.13, *P*=0.013; MELD-Na: HR: 1.06, 95%CI: 1.01, 1.12, *P*=0.044).



Conclusions: Serum GDF-15 concentrations were higher in patients with decompensated cirrhosis experiencing malnutrition risk. Furthermore, this biomarker was closely linked to increased risk of adverse outcome and health deficit. It is tempting to develop therapeutic approach targeting GDF-15 signaling pathway in hopes of reversing energy dysregulation and improving poor clinical endpoint.

Keywords: GDF-15, Malnutrition Risk, Frailty, Liver Cirrhosis, Prognosis, Health Deficit

PE-3

Efficacy of Terlipressin in Cirrhosis with Acute Kidney Injury HRS AKI at Gastroenterology - Hepatology Center, Bach Mai Hospital, Viet Nam

Lon Dang, Cong Long Nguyen, Diep Luu Thi Minh

Bach Mai Hospital, Vietnam

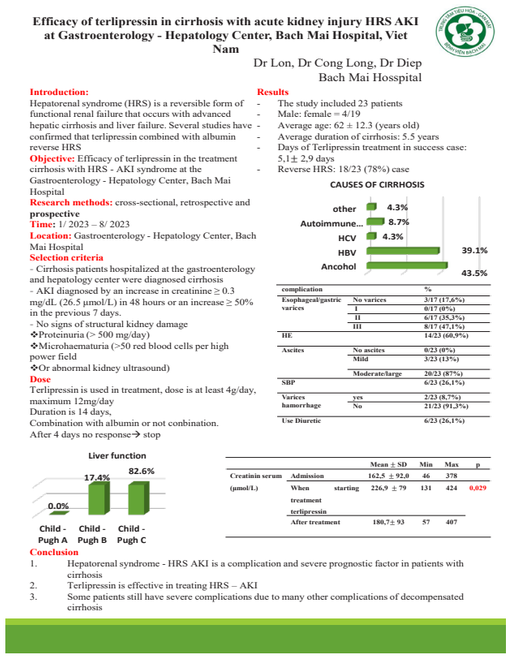
Aims: Hepatorenal syndrome (HRS) is a reversible form of functional renal failure that occurs with advanced hepatic cirrhosis and liver failure. Several studies have confirmed that terlipressin combined with albumin reverse HRS. Objective: Efficacy of terlipressin in the treatment cirrhosis with HRS - AKI syndrome at the Gastroenterology - Hepatology Center, Bach Mai Hospital

Methods: Research methods: cross-sectional, retrospective and prospective. Time: 1/ 2023 – 8/ 2023. Location: Gastroenterology - Hepatology Center, Bach Mai Hospital. Selection criteria: Cirrhosis patients hospitalized at the gastroenterology and hepatology center were diagnosed cirrhosis, AKI diagnosed by an increase in creatinine ≥ 0.3 mg/dL (26.5 μmol/L) in 48 hours or an increase ≥ 50% in the previous 7 days, no signs of structural kidney damage, proteinuria (> 500 mg/day), microhaematuria (>50 red blood cells per high power field, or abnormal kidney ultrasound). Dose: terlipressin is used in treatment, dose is at least 4g/day, maximum 12mg/day. Combination with albumin or not conbination. After 4 days no response stop

Results: Results: the study included 23 patients. male: female = 4/19. average age: 62 ± 12.3 (years old). average duration of cirrhosis: 5.5 years, days of Terlipressin treatment in success case: 5,1 2,9 days, reverse HRS 18/23 case (78%).

Conclusions: Conclusion: hepatorenal syndrome - HRS AKI is a complication and severe prognostic factor in patients with cirrhosis, terlipressin is effective in treating HRS – AKI, some patients still have severe complications due to many other complications of decompensated cirrhosis

Keywords: Cirrhosis, Terlipressin, HRS AKI



PE-4

The Etiology of Chronic Liver Disease Is an Independent Prognostic Factor in Patients with Acutely Deteriorated Chronic Liver Disease

Do Seon Song[1], Hee Yeon Kim[2], Young Kul Jung[3], Tae Hyung Kim[3], Hyung Joon Yim[3], Eileen L Yoon[4], Ki Tae Suk[5], Jeong-Ju Yoo[6], Sang Gyune Kim[6], Moon Young Kim[7], Young Chang[8], Soung Won Jeong[8], Jae Young Jang[8], Sung-Eun Kim[5], Jung-Hee Kim[5], Jung Gil Park[9], Won Kim[10], Dong Joon Kim[5], Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

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Aims: The prognosis for patients with acutely decompensated chronic liver disease (CLD) is very poor. There is a lack of research on the prognostic impact of underlying CLD in patients with acutely decompensated CLD.

Methods: We enrolled a total of 1,352 patients, categorized into three groups: those with viral hepatitis (VH) (n=206), alcoholic liver disease (ALD) (n=1,017), and a combination of alcohol and viral hepatitis (Combination) (n=129) based on etiology of underlying CLD. Subgroups analysis were conducted using Propensity Score matching (PSM). Primary outcome was 28-day liver transplantation free survival (TFS).

Results: The VH group had lower Child-Pugh, MELD, MELD-Na, CLIF-SOFA, and CLIF-C OF scores compared to the ALD and Combination groups, while the ALD and Combination groups had similar scores. The 28-day TFS was similar between the VH and ALD groups (*P*=0.661), but significantly lower in the Combination group compared to other groups (*P*<0.05). In the subgroup analysis comparing the VH and ALD groups after PSM (Subgroup 1), VH group (n=193) had significantly lower 28-day TFS than ALD group (n=197) (*P*=0.01). In the subgroup analysis comparing the VH and Combination groups after PSM (Subgroup 2), there was no significant difference in 28-day TFS between VH group (n=132) and Combination group (n=90) (*P*=0.7). In the subgroup analysis comparing the ALD and Combination groups after PSM (Subgroup 3), ALD group (n=234) had significantly higher 28-day TFS than Combination group (n=120) (*P*=0.04). When comparing patients with a precipitating event of excessive alcohol consumption in the ALD group (n=640) to patients with a precipitating event of hepatitis virus in the VH group (n=52), there was no difference in 28-day TFS between the two groups (*P*=1.0). However, after PSM, the patients with a precipitating event of hepatitis virus (n=32) had significantly lower 28-day TFS than the patients with a precipitating event of excessive alcohol consumption (n=35) (*P*=0.04).

Conclusions: Patients with VH as the etiology of underlying CLD exhibit a poorer prognosis compared to those with ALD. Furthermore, the combined ALD and VH group also demonstrates a worse prognosis than the ALD-only group. Thus, different etiologies require different risk prediction methods.

Keywords: Alcohol, HBV, Etiology, Prognosis

PE-5

Reduced COVID-19 Vaccination Effectiveness and Clinical Outcomes for Decompensated Cirrhosis: A Nationwide Population-Based Study

Won Sohn[1], Jae Yoon Jeong[2], Kyoung A Ko[1], Hyunwoo Oh[1], Yong Kyun Cho[1], Byung Ik Kim[1]

[1]Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Division of Infectious Diseases, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of

Medicine, Seoul, Republic of Korea

Aims: The impact of coronavirus disease 2019 (COVID-19) vaccination on patients with decompensated cirrhosis remains controversial. This study investigated the effectiveness of COVID-19 vaccination in decompensated cirrhosis.

Methods: This study comprised a population-based cohort of 1,583,777 patients with chronic liver disease (CLD) including decompensated cirrhosis, from the National Health Insurance Service data in the Republic of Korea. The primary outcome was the risk of COVID-19 infection within 6 months after vaccination between 26 February 2021 and 31 December 2021. Hospitalisation and all-cause mortality rates were also investigated. Target trial specifications with propensity score matching were used to minimise the bias between the unvaccinated and vaccinated groups.

Results: The mean age of patients was 54.2 years and 54.5% of them were men. In total, 61,765 patients (3.9%) had decompensated cirrhosis. Compared to the unvaccinated group, the vaccinated group exhibited a lower risk of COVID-19 infection (hazard ratio [HR]=0.94; 95% confidence interval [CI]=0.91–0.97), hospitalisation (HR=0.86; 95% CI=0.83–0.89), and all-cause mortality (HR=0.27; 95% CI=0.20–0.36) in CLD. However, there was no beneficial effect of the COVID-19 vaccination on the clinical outcomes of patients with decompensated cirrhosis. The multivariable analysis determined that COVID-19 vaccination reduced all-cause mortality in CLD (HR=0.39; 95% CI=0.32–49) and decompensated cirrhosis increased all-cause mortality in patients with COVID-19 infection (HR=2.94; 95% CI=2.15–4.02). These results were consistent during the pre-Delta and Delta-variant periods.

Conclusions: COVID-19 vaccination reduced the risk of COVID-19 infection, hospitalisation, and mortality in patients with CLD. However, patients with decompensated cirrhosis had a poor prognosis and diminished vaccination effectiveness. Early detection and antiviral treatment are warranted to manage COVID-19 infection effectively in patients with decompensated cirrhosis.

Keywords: Liver Cirrhosis, Covid-19, Vaccination, Prognosis

PE-6

Prevalence of Zinc Deficiency in Patients with Liver Cirrhosis and Its Clinical Correlation

Lkhagvasuren Batbaatar, Uranbaigal Dashnyam, Doljinsuren Enkhbayar

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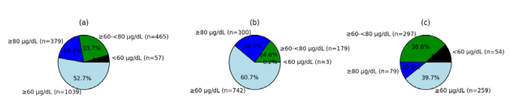
Aims: This study aimed to determine the prevalence of serum zinc deficiency in patients with liver cirrhosis and evaluate its association with clinical characteristics, particularly serum albumin levels.

Methods: A total of 510 patients with liver disease, including 201 diagnosed with liver cirrhosis, admitted to Dornod Medical Center in 2024, were analyzed. Serum zinc levels were measured, and deficiency was categorized as severe (<60 μg/dL) or marginal (<80 μg/dL). The relationship between serum zinc and clinical parameters, including serum albumin levels, was assessed.

Results: Zinc deficiency (<60 μg/dL) was observed in 32.5% of patients, with a higher prevalence among cirrhosis patients (49.7%). When including marginal deficiency (<80 μg/dL), 81.4% of patients were affected, with an even higher rate of 88.3% in cirrhosis cases. Serum zinc levels showed a strong correlation with serum albumin, with 92.2% of patients with low albumin levels presenting zinc deficiency.

Conclusions: Zinc deficiency is highly prevalent in patients with liver cirrhosis, highlighting the importance of routine monitoring and early intervention. Given its strong association with serum albumin levels, nutritional assessment and zinc supplementation should be considered to support disease management and prevent complications in cirrhosis patients.

Keywords: Chronic Liver Disease (CLD), Liver Cirrhosis, Zinc Deficiency, Serum Zinc Levels



PE-7

Comparative Efficacy and Safety of Lactulose Versus Polyethylene Glycol in the Management of Overt Hepatic Encephalopathy: A Comprehensive Meta-Analysis of Randomized Controlled Trials

Roland Helmizar, Wisda Widiastuti

Department of Internal Medicine, Baiturrahmah University, Padang, Indonesia

Aims: Overt hepatic encephalopathy (OHE) is a severe neuropsychiatric complication of cirrhosis, leading to increased morbidity and healthcare burden. Lactulose has long been the standard treatment; however, polyethylene glycol (PEG) has gained attention as a potential alternative due to its purported ability to accelerate clinical recovery. Despite several studies comparing the two treatments, their relative efficacy and safety remain uncertain. This meta-analysis aims to systematically evaluate and compare the effectiveness of PEG and lactulose in managing OHE, focusing on clinical resolution rates, time to symptom improvement, hospital stay duration, and adverse events.

Methods: A systematic search was conducted in PubMed, Embase, Cochrane Library, and and Clinical Trials Registry up to December 2024. Only randomized controlled trials (RCTs) comparing PEG and lactulose for treating OHE were included. The main outcomes analyzed were the rate of complete OHE resolution and the time taken for symptom improvement. Other factors, such as hospital stay length and side effects, were also evaluated. The results were presented as odds ratios (OR) or mean differences (MD) with a 95% confidence interval (CI).

Results: A total of six RCTs were included. PEG showed a higher rate of complete symptom resolution compared to lactulose (OR: 1.62, 95% CI: 1.25–2.38, P=0.001, I^2=38%). Patients treated with PEG experienced faster symptom improvement, with a mean reduction of 10.2 hours compared to lactulose (MD: -10.2 hours, 95% CI: -15.8 to -5.5, P<0.001, I^2=46%). Hospital stay was shorter in PEG-treated patients by approximately 1.5 days (MD: -1.5 days, 95% CI: -2.7 to -0.4, P=0.001, I^2=43%). No significant difference was found in adverse events between PEG and lactulose (P=0.62).

Conclusions: PEG may be a superior alternative to lactulose for managing OHE, though further large-scale studies are warranted to validate these findings and explore long-term outcomes.

Keywords: Lactulose, Polyethylene Glycol, Overt Hepatic Encephalopathy, Efficay

PE-8

Task-Adaptive Transfer Learning for Non-Invasive HVPG Classification with induced Spatially-Aware Feature Localization

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Aims: Hepatic venous pressure gradient (HVPG) measurement, the gold standard for assessing portal hypertension, is invasive, entails complications such as hemorrhage and infection, and necessitates specialized training. Current non-invasive alternatives exhibit limited accuracy and clinical reliability. This study investigates Task-Adaptive Transfer Learning (TATL) as a non-invasive diagnostic adjunct, utilizing segmentation-derived anatomical biomarkers from hepatic and splenic CT imaging to accurately perform HVPG classification, thereby enhancing clinical applicability and safety.

Methods: This study retrospectively analyzed CT data to classify HVPG levels using deep learning-based liver and spleen segmentation. We examined 482 chronic liver disease patients (2007–2014) and 185 normal controls (2022–2023), extracting only portal venous phase images with de-identification. Standardized preprocessing, including intensity normalization and spatial resampling, was applied. TATL was used to extract patient-specific volumetric and anatomical features from segmentation encoders, which were integrated into a classification model for direct HVPG prediction from CT imaging.

Results: We analyzed a balanced cohort of 596 subjects (298 in each HVPG classification group). TATL-based models demonstrated significantly superior diagnostic performance compared to conventional non-invasive methods. As a result, we achieved exceptional clinical performance metrics, including an accuracy of 87.1%, sensitivity of 93.5%, specificity of 80.6%, an F1-score of 87.9%, and an AUC of 0.921.

Conclusions: In this study, we propose a TATL method for non-invasive HVPG classification from CT imaging. By leveraging encoders trained on liver and spleen segmentation tasks, the proposed model effectively enhances anatomical focus, thereby providing robust and clinically applicable HVPG classification.

Keywords: Machine Learning, Portal Hypertension

PE-9

Evaluating The Prognostic Value of the MELD 3.0 Score In Predicting Mortality In Cirrhosis Patients with Acute Variceal Bleeding

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Aims: Variceal hemorrhage is a serious complication that affects up to 70% of cirrhotic patients with upper gastrointestinal bleeding, with a high 6-week mortality rate of up to 15 – 20%. Accurate prediction of early mortality risk after bleeding in cirrhotic patients is vital for optimizing treatment approaches. The MELD 3.0 score, an updated version of the original MELD score, enhances short-term mortality prediction by including additional variables such as gender, sodium levels, albumin concentrations, and a maximum creatinine level of 3.0 mg/dL. This study aimed to evaluate the effectiveness of the MELD 3.0 score in predicting 6-week mortality, comparing its accuracy with the original MELD score, the Glasgow-Blatchford score (GBS), and the AIMS65 score for cirrhotic patients experiencing acute variceal bleeding.

Methods: Prospective data were collected from cirrhosis patients with variceal bleeding at a Vietnamese tertiary hospital between November 2023 and May 2024. The primary endpoint was 6-week mortality, and the secondary was in-hospital mortality. The effectiveness of MELD 3.0 in predicting mortality was assessed using the Area Under the Receiver Operating

Characteristic (AUCROC) curves and compared to MELD, Glasgow-Blatchford (GBS), and AIMS65 scores, providing a comprehensive evaluation of each system's predictive accuracy.

Results: Among the 212 patients analyzed, the mean age was 56.7 ± 12.0 years with a male predominance of 75.0%. The leading cause of cirrhosis was alcoholic hepatitis, followed by viral hepatitis. Endoscopy frequently revealed esophageal varices (88.2%). The observed in-hospital mortality rate was 4.7%, while 6-week mortality reached 19.8%. The MELD 3.0 score demonstrated strong predictive performance, achieving an AUCROC of 0.88 for in-hospital mortality and 0.81 for 6-week mortality.

For in-hospital mortality, the AUCROC values for the scoring systems were as follows: MELD 3.0 (0.88), MELD (0.80), GBS (0.59), and AIMS65 (0.74). Similarly, in predicting 6-week mortality, the MELD 3.0 score outperformed others with an AUCROC of 0.81, compared to MELD (0.75), GBS (0.61), and AIMS65 (0.66). And all differences were statistically significant with a p-value < 0.05.

A MELD 3.0 score threshold of 20 for predicting 6-week mortality was associated with a mortality rate exceeding 25%. This cut-off provided a sensitivity of 69.1%, specificity of 83.5%, a positive likelihood ratio (LR+) of 4.2, and a negative likelihood ratio (LR−) of 0.4.

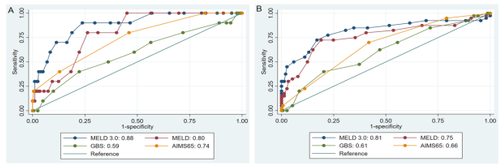

Figure 1. Comparative Analysis of Four Scoring Systems in Mortality Prediction (A) AUCROC for In-Hospital Mortality, (B) AUCROC for 6-Week Mortality..

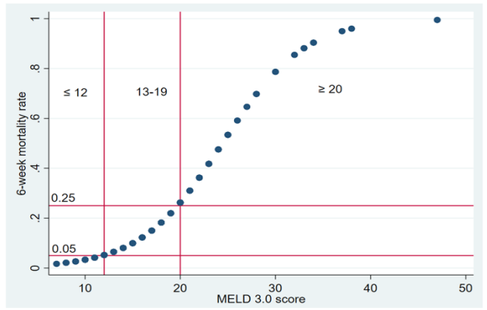

Figure 2. Scatterplot and Identifying Thresholds for MELD 3.0 score..

Conclusions: The MELD 3.0 score effectively predicts in-hospital and 6-week mortality in cirrhotic patients with variceal bleeding due to portal hypertension. Its clinical application is highly recommended for promptly identifying high-risk patients at the time of admission, particularly those with a MELD 3.0 score ≥ 20, who require intensified care.

Keywords: MELD 3.0 Score, Variceal Bleeding, Liver Cirrhosis, Mortality

PE-10

Sarcopenia in Cirrhosis: A Systematic Review of Diagnostic Tools and Interventions

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Aims: Sarcopenia is a prevalent complication of cirrhosis, contributing to worsened outcomes, including hepatic decompensation, poor quality of life, and increased mortality. Despite its clinical relevance, diagnostic consensus and effective interventions remain inconsistent. This systematic review aims to evaluate current diagnostic modalities for sarcopenia in cirrhosis and assess the efficacy of therapeutic interventions to guide evidence-based clinical management.

Methods: Following PRISMA guidelines, we performed a comprehensive search of PubMed, Web of Science, and Scopus databases up to January 2025. Eligible studies included randomized controlled trials (RCTs), cohort studies, and meta-analyses investigating diagnostic techniques or interventions for sarcopenia in adults with cirrhosis. Primary outcomes were diagnostic accuracy, sensitivity, and specificity for various assessment tools. Secondary outcomes included improvement in muscle mass, functional status, quality of life, and survival. Study quality was assessed using the Newcastle-Ottawa Scale and Cochrane Risk of Bias tool.

Results: A total of 53 studies comprising 6,142 patients with cirrhosis were included. Diagnostic assessment varied significantly across studies, with cross-sectional imaging at the L3 vertebral level (CT/MRI) regarded as the gold standard. Cut-offs for skeletal muscle index (SMI) ranged from 39 cm^2/m^2 to 52.4 cm^2/m^2 depending on sex and population. Bioelectrical impedance analysis (BIA) and handgrip strength offered practical alternatives, though with reduced accuracy in fluid-retentive states. Interventions including tailored nutritional support (high-protein diets and branched-chain amino acids), structured resistance exercise, and pharmacologic approaches (testosterone supplementation, myostatin inhibitors) demonstrated consistent improvements in muscle mass and functional outcomes. Combination interventions yielded the most significant benefits, with reported improvements in six-month survival rates by 10–15% in selected cohorts.

Conclusions: Sarcopenia in cirrhosis is underdiagnosed yet clinically impactful. Standardized diagnostic criteria are critical, with imaging-based methods offering the highest reliability. Multimodal interventions combining nutrition, exercise, and pharmacotherapy show promise in reversing sarcopenia and improving patient outcomes. Further large-scale RCTs are warranted to optimize management strategies and validate prognostic impacts.

Keywords: Sarcopenia, Cirrhosis, Diagnostic Tools, Nutritional Intervention

PE-11

A Prospective Multicenter Study for Comparison of Standard Dose Repeated Bolus Injection vs. Low Dose Continuous Intravenous Infusion of Terlipressin for Acute Esophageal Variceal Bleeding in Patients with Liver Cirrhosis

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Aims: Acute esophageal variceal bleeding (AVB) is one of the most serious complications of liver cirrhosis. For the emergent management of variceal bleeding, the administration of a vasoconstrictor is essential for hemostasis together with endoscopic variceal ligation (EVL). Standard-dose repeated bolus injection (SDRBI) of terlipressin 4-6 times daily is most widely employed before and after EVL, but the adverse effects of terlipressin cannot be overlooked. To minimize the ischemic side effect, low-dose continuous infusion (LDCI) of terlipressin has been proposed for hepato-renal syndrome in patients with liver cirrhosis. However, data from prospective comparisons between the two methods for AVB are sparse. This study aims to compare the safety and efficacy of the two methods for the management of AVB.

Methods: This study is a randomized controlled trial to compare SDRBI and LDCI of terlipressin in patients with AVB. A total of 125 patients were enrolled and randomly assigned to the SDRBI group (n=63, 1 mg bolus injection every 6 hours after the initial 2 mg of terlipressin) or LDCI group (n=62, 2 mg/day of terlipressin infusion) after EVL. Patients with gastric varices on the fundus, failure of initial endoscopic therapy, or advanced hepatocellular carcinoma were excluded.

Results: The baseline characteristics of the patients were not significantly different. Re-bleeding incidence after initial successful EVL was observed for 5 days. The success rate of maintaining hemostasis was 98.4% in both groups (Crude odd ratio = 0.98 [0.06-6.09], *P*=0.991). One patient died in the SDRBI group. Decrease of Hb more than 3 g/dL or adjusted blood requirement index over 0.75 to maintain Hb>8.0 g/dL were observed in 7 patients (11.1%) in the SDRBI and 9 (14.5%) in the LDCI group (*P*=0.763), respectively, without newly developed hematemesis or melena. The overall incidence of gastrointestinal, cardiovascular, metabolic, or neurologic adverse events was significantly higher in the SDRBI group than in the LDCI group during 5 days (*P*<0.05).

Conclusions: Compared with SDRBI, LDCI of terlipressin shows comparable efficacy and better safety for managing AVB in patients with liver cirrhosis.

Keywords: Variceal Bleeding, Terlipressin, Liver Cirrhosis

14. Liver Surgery

PE-1

Results of Surgical Treatment of Hepatic Alveolar Echinococcosis in Non-Endemic Region

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Aims: The aim of this study is to evaluate the results of surgical center of the non-endemic region in surgical treatment of liver alveococcosis.

Methods: A total of 17 patients underwent radical liver resection for hepatic alveolar echinococcosis between 2004 and 2024 in the department of liver transplantation and surgery. Patients characteristics, preoperative management, intraoperative dates, short- and long-term postoperative outcomes were analyzed.

Results: The disease was diagnosed in the advanced stages in 15 of 17 patients, which corresponded to IIIa-IV st. PNM WHO classification. Percutaneous transhepatic cholangiostomy was performed in 8 cases, portal vein embolization was performed in 12 cases preoperatively. Extended liver resections were performed in 16 cases, of which in 2 cases – total vascular liver exclusion with in-situ hypothermic perfusion. Clinically relevant 90-day complications (IIIa or more according to Clavien-Dindo classification) occurred in 5 (29,4%) patients. Reoperation was in 2 (11,7%) patients, 1 patient with portal vein thrombosis and compartment syndrome that required portal vein thrombectomy and venoplasty with vascular graft at 1 postoperative day

and abdominal wall reconstruction at 14 postoperative day respectively, other patient required reoperation because of insufficiency of hepaticojejunostomy at 8 postoperative day and because of bleeding from inferior vena cava and portal vein at 33 postoperative day. Incidence of surgical site infections (according to CDC definition) was 33,4%. Incidence of posthepatectomy liver failure (according to ISGLS definition) was 26,3%. Postoperative mortality was 5,9%, 1 patient died due to liver failure and septic shock). All patients are free of recurrence at the time of our study.

Conclusions: Aggressive surgical approach for hepatic alveolar echinococcosis can obtain good short-term outcomes with acceptable perioperative morbidity and mortality rates in experienced centers.

Keywords: Alveolar Echinococcosis, Hepatic Alveolar Echinococcosis, Liver Resection

PE-2

C3aR Deficiency Attenuates Liver Ischemia-Reperfusion Injury by Suppressing Glycolysis-Dependent Macrophage M1 Polarization via STAT3 Signaling

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Aims: Liver ischemia-reperfusion(LIRI) injury is a critical issue in clinical settings, particularly in liver transplantation and resection, leading to severe hepatocellular dysfunction and organ failure. Although the complement component 3a receptor(-C3aR) affects inflammatory responses, its role in LIRI is unclear. Here, we aim to explore the role and mechanism of C3aR in LIRI.

Methods: In vivo experiments, multiple groups including sham operated, C3aR−/−mice, C3aR specific antagonist JR14a treated, Kupffer cell specific C3aR knockout mice(Lyz2-C3aR$^{flox/flox, cre}$)and their control littermates were used to establish 70% LIRI model. Serum and liver tissues were collected to evaluate liver injury through transaminase assays(ALT/AST), hematoxylin-eosin(HE) staining, immunohistochemistry(IHC), Western blot, and qRT-PCR. In vitro experiments, Primary hepatic macrophages and bone marrow-derived macrophages(BMDMs) were isolated and cultured from the aforementioned experimental groups. Cells underwent high-throughput RNA sequencing (RNA-seq), Western blot, qRT-PCR, flow cytometry, Seahorse Glycolysis Stress Test (ECAR/OCR), glucose uptake, lactate production, and immunofluorescence assays to investigate C3aR mediated metabolic reprogramming and polarization dynamics.

Results: C3aR knockout mitigated LIRI induced hepatic damage and inflammation. Specifically, C3aR deficiency reduced macrophage M1 polarization. Macrophage-specific C3aR deletion also attenuated hepatic injury and inflammation while suppressing M1 polarization. In vitro experiments revealed that C3aR deficiency inhibited M1 polarization of macrophages by suppressing glycolysis. Transcriptome analysis showed differential expression of glycolysis-related pathways. Mechanistically, C3aR deficiency inhibited glycolysis via the STAT3 signaling pathway. Treatment with the C3aR antagonist JR14a reduced LIRI progression and suppressed macrophage C3aR expression, glycolysis, M1 polarization and STAT3 phosphorylation.

Conclusions: C3aR deficiency mitigates LIRI through inhibition of glycolysis-dependent macrophage M1 polarization. These findings highlight that targeting C3aR may represent a novel therapeutic strategy for LIRI by disrupting the crosstalk between metabolic reprogramming and pro-inflammatory macrophage activation.

Keywords: Liver Ischemia-Reperfusion Injury, Complement Component 3A Receptor, Macrophage M1 Polarization, Glycolysis

PE-3

Initial Steps of Implementing Liver Cancer Treatment at the National Hospital of Tropical Diseases: Experiences of a New Center

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Aims: The Hepatobiliary - Digestive Surgery Center of the Central Tropical Diseases Hospital was developed from the Department of HBP Surgery established on March 1, 2023 with the function of treating hepatobiliary diseases, including liver cancer. We would like to share our personal experience of the initial implementation of liver cancer treatment as a new center of a specialized infectious disease hospital.

Methods: We develop based on 4 major principles: 1. Focus on our strengths, 2. Make up for the weakness, 3. External coordination, 4. Renew problem approaches.

Results: From March 2023 to September 2024, we have performed liver resection for 138 HCC cases, including complex surgeries such as diaphragm resection, biliary tract resection, vascular thrombosis, ..., TACE for 78 cases.

Conclusions: Treatment of liver cancer requires coordination of many specialties. Each medical facility needs to develop a development orientation that is suitable for its strengths and weaknesses.

Keywords: Liver Cancer

PE-4

Early Outcomes of Anatomical Liver Resection at a Nascent Hepatobiliary Center in Vietnam

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Aims: This study evaluates the early outcomes of anatomical liver resection at a newly established hepatobiliary center in Vietnam, focusing on its feasibility, safety, and efficacy in a setting with limited prior experience

Methods: We retrospectively analyzed 43 patients undergoing anatomical liver resection at the National Hospital of Tropical Diseases, Vietnam, between June 2022 and June 2023. Data collected included patient demographics, operative details, with a particular focus on extrahepatic Glisson's pedicle management, and postoperative outcomes

Results: Most patients were male (86.04%) with underlying hepatitis B or C infection (93.02%). Major hepatectomy was required in 48.84% of cases. Notably, extrahepatic control of the right and left Glisson's pedicles was achieved in 100% of cases, and 93.75% for right anterior and posterior sectional pedicles. Combining intra- and extrahepatic approaches yielded a 0% pedicle injury rate. Mean operative time for major and minor resections were 238.15 and 202.32 minutes, with mean blood loss of 395.86 ml and 296.08 ml, respectively. Postoperative complications occurred in 18.62% of cases, predominantly mild. Patients had a mean postoperative stay of 14.2 days, with 97.67% discharged in stable condition

Conclusions: Despite being a nascent center, our institution demonstrates promising early outcomes in anatomical liver resection, comparable to established centers. The meticulous application of extrahepatic Glisson's pedicle control, particularly when combined with an intrahepatic approach, proves to be a safe and effective technique. These findings underscore the feasibility and safety of performing complex liver surgery in new centers with rigorous surgical techniques

Keywords: Anatomical Liver Resection, Glisson's Pedicle, Hepatobiliary Surgery

PE-5

A Decade of Global Bibliometric Analysis on Research Trends in Minimally Invasive Liver Surgery

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Aims: Minimally Invasive Liver Surgery (MILS) has emerged as a significant innovation in hepatobiliary surgery, offering benefits such as reduced postoperative complications and faster recovery times. This study aims to evaluate the research trends, scientific collaborations, and emerging themes in the MILS field over the past decade through a bibliometric approach.

Methods: A bibliometric analysis was conducted using the Scopus and PubMed databases for the period 2014–2024. Key terms included minimally invasive liver surgery, laparoscopic liver resection, and robotic liver surgery. The data analyzed included publication counts, citations, authors, journals, institutions, and contributions by country. Data visualization was performed using VOSviewer and Bibliometrix software.

Results: There was a significant increase in publications since 2018. Co-occurrence keyword visualization revealed dominant themes such as laparoscopic liver resection, robotic surgical procedures, and hepatocellular carcinoma, reflecting a focus on laparoscopic approaches, robotic technology, liver cancer applications, living donors, and liver transplantation. Technological advances, particularly in robotic surgery and fluorescence imaging, highlight the adoption of cutting-edge technologies in MILS. Keywords such as operative time, length of stay, and postoperative complications emphasize attention to operational efficiency and procedural safety. Countries like Japan, Italy, and France led research contributions, while journals such as Annals of Surgery and Surgical Endoscopy served as key publication sources.

Conclusions: Research on MILS has made significant strides, emphasizing procedural efficiency and technological applications. These findings provide valuable insights into global trends and priority areas for future research development.

Keywords: Bibliometric Analysis, Global, Minimally Invasive Liver Surgery

PE-6

The Transplant Technologies in the Treatment of So-Called "Inoperable Patients" with Liver Alveococcosis

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Aims: The primary target of the study was to assess and improve the outcomes of surgical treatment for patients diagnosed with complicated liver alveococcosis, a parasitic infection caused by *Echinococcus multilocularis* that affects the liver and can become life-threatening if not treated adequately.

Methods: The study reviewed surgical interventions performed between April 2009 and February 2024 at the Department of Surgical Gastroenterology and Endocrinology of the National Hospital. A total of 573 patients with liver alveococcosis were

considered, with 512 of them undergoing surgery. The patients ranged in age from 9 to 73 years, with an average age of 37±2.3 years.

Results: Among the 512 patients who underwent surgery: Resectability rate was 86.2%, meaning most patients had tumors or lesions that were eligible for surgical removal.

Types of liver resections: Extensive liver resections (47.3%): Including procedures like right-side hemihepatectomy (54.3%), extended right-side hemihepatectomy (18.3%), and extended left-side hemihepatectomy (9.4%). Non-anatomical resections (segmentectomy and bisegmentectomy) constituted 52.7% of surgeries.. Average volume of blood loss: for the period 2009-2013. – 2812± 205 ml, for the period 2014-2018. – 1725± 198ml, for the period 2019-2023. - 1145±110ml. 342 (61.4%) patients underwent radical surgery.

A significant innovation discussed in the study involves using transplantation technologies for patients whose alveococcosis has grown into the inferior vena cava (IVC), making the lesions inoperable by conventional liver resection methods. The study describes a technique used in four patients who underwent liver surgery with transplantation technologies:

Tetrafluoroetylene prosthesis: This was used to handle complex cases where the liver resection was not feasible in vivo.

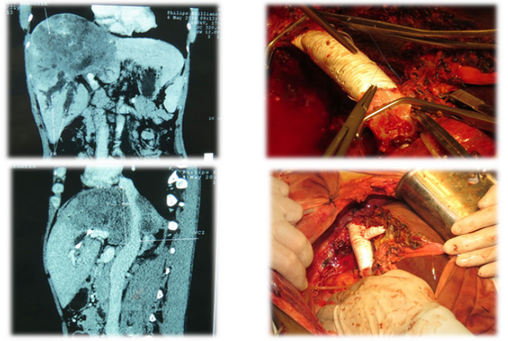
Backtable procedures: This approach involved removing the parasitic lesions outside the body (ex-vivo), especially in patients with damage to the IVC causing critical narrowing (down to 5mm). On the "backtable," surgeons could reconstruct the vascular elements and re-implant them into the patient, which is a critical step in ensuring successful outcomes.

The study noted that three of these surgeries were performed at the Volga Regional Medical Center, and one was performed in Kyrgyzstan

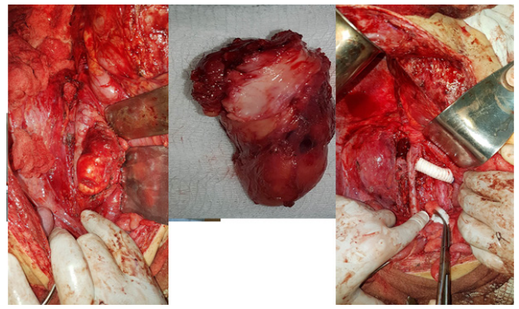
Conclusions: For patients with unresectable alveococcosis involving critical damage to the IVC or other major vessels, liver allotransplantation combined with vascular resection and reconstruction provides a potentially life-saving solution. This method has proven effective not only for the immediate surgical outcomes but also for long-term survival. It represents a radical approach to what was once thought to be a doomed diagnosis for patients with liver alveococcosis that could not be treated with standard surgical techniques.

The findings underscore the importance of advanced surgical technologies and transplantation procedures in offering new hope for patients with otherwise inoperable liver disease due to alveococcosis.

Keywords: Liver Surgery, Liver Alveococcosis, Liver Traspalntation, Trasplant Technologies



Condition after extensive liver resection and IVC replacement, removal of alveolar nodes of the retroperitoneal region (Marginal resection of the IVC and replacement of the left renal vein)



PE-7

Does Digital Aging, Social Capital, and Macroeconomic Factors Matter on Recovery Advancement among Elderly with Liver Disease?

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Aims: Post-treatment recovery in elderly patients with liver disease is influenced by multiple factors, including digital literacy (digital aging), social capital, dietary intake, economic indicators such as GDP per capita, and healthcare expenditure. Digital tools and social networks provide critical support, while economic and dietary factors impact physical recovery.

Methods: This study combines data from the Indonesia Family Life Survey (IFLS), World Bank, and United Nations Development Programme (UNDP) to assess the effects of these factors on recovery outcome. The variabels include digital aging (frequency of digital device use), social capital (participation in community activities, social network size), dietary intake (caloric and protein consumption) gdp per capita (country-level economic data), and healthcare expenditure (public and private healthcare spending per capita). Control variables include age, gender, education, comorbidities, household income.

Results: Recovery outcomes were most strongly associated with dietary protein intake ($\beta = 0.45$, $P<0.01$), emphasizing the critical role of nutrition. Digital aging ($\beta = 0.42$, $P<0.01$) also significantly impacted recovery, highlighting the importance of digital literacy in accessing healthcare resources. Social capital ($\beta = 0.34$, $P<0.05$) contributed positively, indicating that community and social networks support recovery processes. Systemic factors, including GDP per capita ($\beta = 0.28$, $P<0.05$) and healthcare expenditure ($\beta = 0.37$, $P<0.05$), demonstrated significant associations, reflecting the importance of economic and policy-level influences.

Conclusions: This research underscores the need for interventions that prioritize dietary optimization, digital literacy programs, and enhanced social networks. Policy efforts to increase healthcare expenditure and address disparities in economic resources can further improve recovery outcomes for elderly liver disease patients. Future studies should explore longitudinal impacts and personalized recovery strategies to maximize quality of life.

Keywords: Digital Aging, Social Capital, Healthcare Expenditure, Liver Disease Recovery

PE-8

Posthepatectomy Bile Leakage: A Single-Center Experience in Kazakhstan

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Aims: One of the complications after resection, which significantly worsens the postoperative course, is bile leakage (BL). This study shows the experience of one center on this issue.

Methods: 133 liver resections were performed based on the National Research Oncology Center in Astana in the period from 2020 to 2023. All data were retrospectively analyzed.

Results: During the entire follow–up period, there were 14 cases of bile leakage: ICCC – 3 (21.4%), PCCC – 3 (21.4%); HCC+CCC – 1 (7.1%); GBC - 1 (7.1%); CRC LM – 1 (7.1%); 1 (7.1%) EG and 4 (28.5%) EM. The largest number of BL was observed in patients with CCC (42.8%), and in none of the cases of HCC. The average age of patients is 56.07 years, due to the senile age of patients with malignant tumors. Gender ratio: women (71.4%) and men (28.5%). In a way to consider possible predictors of postoperative BL main criteria related to the patient, liver and surgery were analyzed and displayed in Table No. 1. As it shown, the more severe the ECOG status of the patient, the higher the probability of any type of complication, even though this is not observed in the assessment of MUST. Intraoperative blood loss of more than 1000 ml, extent liver resection, resection of extrahepatic bile duct with formation of biliodigestive anastomosis is likely to lead to complications.

Conclusions: The limitation of this study is the small number of patients. Nevertheless, these results may form the basis for a future prospective randomized trial to determine the predictors of BL and the management options for patients with such a complication.

Keywords: Posthepatectomy Bile Leakage, Liver Resection, Single Center Experience, Predictors of PHBL

Table 1.

Variables		Number	%	PHBL A	PHBL B	PHBL C
Etiology						
PCCC		3	21.4	1	2	
ICCC		3	21.4		1	2
HCC+CCC		1	7.1		1	
GBC		1	7.1		1	
CRC LM		1	7.1		1	
Echinococcosis granulosus (EG)		1	7.1		1	
Echinococcosis Multilocularis (EM)		4	28.5	1	2	1
Age >65		4	28.5	1	2	1
EGOC						
ECOG 0		6	42.8	1	4	1
ECOG 1		5	35.7		4	1
ECOG 2		3	21.4	1	1	1
Malnutrition						
MUST 0		11	78.5	2	7	2
MUST 1		1	7.1			1
MUST 2		1	7.1		1	
MUST 3		1	7.1		1	
DiabetesMellitus		3	21.4		2	1
Cirrhosis		2	14.2		2	
Biliary Hypertension		5	35.7	2	2	1
Extent of operation						
Major resection		10	71.4	2	6	2
Minor resection		4	28.5		3	1
Ultrasound device		12	85.7	2	7	3
Ultrasound device (not used)		2			2	
Extrahepatic duct resection						
Roux-en-Y		5	35.7	2	2	1
Bile duct stenting		6	42.8		5	1
Pringle maneuver		2	14.2			
Blood loss >1000 ml		7	50	2	4	1
Duration of surgery		Max – 575 Min – 227 Av – 375.71				
Complication						
Clavien-Dindo						
	Grade I	3	21.4	2	1	
	Grade IIIa	8	57.1		8	
	Grade IIIb	1	7.1			1
	Grade V	2	14.2			2

PE-9

Intraductal Papillary Neoplasm of the Bile Duct (Ipnb) with Invasion to the Stomach and Lef Lobe Atrophy - Case Presentation

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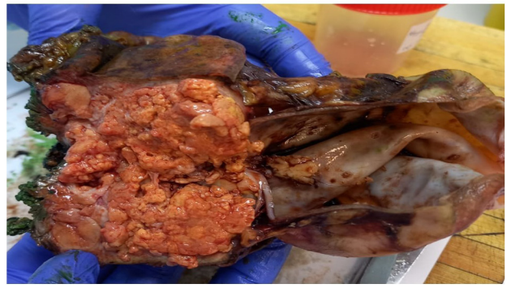
Aims: Intraductal papillary neoplasm of the bile duct (IPNB) is a rare neoplasm of the biliary tract. IPNB develops in any part of the biliary tree, displays papillary exophytic growth pattern. Here we present the clinical case of the patient with IPNB with invasion to the serous layer of the stomach and atrophy of the liver left lobe.

Methods: All data regarding patients were retrieved from electronic records.

Results: 66-year-old male with a history of abdominal pain was admitted to our hospital. 12 month prior to hospitalization, he was found with the lesion in the left lobe of the liver on abdominal ultrasonography. Abdominal computed tomography (CT) and magnetic resonance imaging (MRI) revealed solid soft tissue mass of the left lobe of the liver, irregular in shape, a cystic mass with a walled soft tissue continuing to the left of the lesion. Left liver parenchyma was almost completely atrophied. Resection of the left lateral sector of the liver with gastric serous layer desection, cholecystectomy, and standard lymphadenectomy were performed. Histological examination showed an intraductal papillary liver tumor associated with invasive G2 carcinoma (in the invasive component), biliary type. Invasive component within liver tissue. Retention cyst of the liver The resection margin is negative (R0). Lymph nodes without metastatic lesions. The postoperative period show no complications. The patient was discharged from the hospital on the 7th day after surgery. 3 month follow up showed no reccurence.

Conclusions: Intraductal papillary biliary neoplasm carries a risk of biliary obstruction and increases the risk of progression to invasive carcinoma. Radical liver resection is the treatment of choice, showing better survival. Accurate preoperative imaging evaluation and thorough intraoperative cholangioscopy evaluation are key to curative resection.

Keywords: IPMN-B, Liver Resection, Cholangiocarcinoma



PE-10

Enhanced Recovery after Surgery in Liver Resection: A Systematic Review of Clinical Outcomes

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Aims: Enhanced Recovery After Surgery (ERAS) protocols are structured, evidence-based perioperative care pathways designed to reduce surgical stress, enhance recovery, and improve clinical outcomes. While ERAS has demonstrated benefits across various surgical disciplines, its application in liver resection remains under continued investigation. This systematic review aims to evaluate the clinical outcomes associated with ERAS protocols in patients undergoing liver resection, including morbidity, length of hospital stay, and postoperative recovery.

Methods: A comprehensive literature search was conducted in PubMed, Web of Science, and Scopus databases according to PRISMA guidelines up to January 2025. Randomized controlled trials (RCTs), cohort studies, and case-control studies comparing ERAS protocols to conventional perioperative care in liver resection were included. Outcomes analyzed included postoperative complications, length of hospital stay, readmission rates, mortality, and patient-reported outcomes. The methodological quality of included studies was assessed using the Cochrane Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale for observational studies.

Results: A total of 34 studies encompassing 5,482 patients met the inclusion criteria. ERAS protocols were associated with a significant reduction in postoperative complications (odds ratio [OR] 0.68; 95% confidence interval [CI]: 0.55–0.83; P<0.001) and a shorter length of hospital stay (mean difference: -2.8 days; 95% CI: -3.4 to -2.2). The implementation of ERAS protocols did not increase readmission rates or postoperative mortality. Additionally, ERAS was associated with improved patient satisfaction scores and earlier return to baseline functional status. Subgroup analyses indicated that benefits were consistent across both open and laparoscopic liver resections.

Conclusions: Enhanced Recovery After Surgery protocols significantly improve clinical outcomes following liver resection by reducing complications and accelerating postoperative recovery without compromising patient safety. Widespread adoption and standardization of ERAS protocols in liver surgery are warranted to optimize perioperative care and enhance patient outcomes.

Keywords: Enhanced Recovery, Liver Resection, Postoperative Outcomes, Perioperative Care

PE-11

Prognostic Value of an Integrated AFP-PIVKA-II Based Tumour Biology Characteristics Score Following Curative-Intent Resection of Hepatocellular Carcinoma: A Multicenter Cohort Study

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Aims: Current staging systems for hepatocellular carcinoma (HCC) lack comprehensive biological assessment. We developed a tumor biology characteristics score (TBCS) incorporating AFP and PIVKA-II to predict post-resection outcomes.

Methods: We analyzed 695 HCC patients who underwent curative resection across four centers. The TBCS (range: 2-6) combined preoperative AFP (<20/20-199/≥200 ng/mL) and PIVKA-II (<40/40-399/≥400 mAU/mL) levels, stratifying patients into low (2), medium (3-4), and high (5-6) risk groups.

Results: Patient distribution was: low TBCS (19.0%), medium TBCS (33.5%), and high TBCS (47.5%). Five-year recurrence-free survival rates were 30.4%, 14.7%, and 9.7% respectively (P<0.001). Five-year overall survival rates were 42.1%, 35.5%, and 23.5% respectively (P<0.001). Multivariate analysis confirmed TBCS as an independent predictor of both endpoints (medium TBCS: HR=1.583, high TBCS: HR=1.895 for recurrence; high TBCS: HR=1.781 for survival; all P<0.001).

Conclusions: This novel biomarker-based scoring system effectively stratifies post-resection prognosis in HCC patients, potentially guiding surveillance intensity and adjuvant therapy decisions.

Keywords: Hepatocellular Carcinoma, Alpha-Fetoprotein, Protein Induced By Vitamin K Absence or Antagonist-II

PE-12

Development and Validation of a Risk Stratification Model for Post-Hepatectomy Distant Metastasis in Hepatocellular Carcinoma: A Multi-Center Study

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Aims: Despite advances in surgical techniques for hepatocellular carcinoma (HCC), the occurrence of distant metastasis following curative hepatectomy remains a significant challenge that substantially impacts patient survival. Currently, there is a lack of reliable tools to identify patients at high risk for post-operative distant metastasis, limiting the ability to implement targeted surveillance and early intervention strategies.

Methods: A comprehensive analysis of 2,705 HCC patients who underwent hepatectomy across multiple institutions between 2013 and 2020 was conducted. Using statistical modeling, we integrated clinicopathological variables to identify key predictors of distant metastasis. A novel risk prediction nomogram was developed and validated through rigorous statistical methods, including concordance index calculation and calibration curve analysis. Risk stratification was performed by categorizing patients into three distinct risk groups based on calculated nomogram scores.

Results: Among the study cohort, 342 patients (22.7%) developed distant metastasis as their initial recurrence pattern. Eight independent risks emerged from our analysis: preoperative tumor rupture, tumor diameter exceeding 5 cm, multinodular disease, presence of satellite lesions, macro- and microvascular invasion, surgical margin status, and perioperative blood product administration. The constructed nomogram exhibited exceptional discriminatory ability (C-index >0.85) in predicting distant metastasis risk. Long-term survival analysis revealed striking differences among risk groups, with 5-year overall survival rates of 9.1%, 41.1%, and 90.8% for patients with distant metastasis, intrahepatic recurrence, and no recurrence, respectively (P<0.001).

Conclusions: This validated risk stratification model provides clinicians with a practical tool for identifying HCC patients at elevated risk for distant metastasis, enabling personalized surveillance protocols and timely therapeutic interventions.

Keywords: Hepatocellular Carcinoma, Hepatectomy, Distant Metastasis

PE-13

Development and Validation of an Individualized Prediction Calculator for Postoperative Late Recurrence of Hepatocellular Carcinoma (POLAR-HCC)

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Aims: Postoperative recurrence is a significant concern for patients undergoing hepatocellular carcinoma (HCC) resection. While early recurrence is often attributed to tumor aggressiveness, late recurrence presents its own set of challenges. This multicenter study aimed to develop and validate the POLAR-HCC calculator, a specialized tool for predicting postoperative late recurrence (POLAR).

Methods: Collaborative data from a multicenter database in China were used. Patients free of recurrence for 2 years after surgery were randomly split into development and validation cohorts in a 2:1 ratio. Univariate and multivariate Cox-regression analyses on the development cohort identified independent predictors of POLAR, which were used to create the web-based POLAR-HCC calculator.

Results: In the derivation cohort (n=566), the calculator exhibited a high concordance index (c-index) of 0.660, indicating its superior discriminative ability. Decision curve analysis further validated the model's clinical usefulness, demonstrating its superiority over the 5 traditional HCC staging systems. When tested on the validation cohort (n=283), the calculator maintained its robust predictive performance, with a consistent c-index of 0.626. Based on the nomogram scores, patients were stratified into low-risk and high-risk groups for POLAR. The high-risk group exhibited a significantly increased incidence of POLAR compared to the low-risk group, underscoring the calculator's indispensable clinical utility.

Conclusions: The POLAR-HCC calculator, resulting from multicenter collaboration, offers a practical approach to HCC surgical management. By facilitating precise risk stratification for POLAR, it provides an additional tool for clinicians in guiding individualized surveillance, aiming to enhance long-term survival outcomes for HCC surgical patients.

Keywords: Hepatocellular Carcinoma, Late Recurrence, Individualized Prediction

PE-14

Laparoscopic Glisson Pedicle Priority Hepatectomy Based on Cone Unit

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Aims: Most HCC has the basis of cirrhosis, does not allow large-scale hepatectomy. For patients with small HCC and severe cirrhosis, according to the precise basin of portal vein supply, the liver resection reduces the volume of hepatectomy and achieves the purpose of anatomical hepatectomy, By Glisson Pedicle Priority to find the cone unit's pedicle easily.

Methods: After enhanced CT or MRI, 3D reconstruction constructs the Glisson pedicle composition of the area where the tumor is located, each small pedicle blood supply area acts as a cone unit, two methods determine the cone unit resection range, (1) Glisson Pedicle Priority is applied, one or several cone unit blood supply pedicle is isolated and ligated, ICG reverse staining determines 1 or several cone unit ranges for resection; (2) Another method: ultrasound localization of cone unit Glisson pedicle and puncture portal injection of ICG, anatomical excision by puncture one or several cone unit blood supply pedicles according to preoperative planning.

Results: In all 12 patients with small HCC based on cirrhosis, 8 cases were reverse stained and 4 cases were positive stained. The median duration of surgery was 89±15 minutes and the average estimated blood loss was 103 ml. All 12 recovered successfully. Follow-up results showed that the mean disease-free survival (DFS) was 24.7m and OS 38.9month.

Conclusions: Liver resection based on cone unit is a safe and effective surgical method for small HCCs with severe cirrhosis, which reduces the incidence of postoperative liver failure and reduces bleeding, thereby increasing DFS and OS in patients

Keywords: Cone Unit, Hepatectomy, Glisson Pedicle Priority

PE-15

Modified Extra-Fascial Transfissural Approach- Revisiting Tung's Livers

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Aims: We evaluated our modified extra fascial transfissural technique for liver resection.

Methods: Extra-fascial Transfissural Technique: We mobilize the liver by dividing the triangular ligaments. For right and left hepatectomies, we start by dividing the main portal fissure; for right posterior sectorectomy and left trisegmentectomy, we divide the right portal fissure; and for right trisegmentectomy and left lateral segmentectomy, we divide the left portal fissure. We approach the Glissonian pedicle extrafascially and intrahepatically. The Glissonian pedicle is cut and ligated en masse, followed by liver transection. We reviewed all liver resections performed using our technique over the last 5 years, assessing in-hospital mortality, 90-day mortality, overall complications, and bile leaks. Normality was tested with the Shapiro-Wilk test. Categorical values were evaluated with chi-square tests, continuous variables with the Mann-Whitney U test, and multivariate analysis was conducted using logistic regression.

Results: From November 2019 to August 2024, we performed 74 liver resections: 63 major and 11 minor. The breakdown included 30 right hepatectomies, 16 left hepatectomies, 7 right tri-segmentectomies, 3 left tri-segmentectomies, and 18 parenchyma-preserving resections. The cohort comprised 52 males and 22 females, with a median age of 54. The median operative time was 180 minutes, the median hospital stay was 4 days, and the median blood product requirement was 2 units. In-hospital mortality was 2.7%, 90-day mortality was 6.7%, overall complication rate was 14.8%, and bile leak rate was 8.1%. No factors independently predicted morbidity or mortality.

Conclusions: Our modified extra fascial transfissural approach, is feasible and reproducible.

Keywords: Liver Surgery, Hepatectomy

PE-16

Results of Laparoscopic versus Open Major Hepatectomy for the Management of Hepatocellular Carcinoma in a Vietnamese Tertiary Hospital: A Five-Year Retrospective Comparative Study

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Aims: Laparoscopic techniques are constantly evolving and gradually take the place of open surgery in majorities of abdominal procedures. Nevertheless, for liver resection, the ratio of open surgery is still relatively high, especially for major hapatectomy. This study aimed to compare the results between laparoscopic and open major hepatectomy for managing hepatocellular carcinoma (HCC) in a Vietnamese tertiary hospital over a five-year period.

Methods: A retrospective comparative study between two groups of patients with HCC who underwent major liver resection either by laparoscopic or open approach at Departments of Hepatopancreatobiliary Surgery, Military Central Hospital 108, from January 2019 to December 2023.

Results: A total of 260 major hepatectomies were consecutively performed to manage HCC. 166 resections were performed in the open approach group (63.8%), and 94 resections were performed in the laparoscopic surgery group (36.2%). The laparoscopic approach helps to minimize intraoperative blood loss (257.38 ± 123.84 mL vs. 348.40 ± 165.01 mL, P=0.002) and shorten the length of hospital stay (8.08 ± 2.35 nights vs. 10.98 ± 5.66 nights, P<0.001). For other short-term outcomes, the two groups had no differences in perioperative complications, morbidities, and mortality. Regarding long-term outcomes, the two groups had no differences in overall and disease-free survival.

Conclusions: The application of the laparoscopic approach in major hepatectomy to treat HCC is safe, feasible, and minimizes invasive, which helps faster postoperative with similar long-term outcomes. Laparoscopic major hepatectomy could be an alternative and become the gold standard in selected patients.

Keywords: Hepatectomy, Major Liver Resection, Hepatocellular Carcinoma

PE-17

Modified ALPPS Procedure to Treat Hepatocellular Carcinoma with Macrovascular Invasion

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Aims: HCC with macro vascular invasion is a poor prognosis factor. Liver resection is the only curative treatment according to Asian guidelines. Due to rapid disease progression, ALPPS may be the only option in case of insufficient FLR.

Methods: Method: We performed modified ALPPS in 2 cases. Case 1: Large tumor in the right liver with middle hepatic vein tumor thrombosis. Case 2: Lage tumor in the right liver adjacent to the middle hepatic vein and right portal vein tumor thrombosis (Vp3). Our procedure consisted of: 1. Ligation of right portal vein and middle hepatic vein at their roots, 2) Parenchymal division at the umbilical fissure with the anterior approach, 3) Combined resection of Segment IV.

Results: Both cases have no complications after the first operation. The hypertrophy rate of the FLR was 1.81 and 1.73 after 1 weeks. Both cases were performed right trisectionectomy in the second phase without complications.

Conclusions: By preventing the advance of tumor thrombosis of the hepatic and portal vein, and avoiding parenchymal ischemia, the modified ALPPS could improve the safety and success rates of liver resection.

Keywords: ALPPS, HCC, Macrovascular Invasion

PE-18

Breaking Barriers: The Role of Liver Resection in Giant Hepatocellular Carcinoma

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Aims: Giant hepatocellular carcinoma (HCC), defined as tumors ≥10 cm, poses significant challenges for surgical intervention due to its size, vascular involvement, and risk of postoperative

complications. This study aims to evaluate the role of liver resection in patients with giant HCC, in Makassar, Indonesia.

Methods: A retrospective analysis was conducted on patients with giant HCC who underwent liver resection. Key parameters included patient demographics, tumor characteristics, extent of resection, intraoperative details, complications, and follow-up data.

Results: Between 2021 and 2024, 11 liver resections were performed for giant hepatocellular carcinoma. The mean patient age was 57.4 years, with a predominance of females (55%) and the majority classified as Child-Pugh A (82%). Tumors were mostly located on the right side (73%), with a mean size of 14.9 cm and a maximum tumor volume of 3553 cm^3. Four patients (36%) experienced mortality within the three-year follow-up period. Recurrence occurred in two cases, which were effectively managed with adjuvant lenvatinib therapy.

Conclusions: Liver resection remains a viable and effective treatment option for selected patients with giant HCC, offering favorable survival outcomes when performed with meticulous surgical planning. Despite its challenges, careful patient selection and advanced techniques can break barriers in the management of massive tumors, underscoring the importance of a multidisciplinary approach.

Keywords: GIANT, HCC, Liver Resection

PE-19

Early Experience with Robotic Single-Port Liver Resections Using the Da Vinci SP System in a Small Center

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Aims: Robotic surgical systems have significantly advanced minimally invasive surgery by providing enhanced precision, dexterity, and visualization. Among these, robotic single-port systems offer a notable improvement, allowing complex procedures through a single incision. However, their adoption remains limited due to procedural complexity, especially in smaller centers with constrained resources. Hepatectomy, a demanding procedure requiring careful dissection and hemostasis, presents unique challenges for robotic single-port systems due to the absence of integrated energy devices. This study aims to assess the early experience with the da Vinci SP system for liver resection in a small center, focusing on clinical outcomes and operative efficiency.

Methods: From May 2024, five robotic single-port liver resections were performed at Dong-A University Hospital. These included three monosegmentectomies (Segments 1, 4, and 6), one lateral sectionectomy, and one left hepatectomy, conducted for various liver diseases. All procedures utilized the da Vinci SP system.

Results: Oncologic Outcome Of More Than 10 Cm Resectable Hepatocellular Carcinoma

Conclusions: Our early experience suggests that robotic single-port liver resections is feasible and safe in a small center setting. Despite the challenge of lacking integrated energy devices, the procedures showed acceptable operative times and favorable postoperative outcomes. Further studies with larger case series are needed to validate these results and refine technology for broader implementation in hepatobiliary surgery.

PE-20

Report of Two Cases of Aberrant Hepatic Duct Entering Cystic Duct: Identifying and Preventing Bile Duct Injury

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Aims: Although laparoscopic cholecystectomy has been considered to have more advantages than open cholecystectomy, the incidence of bile duct injury still remains high. The most common cause of biliary tract injury is misidentification of anatomy and variant of the biliary tract.

Methods: We describe two cases of laparoscopic cholecystectomy in patients with the right posterior sectional duct entering the cystic duct.

Results: A 45-year-old female patient and a 53-year-old male patient underwent laparoscopic cholecystectomy due to biliary colic and cholecystitis, respectively. During operation, our team observed an abnormal duct originating from the right lobe of the liver draining into the cystic duct before joining the common bile duct while attempting to clearly define the "critical view of safety." Fundus-first cholecystectomy was performed, and the patients were discharged after 2 and 3 days, respectively.

Conclusions: Anatomical variations of the biliary tract are a significant risk factor for biliary injury during laparoscopic cholecystectomy. Surgeons must know normal and variant biliary anatomy to prevent inadvertent injury.

Keywords: Biliary Ductal Anomalies, Variant Biliary Anatomy, Bile Duct Injury

PE-21

Evaluating the Effectiveness of Surgical Approaches for Hepatolithiasis: Insights from a Bangladeshi Tertiary Care Institution

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Aims: Hepatolithiasis is a significant biliary disorder in Bangladesh, leading to considerable patient morbidity and necessitating effective surgical interventions.

Methods: This prospective study was conducted from January 2018 to December 2023 at the Department of HBP Surgery, Bangabandhu Sheikh Mujib Medical University, Central Hospital and BIRDEM Hospital, Dhaka. A total 62 patients diagnosed with hepatolithiasis enrolled and categorized into open surgery (n=35) and minimally invasive surgery (n=27) groups. Surgical outcomes, including stone clearance rates, postoperative complication incidences, length of hospital stay, were systematically recorded. Data were analyzed using SPSS version 26.0, employing chi-square tests for categorical variables and t-tests for continuous variables. Logistic regression was performed to identify predictors of postoperative complications

Results: Among 62 patients, stone clearance achieved in 32 (91.4%) of open surgery group 25 (92.6%) of minimally invasive group (P=0.85). Open surgery group experienced higher incidence of postoperative complications (15%) compared to minimally invasive group (5%) (P=0.04). Mean length of hospital stay was significantly longer for open surgery patients (10 ± 2 days) versus those undergoing minimally invasive procedures (5 ± 1 days, P<0.001). Logistic regression analysis revealed minimally invasive surgery independently associated with reduced postoperative complications (Odds Ratio = 0.25, 95% CI: 0.07-0.90, P=0.035). Additionally subgroup analysis indicated that laparoscopic approaches specifically resulted in a 35% reduction in hospital stay and a 40% decrease in complication rates compared to open surgery

Conclusions: Minimally invasive surgical approaches for hepatolithiasis in Bangladeshi tertiary care institutions demonstrate comparable stone clearance rates, significantly lower complication incidences, and shorter hospital stays compared to open surgery.

Keywords: Hepatolithiasis, Surgical Approches, Minimal Invasive Surgery

PE-22

Rare Case of Hepatic Epithelioid Hemangioendothelioma Managed with Minimally Invasive Surgery: A Case Report and Literature Review

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Aims: Hepatic epithelioid hemangioendothelioma (HEHE) is a rare malignant vascular liver tumor diagnosed through histopathological evaluation. Standardized treatment is challenging due to its rarity; hepatectomy is preferred for solitary lesions, and transplantation for multiple. There is no consensus on the optimal HEHE treatment, but surgical excision is often considered effective. This report presents a case initially suspected as cholangiocarcinoma or Renal cell carcinoma (RCC) metastasis, later confirmed as HEHE, with no recurrence during follow-up.

Methods: CASE SUMMARY A 52-year-old man with a history of left nephrectomy for RCC presented with an incidentally detected liver mass and nonspecific abdominal discomfort. Imaging showed a 3-cm centripetal enhancing lesion in the right hepatic dome with indeterminate malignant potential. The patient underwent laparoscopic right anterior sectionectomy and remained recurrence-free without complications during the 3-year follow-up period.

Results: The patient underwent laparoscopic right anterior sectionectomy and remained recurrence-free without complications during the 3-year follow-up period.

Conclusions: Managing HEHE is challenging; accurate diagnosis and surgical options like resection or transplantation are essential, with tailored multidisciplinary follow-up.

PE-23

Single Center Experience of ABO-Incompatible Adult-to-Adult Living Donor Liver Transplantation: A Case Report

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Aims: ABO-incompatible living-donor liver transplantation could expand the living-donor pool, reduce waiting times for deceased-donor liver transplantation. We report our first experience of ABO-incompatible adult-to-adult living donor liver transplantation(ABOi LDLT) in a single center.

Methods: A 58-year-old male patient with blood type A and alcoholic liver cirrhosis underwent ABOi LDLT on October 10, 2024. Two months prior to the liver transplantation, the recipient underwent a Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedure to control bleeding from esophageal varices. Following TIPS, the patient developed hepatic encephalopathy. His Model for End-Stage Liver Disease(MELD) score was 10 points. For this ABO-incompatible (ABOi) recipients, the desensitization protocol to overcome the ABO blood group barrier included administering rituximab (RTX) once at a dosage of 375 mg/m^2 of body surface area, three weeks prior to surgery. Additionally, plasma exchange (PE) was performed with the goal of reducing the antibody titer to less than 1:16 before the surgery.

Results: The liver graft was from a son of the recipient, 30 years old, who weighed 61kg, was 1.76 meters tall, and had a blood type of AB. The graft type was modified right lobe, which

weighed 640g, and the Graft-to-Recipient weight ratio(GRWR) was 0.74. This donor was discharged at postoperative 7th days without any complication. The recipient transferred from intensive care unit(ICU) to general ward at postoperative 7th days and discharged at 28th days.

Conclusions: ABOi LDLT may be considered as a treatment option for patients with liver failure when their condition is expected to worsen while waiting for deceased donor liver transplantation.

Keywords: ABO-Incompatible, Liver Transplantation, Living Donor

PE-24

Analysis of the Results of Surgical Treatment of Benign Liver Tumors

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Aims: To analyze the results of surgical treatment of patients with benign liver tumors (BLT).

Methods: The results of surgical treatment of 70 patients with DOP, operated on over the past 15 years, were analyzed. There were 35 men and 35 women. Echinococcal liver cyst (ELC) was present in 41 patients, liver hemangioma (HL) - in 7, non-parasitic cysts (NPC) - in 13, liver abscesses (LA) - in 9.

Results: Cavernous HL were present in 71.4% cases, capillary - in 28.6%. The HL diameter varied from 2.5 to 12.5 cm, the volume - from 4.0 cm^3 to 976 cm^3. Liver resections were performed in all cases. NC (n=13) and LA (n=9) were eliminated by ultrasound-guided interventions. In our observations, laparoscopy was used (n=2) after all non-invasive research methods were performed for the differential diagnosis of hemangioma and its complications from malignant liver neoplasms. The most common type of liver resection in ELC were atypical resections of the right and left lobes of the liver. Right-sided (n=5) and left-sided hemihepatectomies (n=3), which were performed in 16.7% of cases and were considered primarily when the entire lobe was covered by the BLT. The need to perform resection of up to 3 liver segments was caused by the spread of HL (n=2) and ELC (n=5) beyond the limit of 3. Postoperative complications were observed in 14.3% of patients, and postoperative mortality was 4.3%.

Conclusions: According to indications, resection and minimally invasive interventions under ultrasound control are considered the methods of choice for BLT.

Keywords: Benign Liver Tumors, Echinococcal Liver Cyst, Liver Hemangioma

15. Liver Transplantation

PE-1

Two Cases of Living Donor Liver Transplantation for Colorectal Liver Metastases in Korea

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Aims: Colorectal cancer (CRC) with liver metastases (CRLM) poses a significant challenge, with many patients ineligible for resection due to unresectable or recurrent disease. Liver transplantation (LT) has emerged as a potential curative option for select CRLM cases. This study evaluates the feasibility and outcomes of living donor liver transplantation (LDLT) in two complex CRC patients with liver metastases.

Methods: We report two cases of LDLT performed in 2023 at Samsung Medical Center, Seoul, Korea. Patient 1, a 56-year-old male with a 16-year history of CRLM, underwent multiple interventions (radiofrequency ablation, pulmonary resections, proton beam therapy) before LDLT with a right lobe graft from his spouse. Patient 2, a 49-year-old male with CRLM received a left lobe graft from a friend after chemotherapy and rectal resection. Pre-transplant assessments, donor evaluations, and surgical details were analyzed, with outcomes tracked post-transplantation.

Results: Both patients underwent successful LDLT with no immediate complications. Patient 1's procedure (May 30, 2023) used an 808 mL right lobe graft (381-minute surgery, 29-day hospitalization). Patient 2's procedure (August 22, 2023) used a 542 mL left lobe graft (304-minute surgery, 14-day hospitalization). Donors (55-year-old female, 49-year-old male) recovered uneventfully, discharged after 7–8 days. Pre-transplant tumor burden was controlled, and post-operative imaging showed no early recurrence. Long-term survival data are pending ongoing follow-up.

Conclusions: LDLT is a viable and promising option for carefully selected CRLM patients with complex histories, offering potential long-term disease control. These cases highlight the importance of meticulous patient/donor selection and post-transplant monitoring. Further research is needed to refine criteria and establish standardized guidelines for LDLT in CRLM.

Keywords: Patient Selection, Donor Selection, Living Donors, Colon Cancer, Rectal Cancer

Table 1. Demographic and surgical details of case 1 and 2

Detail	Case 1	Case 2
Patient detail		
Diagnosis	CRLM	CRLM
Progress	Cirrhosis	Cirrhosis
Sex	Male	Male
Age (yr)	56	49
Height (cm)	173.0	172.0
Weight (kg)	82.6	62.0
BMI (kg/m^2)	27.6	21.0
Donor detail		
Sex	Female	Male
Age (yr)	55	49
Height (cm)	162.5	175.0
Weight (kg)	68.6	82.2
BMI (kg/m^2)	26.0	26.8
Surgery detail		
Whole liver (mL)	1,205	1,492
GRWR	0.94	1.53
Graft type	Rt. lobe	Lt. lobe
Warm ischemia time (sec)	370	350
Cold ischemia time (min)	97	50

CRLM, colorectal liver metastasis; BMI, body mass index; GRWR, graft-to-recipient weight ratio; Rt, right; Lt, left.

PE-2

Application of Machine Learning Algorithm in Diagnosing Post-Operative Complications in Hepatitis C Patients after Liver Transplantation

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Aims: One of the efforts to treat hepatitis C is liver transplantation. However, traditionally, the risk after liver transplantation is very high. So, to minimize the risk of complications, currently there is technological assistance through machine learning in detecting complications in hepatitis C patients after liver transplantation. This study aims to analyze the role of machine learning algorithms in diagnosing risk factors for post-operative complications in hepatitis C patients after liver transplantation.

Methods: The method used is a systematic literature review. Data sourced from Pubmed, Scopus, CoSciTeh, aeXiv. The keywords used are hepatitis c, liver transplantation, machine learning. After filtering the data through the PRISMA stage, 10 journals were analyzed.

Results: The results show that the models used in the journal, including random forest, decision tree, deep learning transformer, gradient boosting, Support Vector Machine (SVM). The indicators of risk factor diagnosis variables include age, gender, comorbid conditions, donor type, liver function, biochemical markers, medical history, early postoperative data, waiting time, body weight, bilirubin levels, hepatitis genotype, and liver biochemical data. Machine learning models generally provide high accuracy, which is above 86% in determining risk factors for complications in hepatitis C patients.

Conclusions: So, the machine learning model is very good because it can receive faster treatment and prevent complications after liver transplantation in hepatitis C patients. This analysis contributes to the development of liver disease diagnostic and therapeutic technology, providing a better understanding of risk factors and support for clinical decision making, more accurate predictions and reducing treatment costs.

Keywords: Hepatitis C, Transplantation Liver, Machine Learning

PE-3

MALS (Median Arcuate Ligament Syndrome) associated HAT after LDLT; Successful Treatment by Interventional Balloon Dilatation of Anastomosis and Stent Placement at Celiac Artery

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Aims: The median arcuate ligament is the fibrous arch that unites the diaphragmatic crura forming the anterior arc of the aortic hiatus. In some, the ligament is positioned more inferiorly relative to the celiac trunk, resulting in compression. This median arcuate ligament syndrome (MALS) can induce hepatic artery thrombosis (HAT) after liver transplantation (LT).

The authors experienced a case of MALS-associated HAT after living donor liver transplantation (LDLT) that was successfully treated by interventional thrombectomy, balloon dilatation of anastomosis and stent placement at celiac artery.

Methods: A 60 years old male patient underwent LDLT with a modified right liver graft for single hepatocellular carcinoma of 5.5cm in size. Donor was his daughter. GRWR was 1.0. Donor right hepatic artery was 2 mm in diameter and was anastomosed to recipient right anterior hepatic artery (2 mm in diameter) under microscope. Immediate postop AST/ALT was 220/241 IU/L. On Doppler US at postoperative 1 day, hepatic artery (HA) signal could be detected with RI > 0.5. But AST/ALT level rose to 772/844 IU/L next day. On dynamic CT intrahepatic arterial blood flow was barely visible. HAT was suspected. And MALS was identified, which was not noticed before surgery (Fig 1)

Results: Angiography was done. The flow of the gastroduodenal artery (GDA) – common hepatic artery (CHA) is reversed, filling the celiac trunk and splenic artery from the GDA, indicating an obstruction of the celiac trunk orifice. After selecting the

obstruction site of the celiac trunk with a guide wire, the obstruction site was dilated with a 6 mm diameter balloon, after which a 6Fr stent was installed. Thrombotic occlusion of CHA to the level of the arterial anastomosis was identified. After inducing thrombolysis by infusing 1 mg of tPA through a microcatheter, residual adherent thrombi were removed with a balloon and suction. Subsequently, angioplasty was performed on the HA anastomosis stricture site with a balloon (diameter 2 mm). Finally, the angiogram showed that the HA anastomosis was patent and not stenotic. HA blood flow to the liver graft was significantly improved. On CT scan checked 2 days later, HA blood flow was well maintained with good hepatic parenchymal enhancement (Fig 1). AST/ALT level was 90/215 IU/L.

Conclusions: Early identification of MALS-associated HAT after LDLT could be treated successfully by interventional thrombectomy, balloon dilatation of artery anastomosis site and stent placement at celiac artery.

Keywords: Liver Transplantation, Hepatic Artery Thrombosis, Median Arcuate Ligament Syndrome, Living Donor Liver Transplantation

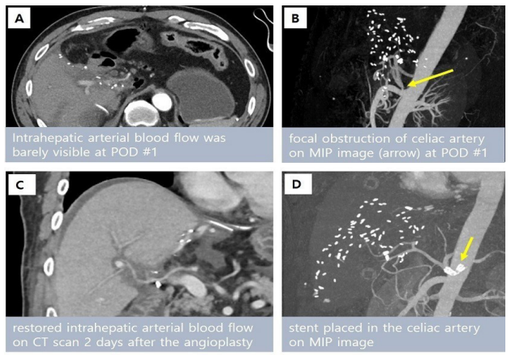

Fig 1. A&B. CT and angiography at POD#1, before interventional hepatic artery thrombectomy and stent placement at celiac artery. C&D. CT and angiography at POD#3, after angioplasty.

PE-4

Significance of Clinical Laboratory Evaluations in Post-Liver Transplant Recipients: The Impact on Management Strategies

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Aims: Over the past few decades, liver transplantation (LT) has markedly enhanced survival rates and outcomes. Effective surgical results for patients are heavily reliant on consistent laboratory evaluations and precise monitoring of blood biochemistry. Thus, the management of these patients depends on the thorough investigation of specific clinical and biochemical parameters.

Methods: We conducted a study on 12 post-operative liver transplant recipients over 2 year period. We monitored a range of parameters including clinical parameters (hematocrit, hemoglobin, mean corpuscular volume, white blood cell count, platelet count, prothrombin time, and international normalized ratio); biochemical markers (urea, creatinine, sodium, potassium, magnesium, calcium, phosphate, glucose, amylase, and C-reactive protein); and liver function tests (alanine transaminase [ALT], aspartate aminotransferase, alkaline phosphatase, albumin, common bilirubin, gamma-glutamyl transpeptidase, and bilirubin drainage). Venous blood samples were analyzed, and data were processed using statistical software. Statistical significance was determined with a threshold of $P<0.05$.

Results: Our study evaluated clinical parameters, biochemical markers, and liver function tests in post-liver transplant recipients. Significant changes were observed in hematocrit, hemoglobin, platelet count, prothrombin time, and international normalized ratio ($P<0.05$). Biochemical markers, including creatinine, sodium, potassium, phosphate, glucose, amylase, and C-reactive protein, also showed significant variations ($P<0.05$). Conversely, urea, magnesium, and calcium indicated trends without statistical significance. Liver function tests revealed significant changes in alanine transaminase, aspartate aminotransferase, alkaline phosphatase, albumin, common bilirubin, and gamma-glutamyl transpeptidase ($P<0.05$), with bilirubin drainage at the threshold of significance ($P=0.05$). These results underscore the need for comprehensive monitoring of these parameters to enhance postoperative care and address complications effectively.

Conclusions: Comprehensive laboratory monitoring in post-LT patients is crucial for early detection of complications and informed clinical decision-making, ultimately improving patient outcomes and postoperative care strategies.

Keywords: Clinical Laboratory, Post-Liver Transplant Recipients

PE-5

Liver Regeneration and Organoid Technology: Engineering Functional Hepatocytes for Transplantation and Drug Discovery

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Aims: Liver transplantation remains the only curative option for end-stage liver disease, but organ shortages and immunological challenges limit its accessibility. Liver organoid technology has emerged as a groundbreaking approach to generate functional hepatocytes for transplantation, disease modeling, and drug screening. This review explores advancements in stem cell-derived liver organoids, bioprinting strategies, and their translational potential in hepatology.

Methods: A systematic review of studies on induced pluripotent stem cell (iPSC)-derived hepatic organoids, biomaterial scaffolds, and 3D bioprinting approaches was conducted. The efficacy of organoid-derived hepatocytes in liver regeneration, fibrosis modeling, and high-throughput drug toxicity screening was analyzed.

Results: **Liver Organoids as Functional Hepatic Units:**

iPSC-derived hepatocyte-like cells (HLCs) self-organize into 3D liver organoids, exhibiting bile acid secretion, albumin production, and cytochrome P450 activity.

Co-culture systems incorporating Kupffer cells, stellate cells, and endothelial cells enhance organoid maturation and disease modeling capabilities.

Organoids in Liver Regeneration and Transplantation:

Organoid-based liver patches restore hepatic function in animal models of acute liver failure.

CRISPR-edited patient-derived liver organoids offer autologous transplant potential without immune rejection.

Organoids for Drug Discovery and Toxicology:

Liver organoids recapitulate idiosyncratic drug-induced liver injury (DILI), enabling personalized drug safety screening.

High-throughput organoid-on-a-chip systems provide predictive models for hepatotoxicity screening and regenerative medicine applications.

Conclusions: Liver organoid technology is revolutionizing hepatology, offering a scalable and patient-specific solution for transplantation, drug testing, and disease modeling. Future research should focus on enhancing organoid vascularization, optimizing CRISPR-based genetic corrections, and integrating AI-driven bioengineering approaches to accelerate clinical translation.

Keywords: Liver Regeneration, Organoids

PE-6

A Successful Case of Coordination of Brain-Dead Donor with The Highest Number of Organ and Tissue Transplantation in Vietnam: Case Report and Review of the Literature

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Aims: The demand for organ transplantation is immense, and multi-organ donation from brain-dead or cardiac death donors is a global trend, particularly in Europe and America. National Organ Procurement Organizations play a crucial role in managing and maximizing the utilization of donated organs. This report presents a successful case of multi-organ donation and transplantation at the 108 Military Central Hospital, involving the procurement and transplantation of seven organs: one liver, two kidneys, one pancreas, one heart, two upper limbs, and two corneas. Additionally, the lungs were coordinated for transplantation at the National Lung Hospital by the National Organ Procurement Organization.

Methods: This is a retrospective clinical case report of a brain-dead organ donor who donated the most organs in Vietnam to date, according to current statistics, with a total of eight organs: one liver, two kidneys, one pancreas, one heart, one lung, two upper limbs, and two corneas in January 2024.

Results: The multi-organ donor was a 26-year-old male, treated at the Department of Surgical Intensive Care and Organ Transplantation at the 108 Military Central Hospital. To date, all organ recipients have shown good progress.

Conclusions: The successful case of multi-organ donation and transplantation from a brain-dead donor, with a record number of transplanted organs coordinated by the National Organ Procurement Organization, demonstrates the effectiveness of organ donation and transplantation coordination in Vietnam, as well as the capability to master transplantation techniques.

Keywords: Organ and Tissue Transplantation, Brain Dead Donor

PE-7

Leveraging Machine Learning Algorithms for Prognosis Stratification in Salvage Liver Transplantation

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Aims: Salvage liver transplantation (SLT) is a crucial treatment option for patients with recurrent hepatocellular carcinoma (HCC) following primary liver resection. The complexity of clinical, pathological, and treatment-related factors makes prognosis classification in SLT particularly challenging. However, recent advancements in machine learning (ML) have introduced promising methods for improving prognostic accuracy and facilitating personalized treatment approaches.

Methods: A comprehensive literature review was conducted by searching PubMed, EBSCO, and Scopus for studies published between 2013 and 2023. Studies that employed ML algorithms to predict outcomes in SLT patients were included. Data were extracted on ML model types, input variables, prediction accuracy, and clinical utility. The QUADAS-2 tool was used to assess the potential risk of bias.

Results: Thirteen studies utilizing ML models, including Random Forest, Support Vector Machines, and Neural Networks, met the inclusion criteria. Common predictive variables included patient demographics, liver function tests, and tumor recurrence. The models demonstrated strong accuracy, with AUC values ranging from 0.80 to 0.95. These findings suggest that ML-based prognosis classification can significantly improve patient selection for SLT and enable personalized post-operative care, leading to better survival outcomes.

Conclusions: ML algorithms hold significant promise for enhancing prognosis stratification in SLT, offering superior predictive accuracy compared to traditional methods. Integrating ML into clinical practice could improve patient outcomes by enabling more informed decision-making in SLT. However, further research is needed to validate these findings across diverse clinical settings and patient populations.

Keywords: Prognosis, Stratification, Salvage Liver Transplantation, Machine Learning

PE-8

Outcomes and Complications of Living Donor Liver Transplantation in Pediatric Patients

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Aims: Living Donor Liver Transplantation (LDLT) is a critical therapeutic option for pediatric patients with end-stage liver failure. Despite its potential benefits, LDLT presents various technical, immunological, and psychosocial challenges. This study aims to evaluate the outcomes and complications of LDLT in pediatric patients.

Methods: A systematic review was conducted following Cochrane guidelines. Relevant literature was retrieved from PubMed, ScienceDirect, DOAJ, NLM, and Epistemonikos. Studies reporting survival rates, postoperative complications, and quality-of-life assessments in pediatric LDLT recipients were included.

Results: LDLT in pediatric patients demonstrates favorable long-term outcomes, with survival rates of 90% at five years and 75% at twenty years. However, early postoperative complications, including infections, graft rejection, and bleeding, remain significant challenges. Biliary leakage is a common cause of early relaparotomy. Despite these complications, the quality of life for both patients and their families improves over time, although psychosocial burdens persist. Advances in surgical techniques, preoperative planning, and donor evaluations continue to enhance the safety and success of LDLT.

Conclusions: LDLT in pediatric patients yields satisfactory survival outcomes. However, comprehensive postoperative management and psychosocial support are essential to reduce complications and enhance overall patient and family well-being. Continued innovations in surgical approaches and donor selection criteria will further optimize the procedure's success.

Keywords: Living Donor Liver Transplantation, Pediatric Transplantation, Survival Outcomes, Postoperative Complications

PE-9

Global Research Trends in Pediatric Living Donor Liver Transplantation

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Aims: Living donor liver transplantation (LDLT) has become a crucial alternative to deceased donor transplantation for children with end-stage liver disease. Despite the rapid growth of research in this field, a comprehensive understanding of global trends, key contributors, and dominant themes remains limited. This study aims to conduct a bibliometric analysis to identify research trends, influential contributors, and collaboration patterns in pediatric LDLT.

Methods: A systematic search was conducted in Scopus and PubMed for articles published between 2014 and 2024. Studies related to pediatric LDLT were selected based on relevance. Extracted data included publication year, authors, institutions, journals, countries, keywords, and citations. Bibliometric analysis was performed using VOSviewer and Biblioshiny to assess publication trends, co-authorship networks, and keyword clusters.

Results: The number of publications on pediatric LDLT has significantly increased over the past decade. Key research themes include surgical techniques, post-transplant complications, and long-term outcomes. The United States, Japan, India, and several European countries have been major contributors, with institutions such as the National Center for Child Health and Development in Tokyo playing a central role. Keyword analysis highlights a growing interest in immunosuppression, graft survival, and ethical issues related to living donation. Additionally, international collaborations, particularly between institutions in Asia and the Americas, have expanded significantly.

Conclusions: This bibliometric analysis highlights the rapid growth and evolving focus of pediatric LDLT research. The findings emphasize the importance of international collaboration and the contributions of leading institutions in advancing this field. Further studies are needed to address challenges related to graft rejection, long-term quality of life, and ethical considerations in living donor transplantation.

Keywords: Bibliometric Analysis, Living Donor Liver Transplantation, Pediatric Transplantation

PE-10

Blockchain-Enhanced Liver Transplantation: A Paradigm Shift in Ethical Allocation, Data Security, and Transplant Logistics

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Aims: Liver transplantation faces persistent challenges related to organ allocation inefficiencies, data security breaches, and ethical concerns surrounding donor-recipient matching. Blockchain technology, characterized by decentralized ledger mechanisms, cryptographic security, and immutable record-keeping, presents a transformative solution. This systematic review evaluates the integration of blockchain in liver transplantation, emphasizing its potential in optimizing organ distribution, enhancing transparency, mitigating fraudulent practices, and ensuring regulatory compliance.

Methods: A systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive search of PubMed, IEEE Xplore, Scopus, and Web of Science was performed using the keywords blockchain, organ transplantation, liver transplant logistics, decentralized data governance, and ethical allocation systems. Peer-reviewed studies, institutional white papers, and clinical trial registries were screened for eligibility. Studies analyzing blockchain frameworks in transplant logistics, smart contract applications in healthcare, and security challenges in medical data integration were included. Reference lists of selected studies were manually examined to identify additional relevant sources.

Results: The review synthesizes data from 47 high-impact studies, revealing that blockchain-based systems can significantly enhance transparency in liver transplantation by establishing tamper-proof donor-recipient matching protocols. Smart contracts facilitate automated enforcement of allocation policies, reducing human bias and bureaucratic inefficiencies. Furthermore, blockchain ensures real-time interoperability among transplant centers, minimizing organ wastage due to logistical delays. Ethical concerns, such as inequitable access and black-market organ trade, can be mitigated through transparent, permissioned blockchains integrated with biometric verification. However, limitations include the scalability of blockchain networks in handling large-scale transplant data, the computational burden of cryptographic validation, and unresolved regulatory frameworks.

Conclusions: Blockchain technology offers an unprecedented opportunity to revolutionize liver transplantation by improving organ allocation fairness, fortifying ethical oversight, and strengthening cybersecurity in transplant registries. Despite its promise, full-scale clinical adoption requires cross-disciplinary collaboration, regulatory harmonization, and the integration of artificial intelligence-driven predictive analytics to refine organ distribution models. Future research should focus on developing hybrid blockchain architectures that balance decentralization with regulatory oversight to ensure the seamless, secure, and ethical transformation of liver transplantation.

Keywords: Organ Trade, Bureaucratic Inefficiencies, Blockchain Technology, Hybrid Blockchain

PE-11

Post-Liver Transplantation Depression and Anxiety: Prevalence and Risk Factors

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Aims: Liver transplantation (LT) is a life-saving intervention, yet post-transplant psychiatric complications remain underrecognized. This review aims to evaluate the prevalence, risk factors, and pathophysiological basis of depression and anxiety in LT recipients, highlighting the impact on graft survival and long-term prognosis.

Methods: A systematic literature review was conducted using PubMed, Scopus, and Web of Science, focusing on studies assessing psychiatric outcomes in adult LT recipients. Inclusion criteria encompassed cohort studies, meta-analyses, and clinical trials analyzing depression, anxiety, and cognitive dysfunction post-transplantation.

Results: **Prevalence & Onset:** Post-transplant depression (PTD) affects up to 40% of LT recipients, while anxiety disorders range from 20-35%. Symptoms often emerge within the first six months post-transplant, with a second peak after 3–5 years.

Pathophysiology: Neuroinflammatory changes from chronic immunosuppression (calcineurin inhibitors, corticosteroids) alter neurotransmitter regulation, increasing susceptibility to mood disorders. Dysregulated HPA axis function further exacerbates psychiatric vulnerability.

Psychosocial & Biological Risk Factors: History of psychiatric illness, pre-transplant hepatic encephalopathy, social isolation, financial burden, and poor coping mechanisms significantly elevate depression and anxiety risk. Additionally, IL-6 and TNF-α elevations post-transplant correlate with neuroinflammatory-driven mood disturbances.

Impact on Graft & Patient Survival: PTD is associated with increased graft rejection due to medication non-adherence,

while severe anxiety leads to autonomic dysregulation, affecting long-term transplant outcomes.

Conclusions: Depression and anxiety significantly impair post-LT recovery, yet psychiatric screening remains inadequate. A multidisciplinary approach integrating hepatology and psychiatry is essential to improve patient outcomes. Future research should focus on neuroimmune mechanisms and targeted interventions to mitigate psychiatric morbidity post-transplantation.

Keywords: Post-Liver Transplantation Depression, Post-Liver Transplantation Anxiety

PE-12

Extended Indications for Robotic Donor Right Hepatectomy: Risk Factor Analysis and Surgical Step-Based Recommendations

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Aims: Robot donor right hepatectomy (RDRH) is an emerging surgical procedure that a growing number of groups have increasingly reported. This study aims to evaluate extended donor anatomical criteria at each surgical step to enhance safety and improve outcomes.

Methods: From March 2016 to December 2021, 97 RDRH donors were performed, with operative times recorded for each surgical step. After excluding 17 cases conducted before overcoming the learning curve, 80 cases were included in the analysis. Surgical steps, including liver mobilization, hilar dissection, parenchymal transection, and warm ischemic time, were evaluated using multivariate logistic regression to identify risk factors, such as anatomical variations and graft size, contributing to longer operative times.

Results: The presence of multiple right inferior hepatic veins(RIHVs) was identified as a significant risk factor for prolonged mobilization time. Bile duct variations and BMI ≥ 23 were determined to be risk factors for prolonged hilar dissection times, while a total liver volume ≥ 1200 mL was a significant risk factor for longer parenchymal transection time. Warm ischemic time was significantly prolonged in donors with multiple RIHVs or portal vein(PV) variation. Overall, the presence of PV variations was identified as a key risk factor for longer total operative times until graft retrieval.

Conclusions: In RDRH, each anatomical variation and large graft size increase the complexity of surgical steps. PV variations and multiple RIHVs, which prolong warm ischemic time, require caution to preserve graft quality and careful consideration for extended indications. Beginners should comprehensively assess these risk factors to ensure safe donor selection.

Keywords: Robot Donor Hepatectomy, Anatomic Variation, Extended Criteria

PE-13

Identifying Risk Factors for Diffuse Intrahepatic Biliary Stricture in ABO-Incompatible Living Donor Liver Transplantation: An Analysis of 1,000 Cases

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Aims: Diffuse intrahepatic biliary stricture (DIHBS) is a critical and refractory complication of antibody-mediated rejection (AMR) following ABO-incompatible living donor liver transplantation (LDLT). This study aims to assess the clinical outcomes of DIHBS in AMR patients and identify key risk factors associated with its development in a cohort of 1,000 ABO-incompatible LDLT recipients.

Methods: We retrospectively reviewed the medical records of 1042 patients undergoing ABO-incompatible LDLT between November 2008 and June 2024 performed at a single institution in Korea.

Results: DIHBS occurred in 52 out of 1,042 ABO-incompatible LDLT recipients, resulting in an incidence rate of 4.99%. DIHBS was associated with significantly lower overall survival and graft survival in recipients compared to those without DIHBS (P=0.001 for both). Multivariable analysis revealed that recipient blood type O (odds ratio [OR]: 3.691, 95% confidence interval [CI]: 1.439-9.469; P=0.007), the number of preoperative plasma exchanges (OR: 1.118, 95% CI: 1.021-1.235; P=0.028) and postoperative plasma exchanges (OR: 1.066, 95% CI: 1.011-1.123; P=0.018), and a diagnosis of rejection on biopsy were independent risk factors for DIHBS. Additionally, elevated peak anti-ABO antibody titers within the first month post-transplantation were strongly predictive of DIHBS, with titers ≥ 1:1024 (OR: 17.312, 95% CI: 2.824-88.687; P=0.002) showing the highest risk.

Conclusions: The Rituximab-based desensitization protocol for ABO-incompatible LDLT demonstrated feasibility with acceptable DIHBS outcomes. However, due to the significant impact of DIHBS on survival, especially in high-risk patients, tailored desensitization protocols and vigilant management are crucial to improving outcomes.

PE-14

Artificial Intelligence in Predicting Liver Transplant Graft Rejection

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Aims: Graft rejection remains a significant challenge in liver transplantation. Artificial intelligence (AI) offers the ability to analyze large datasets to predict rejection risks.

Methods: A machine learning algorithm was trained on clinical, genomic, and biochemical data from 5,000 liver transplant recipients. External validation was performed using 1,000 patients from three transplant centers.

Results: The AI model achieved 93% sensitivity and 90% specificity in predicting acute rejection within the first year post-transplant. Integration into clinical workflows reduced rejection episodes by 25%.

Conclusions: AI-driven prediction models have the potential to revolutionize post-transplant care, improving graft survival and patient outcomes.

Keywords: Artificial Intelligence, Graft Rejection, Transplant

PE-15

Gut-Liver Axis: The Role of Probiotics in Accelerating Recovery after Liver Surgery

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Aims: Postoperative liver dysfunction often delays recovery after surgery. Modulating the gut-liver axis with probiotics may enhance recovery.

Methods: A randomized trial involving 150 patients undergoing liver resection evaluated the impact of a probiotic regimen on postoperative liver function and complications.

Results: Probiotic-treated patients had a 20% faster normalization of liver enzymes and a 15% reduction in complications compared to controls.

Conclusions: Probiotics offer a safe, non-invasive strategy to enhance recovery and reduce complications after liver surgery.

Keywords: Gut Liver Axis, Probiotics, Transplant

PE-16

Comprehensive Management and Liver Transplantation for Huge Hepatocellular Carcinoma with Main Portal Vein Tumor Thrombosis: A Five-Year Case Report

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Aims: The prognosis for huge hepatocellular carcinoma (HHCC) with portal vein tumor thrombosis (PVTT) is generally poor. However, this case highlights the potential benefits of aggressive, multidisciplinary treatment.

Methods: A 46-year-old male HBV carrier with an 11 cm HHCC and PVTT extending to the main portal vein (PV) presented with elevated AFP (76,430 ng/mL) and PIVKA-II (1,478 mAU/mL). He underwent right hemihepatectomy and PV thrombectomy, with postoperative pathology confirming a 12 cm HHCC with PVTT. The patient was discharged on postoperative day 13 without complications. Six months later, recurrent tumors were detected on follow-up imaging, leading to six transarterial chemoembolization (TACE) procedures and radiotherapy over the next 42 months. At 41 months post-surgery, the patient developed acute-on-chronic liver failure (MELD score: 40), requiring continuous renal replacement therapy and ventilator support. Due to worsening condition, he underwent emergency deceased donor liver transplantation (DDLT) with IVC anastomosis (Modified Piggyback technique), maximal PV resection, and duct-to-duct bile duct anastomosis

Results: Pathology after DDLT revealed two small viable HCCs (2.2 cm and 1.1 cm). Postoperative complications included minor bleeding, delirium, and pleural effusion, but the patient recovered and was discharged on day 42. One year later, recurrence necessitated further TACE procedures. After three additional TACEs, AFP and PIVKA-II levels normalized, and the patient remained stable.

Conclusions: This case underscores that aggressive surgical and medical interventions, including liver transplantation, can significantly extend survival in HHCC with PVTT.

Keywords: Huge Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis, Hepatectomy, Liver Transplantation

PE-17

Feasibility of Pure Laparoscopic Donor Right Hepatectomy Compared to Open Donor Right Hepatectomy: A Large Single-Center Cohort Study

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Aims: Donor and recipient morbidity have not been sufficiently reported in large-scale comparisons of pure laparoscopic donor right hepatectomy (PLDRH) and open donor right hepatectomy (ODRH). This study aimed to compare morbidity of living donors and recipients after PLDRH and ODRH.

Methods: This retrospective study reviewed 3348 donors who underwent PLDRH (n=329) and ODRH (n=3019) and their corresponding recipients (n=3348) between January 2014 and August 2023. Donor complications and recipient biliary complications within 90 days were evaluated before and after 1:3 propensity score mathcing (PSM). Multivariate logistic regression analyses identified significant risk factors for donor major and biliary complications, as well as recipient bile leakage and

biliary stricture.

Results: For donors, PLDRH had fewer overall complications than ODRH (0.9% vs. 3.7%, *P*=0.009), with no significant differences in major (Clavien-Dindo III/IV) complications (*P*=0.057) and biliary complications (*P*=0.067), despite the absence of biliary complications in PLDRH. However, PLDRH showed longer warm ischemic time and operation time, and higher peak aspartate aminotransferase and alanine aminotransferase levels compared to ODRH in donors (*P*<0.001). These results remained consistent after PSM. Recipient biliary complications were comparable between PLDRH and ODRH, both before (*P*=0.806) and after PSM (*P*=0.264). Multiple portal veins were significant donor risk foctor for major (*P*=0.022), and biliary complications (*P*=0.001). Separated multiple bile ducts were common significant recipient risk factor for bile leakage (*P*=0.007) and biliary stricture (*P*=0.022).

Conclusions: PLDRH could become the standard for donor right hepatectomy with careful consideration of portal and biliary variations for donor and recipient safety.

Keywords: Donor Right Hepatectomy, Laparoscopic, Open

PE-18

Liver Transplantation by a Single Surgeon

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Aims: Liver transplantation (LT) is typically performed by a highly skilled medical team with specialized training; however, the current shortage of physicians presents a practical challenge that must be addressed in resource-limited LT settings.

Methods: This analysis includes 14 LT cases performed April to October 2024, a single surgeon conducted all procedures for donors and recipients, supported by a minimal team of one coordinator, 1 physician assistant(RN), 4 surgical assistants(RN). Four recipients underwent deceased donor liver transplantation, with grafts sourced from hospitals in Pohang, Daegu, Daejeon, and Hwaseong. Ten recipients underwent living donor liver transplantation, six laparoscopically and four converted to open surgery due to intraoperative bleeding.

Results: The median age of recipients was 49.5 ± 11.8 years, donors were 33.14 ± 13.98 years. Primary recipient etiologies included two of hepatic malignancy, one Wilson's dz, and 11 liver cirrhosis or hepatic failure cases. The mean MELD score was 30 ± 8. Operative times averaged 267.2±100.9min for LDLT donors and 341±68.64min for recipients. Key surgical outcomes included cold ischemia time of 226.74±105.16min, warm ischemia time of 31.57±5.77min, and no cases of hepatic artery thrombosis or biliary complications. Recipient hospital stays from 3 to 4 weeks, with no mortality. All donors fully recovered without complications, with hospital stays of 7–14 days.

Conclusions: This study demonstrates that a liver transplantation program can achieve excellent outcomes with a small surgical team under the supervision of a single, highly skilled surgeon. These findings challenge the conventional perception that LT requires extensive manpower and resources, highlighting the potential for streamlined approaches in specialized settings.

Keywords: Liver Transplantation, Surgeon, Manpower

16. MASLD, Basic

PE-1

Researching the Role of the Advanced Biomarker Kallistatin in MASLD

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Aims: Cirrhosis of liver is a pathological condition characterized by diffuse fibrosis, severe disruption of intra hepatic arterial and venous flow, portal hypertension and finally liver failure. Liver fibrosis/cirrhosis is generally the end result of majority of chronic liver insults; major global health concern associated with a significant morbidity and mortality. It is 14thcommon cause of death globally.

In the present study, Kallistatin is the newly discovered protein biomarker candidate; known as kallikrein inhibitory protein belongs to serine proteinase inhibitor family, documented to play a vital role in screening, diagnosis and prognosis of cirrhosis of liver. This molecule of research interest needs further research among the population. It is also known to have inhibitory action on tissue kallikrein and a role in inhibiting inflammation, oxidative stress, angiogenesis and apoptotic reactions.

Methods: Blood samples were collected from MASLD (n=25) age and gender matched healthy subjects (n=25) from Department of Medicine and analysed in Department of Biochemistry, RDMC, Banda U.P, India. Serum was used to estimate Kallistatin, serum transaminases (Aspartate transaminase [AST] &Alanine Transaminase (ALT), γ -Glutamyl Transferase (γ -GT), Total protein, albumin, total bilirubin, uric acid, total antioxidant capacity and total oxidative stress.

Results: Hyperuricemia with significant reducation of kallistatin levels in MASLD patients compared to healthy subjects were observed. There was an increase in total oxidative stress with decreased antioxidant capacity in MASLD compared to healthy subjects. Serum levels of Kallistatin was positively correlated with activities of ALT, AST and γ -GT with concentration of Total Bilirubin, total oxidative stress. Negative correlation was observed between serum levels of uric acid, Kallistatin to serum levels of total protein, albumin and total antioxidant capacity.

Conclusions: Kallistatin expression decreased during disease progression and can serve as direct biomarkers of MASLD which needs to be validated in diverse population. Hyperuricemia with elevated liver enzymes activity lead to poor prognosis.

Keywords: Endothelial Dysfunction, Hyperuricemia, Kallistatin, Inflammatory CytokinES

Table 1: Statistical analysis of biochemical parameters (n=25 cases and controls)

Variables	Groups	Mean ± SD	p-Value
RBS (mg/dl)	I	100.10 ± 10.08	0.49
	II	102.12 ± 10.86	
Blood Urea (mg/dl)	I	30.19 ± 5.90	0.23
	II	35.10 ± 6.24	
Creatinine (mg/dl)	I	1.06 ± 0.20	0.47
	II	1.08 ±0.18	
Kallistatin (pg/ml)	I	4000.66 ± 550.40	0. 01*
	II	1680.54 ± 470.40	
Uric acid (mg/dl)	I	3.40 ± 0.30	0.01*
	II	6.50±0.60	

*p<0.05: significant; **Group II**: Clinically& diagnostically proven MASLD subjects; **Group I**: Healthy subjects; **SD**: Standard Deviation

Table 2: Statistical analysis of biochemical parameters (n=25 cases and controls)

Variables	Groups	Mean ± SD	p-Value
AST (U/L)	I	36.90 ± 12.40	0.01*
	II	220.90 ± 50.20	
ALT (U/L)	I	32.50 ± 12.20	0.01*
	II	280.78 ± 50.48	
ALP (U/L)	I	120.50 ± 20.30	0.01*
	II	340.70 ± 45.40	
γ-GT (U/L)	I	36.50 ± 12.00	0.01*
	II	280.00 ± 50.00	
Total Protein (g/dl)	I	6.00 ± 0.32	0.01*
	II	4.50 ± 0.50	
Albumin (g/dl)	I	3.50 ± 0.30	0.01*
	II	2.50 ± 0.40	
Total Bilirubin (mg/dl)	I	0.80 ± 0.20	0.01*
	II	5.60 ± 1.48	

*p<0.05: significant; **Group II**: Clinically& diagnostically proven MASLD subjects; **Group I**: Healthy subjects; **SD**: Standard Deviation; **AST**: Aspartate Transaminase; **ALT**: Alanine Transaminase; **ALP**: Alkaline Phosphatase; **γGT**: Gamma Glutamyl Transferase

Table 3: Statistical analysis of biochemical parameters (n=25 cases and controls)

Variables	Groups	Mean ± SD	p-Value
TAC (nmol/µL)	I	32.34 ± 6.00	0.01*
	II	22.70 ± 5.00	
TOS(µmol H_2O_2 Equiv/L)	I	12.12 ± 4.00	0.01*
	II	34.18 ± 5.98	

*p<0.05: significant; **Group II**: Clinically& diagnostically proven MASLD subjects; **Group I**: Healthy subjects; **SD**: Standard Deviation; **TAC**: Total Anti-oxidant Capacity; **TOS**: Total Oxidative Status

PE-2

Thiazole-Naphthyl Derivatives as PPARγ/NRF2/COX-2 Modulators for Fibrosis Prevention in Metabolic Dysfunction-Associated Steatohepatitis: Molecular Docking and ADMET Profiling

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Aims: Metabolic dysfunction-associated steatohepatitis (MASH) is a leading cause of liver fibrosis, a key predictor of mortality and liver transplantation need. Despite its clinical burden, no approved antifibrotic therapies exist. Peroxisome proliferator-activated receptor (PPAR) agonists improve lipid metabolism and inflammation, while nuclear factor erythroid 2-related factor 2 (NRF2) activation combats oxidative stress. Cyclooxygenase-2 (COX-2) inhibitors further modulate inflammatory prostanoid signaling, reducing hepatic stellate cell activation. This study explores thiazole-naphthyl derivatives as potential PPAR/NRF2/COX-2 multi-target modulators with optimized pharmacokinetics and hepatocyte-targeted delivery for fibrosis prevention.

Methods: Molecular docking (AutoDock Vina) was performed to evaluate binding affinity of thiazole-naphthyl derivatives against PPARγ (PDB: 1FM9), NRF2-Keap1 (PDB: 5CGJ), and COX-2 (PDB: 5JW1). ADMET profiling (pkCSM) predicted hepatic metabolism, toxicity, and bioavailability. β-Cyclodextrin (β-CD) complexation modeling was conducted.

Results: Lead thiazole-naphthyl derivatives (HL1, HL2) exhibited strong multi-target binding to PPARγ (−9.4 to −11.6 kcal/mol), NRF2-Keap1 (−9.7 to −10.6 kcal/mol), and COX-2 (−9.2 to −10.3 kcal/mol), with HL2 showing the highest affinity. Despite moderate lipophilicity (Log *P*=5.12–5.23) and low water solubility (log mol/L = −4.686 to −5.396), β-cyclodextrin complexation predicted improving bioavailability. Pharmacokinetics predicted high intestinal absorption (~89%), moderate clearance (log ml/min/kg = 0.271–0.31), and low BBB permeability (log BB = −0.022 to 0.285), favoring hepatoselectivity. Both compounds were CYP1A2 inhibitors, indicating potential drug-drug interactions. Drug-likeness evaluation showed no Lipinski violations, a bioavailability score of 0.55, and moderate synthetic accessibility (3.37–3.49). Toxicity profiling predicted an oral LD50 of 2.311–2.401 mol/kg, suggesting an acceptable safety profile. These findings highlight PPARγ/NRF2/COX-2 modulation as a promising synergistic strategy for fibrosis prevention in MASH, offering a potential multi-target therapeutic approach to mitigate disease progression.

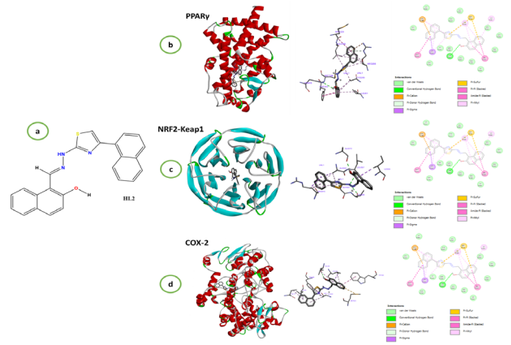

Figure 1. a) molecule structure of HL2 (thiazole-naphthyl derivative), 2D and 3D Molecular interaction between HL2 toward b) PPARγ, c) NRF2-Keap1, and d) COX-2.

Table 1. ADMET Profile.

GENERAL PROFILES		
Molecules/Pubchem ID	**HL1**	**HL2**
MW	375.45	395.48
Binding Affinity		
PPARγ (kcal/mol)	-9.4	-11.6
NRF2-Keap1 (kcal/mol)	-9.7	-10.6
COX-2 (kcal/mol)	-9.2	-10.3
LIPOPHILICITY		
Consensus Log P	5.12	5.23
WATER SOLUBILITY		
Log solubility (log mol/L)	-4.686	-5.396
PHARMACOKINETICS		
BBB Permeability (log BB)	-0.022	0.285
CYP1A2 inhibitor	yes	yes
Intestinal Absorption (Human) (% Absorbed)	89.085	89.139
Total Clearance (log ml/min/kg)	0.271	0.31
DRUGLIKENESS		
Lipinski #violations	0	0
Bioavailability Score	0.55	0.55
MEDICINAL CHEMISTRY		
Leadlikeness #violations	2	2
Synthetic Accessibility	3.37	3.49
TOXICITY		
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.311	2.401

Conclusions: Thiazole-naphthyl derivatives demonstrate strong multi-target receptor activation, bioavailability, and antifibrotic potential, offering a promising therapeutic strategy for MASH-related fibrosis. Future studies should focus on molecular dynamics simulations and experimental validation.

Keywords: Metabolic Dysfunction-Associated Steatohepatitis, Fibrosis Prevention, Thiazole-Naphthyl, Molecular Docking

PE-3

B Cell Activation to Produce Autoantibodies Are Promoted in the Spleen of MASH-Induced Mice Model

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Aims: Among the autoantibodies associated with autoimmune hepatitis (AIH), antinuclear antibodies (ANA) are frequently detected in MAFLD patients. Autoantibodies are immunoglobulins that react against normal host proteins, potentially exacerbating inflammation. In MASH, autoantibody responses may contribute to disease progression. Therefore, characterizing autoantibody-producing plasma cells in MASH could provide insights into disease mechanisms and help identify potential therapeutic targets. In this study, we investigated the characteristics of autoantibody-producing plasma cells in MASH.

Methods: We utilized a MASH mouse model induced by a fat, phosphate, and cholesterol (FPC) diet. Immunofluorescence staining was performed on spleen tissue to examine germinal centers and plasma cells. The IgG and IgM phenotypes of plasma cells were analyzed using flow cytometry. Additionally, plasma from MASH mice was assessed for antibody types and autoantibodies using ELISA and ELISpot assays. To investigate the role of splenic plasma cells in MASH progression, splenectomy was performed, followed by histological evaluation of liver injury and fibrosis markers.

Results: In the FPC diet-induced MASH mouse model, we observed an active germinal center reaction and a significant increase in plasma cell numbers within the spleen. Notably, the expanded plasma cell population was predominantly IgG- and IgM-positive. Consistently, plasma from both MASH mice and MASH patients exhibited elevated levels of IgG and IgM antibodies. Further analysis confirmed that these increased antibodies included autoantibodies, as evidenced by ANA detection. Interestingly, histological evaluation revealed a significant reduction in disease progression in splenectomized MASH mice fed the FPC diet Additionally, splenectomy reduced plasma ALT and AST levels in MASH mice. These findings suggest a potential link between splenic antibody production and MASH.

Conclusions: Our findings indicate that autoantibodies play a detrimental role in MASH progression and highlight the potential of targeting plasma cells involved in autoantibody production as a novel therapeutic strategy for MASH management.

Keywords: B Cell, Autoantibody, Inflammation, Splenectomy

PE-4

Trends in Metabolic Dysfunction-Associated Steatotic Liver Disease by Household Income, 2007-2022: A National Representative Study in South Korea

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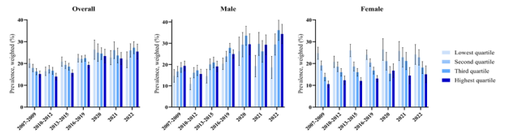
Aims: Metabolic dysfunction–associated steatotic liver disease (MASLD) could lead to liver-related life-threatening conditions. However, relatively little research has been conducted on trends in MASLD based on household income. This study aimed to examine trends in MASLD prevalence stratified by household income and identify socioeconomic factors associated with a risk of MASLD.

Methods: Data from the Korea National Health and Nutrition Examination Survey from 2007 to 2022 were analyzed to examine MASLD prevalence among adults in South Korea, stratified by household income levels. Weighted logistic regression analysis was conducted to assess the prevalence of MASLD for each variable across the four household income levels and to calculate weighted odds ratios along with the associated risk factors for MASLD.

Results: A total of 70,276 individuals aged ≥19 years (male: 29,169 [41.51%]) from 2007 to 2022 were included in the analysis. MASLD prevalence increased over the study period across all household income levels. Particularly, in the medium-high and high household income levels, prevalence increased from 16.30% (95% CI, 14.83-17.76) in 2007 to 27.25% (95% CI, 24.46-30.04) in 2022 and from 15.15% (95% CI, 13.71-16.58) in 2007 to 25.44% (95% CI, 22.01-28.86) in 2022, respectively. The prevalence of MASLD exhibited a sex-specific trend, being higher among low-income females while tending to be higher among high-income males. Sex, middle-aged individuals, high-stress levels, and smoking status were statistically significant risk factors for MASLD.

Conclusions: This is the first study to analyze the trends of MASLD stratified by household income level in South Korea. These findings indicate the necessity of nationwide campaigns and programs to promote healthy diets and lifestyles and enhance public awareness.

Keywords: Epidemiology, Household Income Level, Metabolic Dysfunction-Associated Steatotic Liver Disease, South Korea



PE-5

Palmitic Acid Reduces LDLR-Dependent Uptake of Macrophage-Derived Extracellular Vesicles by Hepatoma Cells

Bootsakorn Boonkaew[1,2], Nantawat Satthawiwat[1,2], Pisit Tangkijvanich[1,2], Chaiyaboot Ariyachet[1,2]

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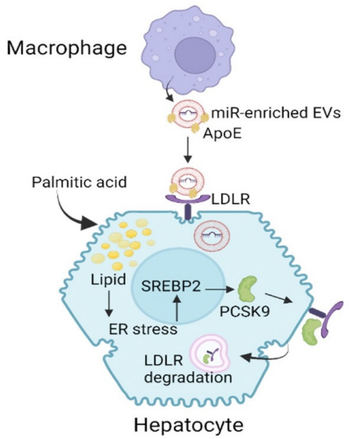
Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) involves complex interactions between lipotoxicity and inflammation, yet the mechanisms connecting these processes remain unclear. This study aims to investigate the uptake mechanisms of extracellular vesicles (EVs) derived from macrophages into palmitic acid (PA)-induced lipotoxic hepatoma cells.

Methods: Macrophages were co-cultured with PA-treated Huh7 cells using a transwell system to assess EV transfer efficiency. The levels of macrophage-derived microRNA-223 (miR-223) in Huh7 cells were measured after co-culture, along with the expression of miR-223 target genes. Low-density lipoprotein receptor (LDLR) expression and EV uptake activity in PA-treated Huh7 cells were analyzed. Gain- and loss-of-function experiments were conducted to evaluate the role of LDLR in EV uptake. Additionally, the effects of endoplasmic reticulum (ER) stress-induced proprotein convertase subtilisin/kexin type 9 (PCSK9)-mediated LDLR degradation and PCSK9 inhibition on EV uptake were examined. The role of apolipoprotein E (ApoE) in EV transfer was also investigated.

Results: PA-treated Huh7 cells exhibited reduced uptake of macrophage-derived EVs, resulting in decreased miR-223 levels and increased expression of miR-223 target genes. PA treatment also led to LDLR downregulation, which in turn impaired EV uptake. Gain- and loss-of-function studies confirmed the crucial role of LDLR in EV uptake. Mechanistically, PA induced ER stress, activated the ER-resident transcription factor sterol regulatory element-binding protein 2 (*SREBP2*), and subsequently stimulated PCSK9-mediated LDLR degradation. Administration of a PCSK9 inhibitor alirocumab rescued LDLR levels and increased EV uptake of PA-treated Huh7 cells from macrophages. Furthermore, macrophage-derived EVs lacking ApoE were less efficiently internalized by Huh7 cells, indicating the role of ApoE in facilitating EV transfer.

Conclusions: Overall, our study sheds light on the intricate mechanisms underlying EV-mediated communication between macrophages and Huh7 cells during lipotoxicity and provides insight toward the development of EV-based therapy for MASLD.

Keywords: Extracellular Vesicles, Metabolic Dysfunction-Associated Steatotic Liver Disease, Lipotoxicity, Inflammation, Low-Density Lipoprotein Receptor



PE-6

MASLD-Related Oral Microbes Were Associated with Obesogenic Metabolites and Clinical Parameters

In Young Kang[1], Seung Min Lee[1], Hye Young Kim[1], Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], Jin Kim[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: Previous studies have primarily focused on the role of the intestinal microbiome in metabolic dysfunction-associated steatotic liver disease (MASLD). While the impact of the gut microbiome is well-documented, the role of the oral microbiome in influencing the gut microbial environment and metabolic pathways has been unveiled. We aimed to investigate the association between the oral microbiome and its potential impacts on gut microbiomes, metabolites, and metabolic risk factors.

Methods: This study was conducted as a multicenter cross-sectional study involving 206 healthy individuals and 206 diagnosed with MASLD. The oral and stool microbiomes were analyzed using the V3–V4 hypervariable region of the 16S rRNA gene, following the Illumina 16S Metagenomic Sequencing Library Preparation protocol. Serum and stool metabolites were also analyzed using LC-MS.

Results: There was a lower diversity of oral microbiota and distinct microbial distributions in MASLD compared to controls. Notably, prevalence of oral Neisseria sp. 0031, Veillonella sp. 0011, and Streptococcus sp. 0009 were higher in MASLD compared to non-SLD. These oral microbiomes showed positive associations with body mass index, waist circumference, and adverse lipid profiles, alongside a correlation with elevated liver enzymes. Additionally, specific gut microbes like Weissella sp.001 and Tyzzerella sp. 001 were more abundant in MASLD. Interestingly oral Neisseria sp. 0031, Veillonella sp. 0011, and Streptococcus sp. 0009 showed positive correlation with intestinal Weissella sp.001 and Tyzzerella sp. 001. Presence of Streptococcus sp. 0009 in MASLD was associated with higher levels of lysophosphatidylcholines (15:0), (17:0) and negative correlation with correlation with N-(1-Deoxy-1-fructosyl) aline, succinylcarnitine in serum.

Conclusions: The oral microbiome, specifically Streptococcus sp. 0009, showed a positive correlation with intestinal microbiome, obethogenic metabolites as well as cardiometabolic parameters in patients with MASLD.

Keywords: MASLD, The Intestinal Microbiome, Streptococcus SP. 0009, Cardiometabolic Parameters

PE-7

11β-HSD1 Inhibition on Non-alcoholic Fatty Liver Disease: Investigating Immune Cell Dynamics via Single-Cell Mass Cytometry

Sun Mi Park[1], Hye Won Jang[1], Yoo Jeong Lee[1], In Young Kang[1], Seung Min Lee[1], Hye Young Kim[1], Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], Jin Kim[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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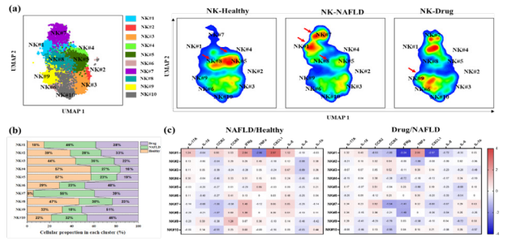
Aims: Metabolic dysfunction associated steatosis liver disease (MASLD) affecting one-fourth of the world's population. However, non-invasive diagnostic tools and effective drug treatments for patients with MASLD are still lacking. Systemic immune dysregulation, such as inflammation, plays a pivotal role in MASLD development, indicating the possibility of utilizing quantitative and phenotypic changes in the peripheral immune cells to diagnose and treat MASLD.

Methods: We compared the immune cell populations in samples of healthy patients and patients with MASLD using high-dimensional mass cytometry at the single-cell level. Using a multi-parametric mass cytometry approach, we analyzed peripheral blood mononuclear cells (PBMCs) from MASLD, healthy, and drug-treated groups. Isolated PBMCs were stained with 29 markers, and 15 cell types were identified.

Results: Comparison of manually gated immune cell percentages in total leukocytes revealed elevated frequencies of total $CD8^+$ T cells, early NK cells, and monocytes, and decreased T_H2, late NK, T_H1, and Treg cells in patients with MASLD. Automated clustering was used to identify subsets of NK and phagocytic cells. These subsets were further investigated for specific marker expression. We demonstrated that an 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor significantly downregulated inflammatory cytokines in late NK cells and pDCs, suggesting its potential therapeutic efficacy in MASLD treatment.

Conclusions: Our findings illuminate the complex immune landscape of MASLD and suggest that 11β-HSD1 inhibition may offer a novel therapeutic strategy. These insights contribute to our understanding of the immunological dimensions of MASLD and propose a targeted approach for future interventions.

Keywords: MASLD, 11 B -HSD1, NK Cells, PBMC



PE-8

Microbiome Analysis in MASLD and Obesity: Identifying a Beneficial Strain and Its Hepatoprotective Effects in a Western Diet Mouse Model

Moon Gyeong Yoon[1], Se Ha Jang[1,2], Geum Ok Baek[1], Hyun Sun Jung[1], Ji Eun Han[1], Jae Youn Cheong[1], Jung Woo Eun[1], Soon Sun Kim[1]

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Aims: The gut microbiome plays a crucial role in the pathogenesis of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), yet microbiome-based therapeutic strategies for MASLD in humans remain unclear. This study aimed to identify a gut microbiome composition associated with MASLD prevention or treatment in both obese and non-obese individuals and to validate its efficacy in animal model.

Methods: Gut microbiome profiling was performed using 16S rRNA sequencing on the fecal samples from healthy individuals and subjects with MAFLD, including both obese and non-obese individuals. A Western diet-induced MASLD mouse model was established using male C57BL/6 mice, which were divided into three groups: normal diet (ND), Western diet + PBS (WD), and Western diet + identified strain. The mice were administered their respective diets for 13 weeks. Serum biochemical analyses, liver histopathology, and gene expression studies were conducted to elucidate the hepatoprotective effects the identified strain.

Results: In the WD group, body weight, liver weight, fat content, and serum levels of AST and ALT were significantly increased compared to the ND group. However, these parameters were significantly reduced in the WD+identified strain group.

Histological analysis using H&E staining and Masson's trichrome staining revealed significantly increased NAS score and fibrosis stage in the WD group compared to the ND group, which were notably ameliorated in the WD+identified strain group. Additionally, gene expression levels of Farnesoid X receptor (*FXR*), Peroxisome proliferator-activated receptors (PPAR-α), and Intestinal fatty acid binding protein (I-FABP) were markedly decreased in the WD group compared to the ND group but significantly recovered in the WD+identified strain group.

Conclusions: These findings suggest that the identified gut microbial strain exerts hepatoprotective effects and mitigates MASLD progression, highlighting its potential for microbiome-targeted interventions in MASLD and obesity.

Keywords: Gut Microbiome, NAFLD, 16S RRNA Sequencing, Western Diet

PE-9

Lobeglitazone Alleviates Palmitic Acid-Induced Hepatic Steatosis by Enhancing Mitochondrial Function and Regulating Lipid Metabolism in HepG2 Cells

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Aims: Lobeglitazone, a thiazolidinedione oral antidiabetic agent, predominantly activates peroxisome proliferator-activated receptor γ to enhance insulin sensitivity. Recent studies suggested that lobeglitazone may also improve hepatic steatosis, but its precise mechanism remains unclear. In this study, we aimed to elucidate the mechanism by which lobeglitazone improves hepatic steatosis in HepG2 cells treated with palmitic acid (PA).

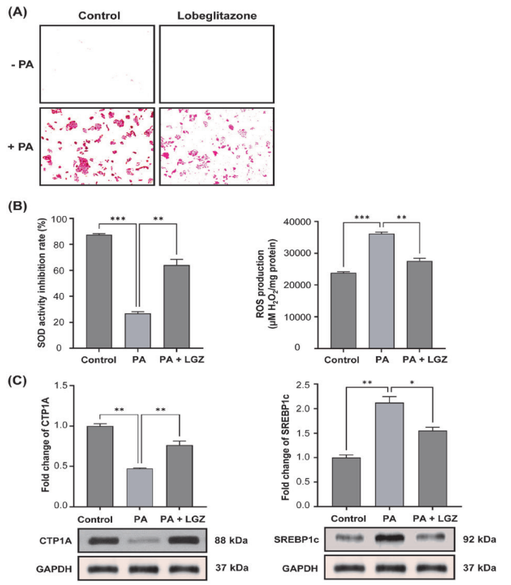
Methods: HepG2 cells were pretreated with 100 μM PA for 16 hours, followed by treatment with or without 70 μM lobeglitazone for an additional 18 hours. Hepatic lipid accumulation was assessed using oil Red O (ORO) staining, while the expression of mitochondrial function-related factors was analyzed through enzyme-linked immunosorbent assay (ELISA), real-time polymerase chain reaction, and Western blotting.

Results: Lobeglitazone significantly reduced hepatic lipid accumulation in PA-treated HepG cells, as shown by ORO staining (Figure 1A). ELISA showed an increase in superoxide dismutase levels and a decrease in reactive oxygen species production, suggesting an improvement in mitochondrial function. (Figure 1B). Additionally, lobeglitazone increased the expression of carnitine palmitoyltransferase 1A, which is involved in fatty acid oxidation. In contrast, the expression of sterol regulatory element-binding protein-1c, which is involved in hepatic lipogenesis, was decreased (Figure 1C).

Conclusions: Lobeglitazone restored mitochondrial function involved in fatty acid oxidation and reduced lipogenesis in HepG2 cells with palmitic acid-induced hepatic steatosis. Therefore, lobeglitazone could serve as a therapeutic agent

for improving metabolic dysfunction-associated steatotic liver disease.

Keywords: Fatty Liver, HEPG2, Thiazolidinedione, Lipid Metabolism



PE-10

AI-Driven Single-Cell Spatiotemporal Metabolic Trajectory Mapping Identifies Hepatic Fibrosis Onset in MASLD: A Transformer-Based Multi-Scale Predictive Framework

Rini Winarti[1], Sahnaz Vivinda Putri[2], Elfiany[3], Andi Nursanti[4], Prihantini Prihantini[5], Rifaldy Fajar[5]

[1]Department of Biology, Yogyakarta State University, Indonesia; [2]Health Management Laboratory, International University Semen Indonesia, Indonesia; [3]Computational Science Research Laboratory, BLK Muhammadiyah University, Indonesia; [4]Department of Pharmacy, Wallacea University, Indonesia; [5]Mathematical and Computational BioMedicine Research Group, The Integrated Mathematical, Computational, and Data Science for BioMedicine Research Community Foundation, Indonesia

Aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a leading cause of fibrosis-related liver failure, yet current diagnostic models lack the ability to resolve fibrosis-driving metabolic shifts at the single-cell level. This study develops an AI-based predictive model that reconstructs hepatic metabolic trajectories using spatiotemporal single-cell transcriptomics, lipidomics, and metabolic fluxomics, enabling early MASLD fibrosis risk stratification with enhanced accuracy.

Methods: We integrated multi-omics data from the Human Cell Atlas (single-cell transcriptomics of hepatocytes, Kupffer cells, and stellate cells), Metabolomics Workbench (spatial lipidomics profiling of liver tissue), the Human Metabolic Atlas (metabolic fluxomics), and longitudinal fibrosis progression data from UK Biobank and the HUNT Study. The model incorporates Spatiotemporal Contrastive Learning to extract lipidomic trajectory shifts, a Multi-Scale Graph Transformer for cross-cellular metabolic interactions, and a Longitudinal Variational Autoencoder for patient-specific fibrosis progression prediction. Model explainability was ensured using SHAP analysis to identify fibrosis-predictive metabolic markers.

Results: The model achieved an AUROC of 0.88 (95% CI: 0.86–0.90) for MASLD fibrosis prediction, with 82.5% sensitivity, 85.1% specificity, and 86.2% accuracy in detecting early-stage fibrosis. SHAP analysis identified *Lysophosphatidylcholine (LPC 16:0, LPC 18:1)* as fibrosis accelerators (HR: 3.92, $P<0.0001$) and *mitochondrial β-oxidation deficits* as fibrosis risk markers (HR: 2.87, $P=0.0003$). MASLD metabolic clustering revealed three fibrosis subtypes: Fibrosis Accelerators (28.3%), Lipid Dysregulated MASLD (35.2%), and Metabolically Stable MASLD (36.5%).

Conclusions: This AI-based metabolic trajectory mapping framework improves MASLD fibrosis prediction by integrating multi-omics data, identifying fibrosis-driving metabolic shifts, and enabling clinically relevant, patient-specific risk stratification for improved disease management.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Single-Cell Multi-Omics, Fibrosis Prediction, Spatiotemporal Metabolic Trajectory Mapping

PE-11

siRNA-Based Modulation of PCSK9 for the Treatment of Liver Metabolic Disorders: A Bioinformatics Study

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Aims: Hepatic cholesterol homeostasis is critical for liver function, and dysregulation contributes to metabolic liver diseases such as non-alcoholic fatty liver disease (NAFLD) and hypercholesterolemia. Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9), predominantly synthesized in hepatocytes, accelerates degradation of hepatic low-density lipoprotein receptors (LDLR), exacerbating circulating LDL-cholesterol (LDL-C) levels and liver lipid accumulation. This study aimed to design small interfering RNAs (siRNAs) targeting *PCSK9* as a novel therapeutic strategy to restore hepatic LDLR expression and ameliorate liver-related metabolic disorders.

Methods: Using bioinformatics tools, we systematically designed and evaluated siRNA candidates for their ability to silence *PCSK9* in hepatocytes. siPRED generated siRNA molecules and predicted their silencing efficacy, with a stringent inhibition threshold of ≥90%. Candidates were filtered using siRNA Scales to optimize specificity and minimize off-target effects. Further analyses included MaxExpect to evaluate siRNA folding free energy and DuplexFold to calculate binding free energy between the guide strand and *PCSK9* mRNA (NM_174936.4).

Results: Ten siRNA candidates were designed, all targeting regions of human *PCSK9*. Bioinformatics analyses identified these siRNAs as potent silencers of *PCSK9*, with a maximum predicted efficacy of 93.43%. indicated stable siRNA structures and strong guide strand-target interactions, critical for hepatic cellular uptake and activity. Furthermore, evaluations of siRNA structural stability (folding free energy) and guide strand-target interaction strength (binding free energy) demonstrated optimal thermodynamic properties.

Conclusions: In conclusion, these findings highlight the potential of siRNA-based *PCSK9* silencing to modulate hepatic cholesterol metabolism, offering a promising RNA therapeutic strategy for liver diseases driven by dyslipidemia. Future work will validate efficacy in hepatocyte models and *in vivo* systems to advance liver-targeted therapies for NAFLD and related metabolic disorders.

Keywords: PCSK9, SIRNA, Hepatic Cholesterol Metabolism, Non-Alcoholic Fatty Liver Disease (NAFLD)

PE-12

Targeting Lipid-Regulating Proteins with Bajakah-Derived Compounds, A Borneo-Native Plant: A Strategy for Managing Hyperlipidemia in MASLD

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Aims: Hyperlipidemia, a major driver of MASLD, involves dysregulated cholesterol and triglyceride metabolism, prompting the use of lipid-lowering agents like statins, though their long-term side effects necessitate alternatives. Bajakah (*Spatholobus littoralis* Hassk.), a Borneo-native plant, shows potential in inhibiting cholesterol synthesis. This study explores recent trends in hyperlipidemia-related MASLD and evaluates Bajakah's compounds for targeting lipid-regulating proteins, offering insights into natural therapeutic strategies for MASLD management.

Methods: A bibliometric analysis was conducted to examine the relationship between hyperlipidemia and MASLD using the Scopus database, focusing on publications from the past decade. Relevant keywords were employed to retrieve data, which were subsequently analyzed and visualized using VOSviewer. Additionally, through molecular docking simulations, 15 bioactive compounds from Bajakah were computationally evaluated for their binding affinity to key lipid-regulating proteins, including ACC, SREBP1c, DGAT, HMG-CoA reductase, and PCSK9.

Results: The bibliometric visualization suggests a strong relationship between Hyperlipidemia and hepatic steatosis (Figure-1A). The overlay visualization emphasize the older research focusing on lipid metabolism, cholesterol, and statins. Recent trends emphasize on gut microbiota and inflammatory pathways linking MASLD and non-statin lipid-lowering agents (Figure-1B). The heatmap displays the binding affinities of Bajakah compounds against key proteins involved in hyperlipidemia and MASLD (Figure-1D). Taxifolin (-9.5 kcal/mol) against DGAT, suggesting its role in reducing triglyceride synthesis, and 6-methoxyeriodictyol (-9.0 kcal/mol) against SREBP1, indicating an impact on fatty acid metabolism. Butin (-9.7 kcal/mol), Liquiritigenin (-9.5 kcal/mol), and Eriodictyol (-9.6 kcal/mol) inhibited PCSK9, suggesting enhanced LDL receptor recycling and lower cholesterol levels. Compared to simvastatin, these natural compounds demonstrate comparable or superior binding affinities, making them promising candidates for therapeutic intervention in hyperlipidemia and MASLD.

Conclusions: This study underscores the critical role of hyperlipidemia in MASLD pathogenesis and highlights the research trends shift. Bajakah compounds demonstrate comparable or superior efficacy to simvastatin, positioning them as promising natural alternatives for managing hyperlipidemia and MASLD

Keywords: MASLD, Hyperlipidemia, BAJAKAH, Bioinformatics

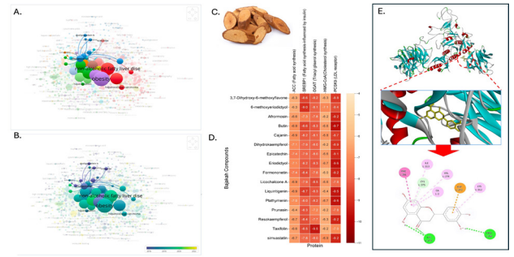

Figure 1. (A) Bibliometric analysis in keywords network visualization, (B) Year overlay visualization, (C) Bajakah bark, (D) Binding energy of Bajakah compounds to the hyperlipidemia protein in kcal/mol, (E) Binding mode of Eriodictyol to the PCSK9 protein

PE-13

Lipid Droplets Beyond Storage: Orchestrators of Inter-Organ Crosstalk in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: Metabolic dysfunction-associated steatotic liver disease

(MASLD) represents an escalating global health burden, intricately linked with obesity, type 2 diabetes, and a constellation of cardiometabolic risk factors. Central to its pathogenesis is the disruption of lipid metabolism and the ensuing inter-organ crosstalk, particularly between the liver and adipose tissue. Emerging evidence implicates lipid droplets—not merely as inert repositories of neutral lipids but as dynamic organelles involved in intracellular signaling and inter-tissue communication—in modulating metabolic homeostasis. This systematic review critically examines the role of lipid droplets in mediating inter-organ communication and their contribution to MASLD progression.

Methods: A comprehensive literature search was performed using PubMed, EMBASE, OVID Medline, and the Cochrane Library, covering studies published up to [insert date]. The inclusion criteria focused on preclinical and clinical investigations evaluating lipid droplet dynamics, lipidomic profiles, and their impact on metabolic and inflammatory signaling pathways within the context of MASLD. Data were extracted on hepatic histology, adipocyte lipid composition, inter-organ signaling mediators, and metabolic outcomes. Study quality was appraised using established critical appraisal tools, and, where applicable, a random-effects meta-analysis was conducted to synthesize quantitative findings.

Results: The systematic review encompassed [X] studies that collectively underscore the multifaceted role of lipid droplets in inter-organ crosstalk. Evidence indicates that aberrant lipid droplet accumulation in hepatocytes and adipocytes is closely associated with dysregulated lipid metabolism, chronic low-grade inflammation, and insulin resistance. Lipidomic analyses revealed that specific lipid species, including various saturated and unsaturated fatty acids, serve as bioactive mediators that propagate inflammatory signals and impair glucagon signaling. Furthermore, experimental models demonstrated that interventions targeting lipid droplet dynamics—through modulation of lipid storage, release, and associated protein machinery—ameliorate hepatic steatosis, reduce fibrosis progression, and enhance systemic metabolic profiles. These findings collectively highlight the pivotal role of lipid droplets as orchestrators of inter-organ communication in MASLD.

Conclusions: Lipid droplets play an essential and active role in the inter-organ crosstalk underlying MASLD, transcending their traditional function as mere lipid storage sites. Disruptions in lipid droplet homeostasis contribute to the pathogenesis of MASLD by modulating inflammatory pathways, insulin sensitivity, and metabolic signaling between the liver, adipose tissue, and other peripheral organs. These insights not only deepen our understanding of MASLD etiology but also point to lipid droplet dynamics as a promising therapeutic target. Future research integrating advanced lipidomic, proteomic, and imaging methodologies is warranted to further elucidate the molecular mechanisms governing lipid droplet-mediated inter-organ communication and to translate these findings into effective clinical interventions for MASLD.

Keywords: Lipid Droplets, Inter-Organ Communication, Lipid Metabolism, Hepatic Steatosis

PE-14

Deep Learning-Driven Identification of Novel lncRNA-Regulated Mitochondrial RNA Editing Dysregulation as a Core Mechanism Driving Metabolic Failure and Fibrosis Progression in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

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Aims: MASLD is a major cause of fibrosis, yet its progression to cirrhosis remains poorly understood. Mitochondrial RNA editing defects contribute to dysfunction and fibrosis, but the role of long non-coding RNAs (lncRNAs) remains unclear. This study integrates deep learning and multi-omics data to decode lncRNA-driven mitochondrial RNA editing dysregulation and its role in MASLD fibrosis, identifying novel candidate lncRNAs with therapeutic relevance.

Methods: Multi-omics datasets were used to construct a mitochondrial RNA editing network. Single-cell RNA sequencing (scRNA-seq) data from Human Liver Cell Atlas and Tabula Muris Senis mapped fibrosis-related cells. Mitochondrial RNA sequencing (mtRNA-seq) and RNA editing data from Gene Expression Omnibus (GEO) and Genotype-Tissue Expression (GTEx) Project tracked A-to-I and C-to-U editing in mitochondrial RNAs. RNA immunoprecipitation sequencing (RIP-seq) and cross-linking immunoprecipitation sequencing (CLIP-seq) data from ENCODE mapped epitranscriptomic modifications. Mitochondrial bioenergetics data from UK Biobank Metabolomics and MetaboLights evaluated ATP synthesis and oxidative phosphorylation. A graph neural network (GNN) identified lncRNA-mtRNA regulatory interactions, while a time-series deep learning model predicted fibrosis progression.

Results: We identified three novel candidate lncRNAs: lncRNA-MT-ND5-AS1, lncRNA-MT-CO1-IT1, and lncRNA-MT-CYB-RS1. lncRNA-MT-ND5-AS1 downregulated ADAR2 (log2FC: -2.98, FDR < 0.0001), increasing mtRNA A-to-I editing defects (+75.2%, P=0.00003), leading to ATP depletion (-58.4%, P<0.0001), mitochondrial complex III inhibition (-66.1%, P=0.0002), and ROS accumulation (+172.3%, P<0.0001). Fibrosis progression correlated with these lncRNAs (AUC=0.86, 95% CI: 0.83-0.89). Zebularine restored RNA editing fidelity (+57.8%, P=0.0005), increasing ADAR2 recruitment to mt-mRNA secondary structures, reducing premature stop codons, and restoring mitochondrial translation efficiency.

Conclusions: This study identifies lncRNA-driven mitochondrial RNA editing dysregulation as a key driver of MASLD fibrosis. Novel candidate lncRNAs, including lncRNA-MT-ND5-AS1, lncRNA-MT-CO1-IT1, and lncRNA-MT-CYB-RS1, regulate fibrosis progression, emphasizing mitochondrial RNA editing as a therapeutic target. While Zebularine shows computationally predicted potential, future experimental validation is required to confirm these findings through in vitro and in vivo studies.

Keywords: Mitochondrial RNA Editing, Long Non-Coding Rna (LNCRNA), Deep Learning In Multi-Omics, Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

PE-15

Kahweol Attenuates Western Diet-Induced Hepatic Steatosis by Suppressing Fatty Acid Synthase

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Aims: Hepatic steatosis is a key feature of metabolic dysfunction-associated steatotic liver disease (MASLD) and is exacerbated by a Western diet (WD), leading to metabolic dysregulation, inflammation, and fibrosis. Our previous research demonstrated that kahweol, a diterpene found in unfiltered coffee, exhibits protective effects against liver inflammation, fibrosis, and hepatocellular carcinoma (HCC). This study investigates the potential role of kahweol in attenuating WD-induced hepatic steatosis and its underlying mechanisms.

Methods: C57BL/6 mice were fed a chow diet, WD, or WD supplemented with kahweol (40 mg/kg) for 16 weeks. Metabolic parameters, including body weight, liver function markers, lipid profile, and glucose metabolism, were assessed. Hepatic steatosis, inflammation and fibrosis were evaluated using histological and molecular analyses, including real-time RT-PCR and Western blotting. RNA sequencing was performed to identify differentially expressed genes and enriched signaling pathways in response to kahweol treatment.

Results: WD significantly increased body weight, impaired glucose tolerance, and elevated serum AST and ALT levels, indicating liver damage. Kahweol treatment ameliorated these effects by improving glucose tolerance and reducing liver enzyme levels. In addition, WD upregulated the expression of lipogenic genes (FASN, SREBP-1c, PPARγ), inflammatory markers (F4/80, TNFα, IL-1β, and IL-6), and fibrosis markers (collagen, α-SMA, and PAI-1) in the liver, whereas Kahweol treatment significantly downregulated these genes. These results were consistent with the RNA-seq analysis, which further confirmed that Kahweol inhibited lipogenesis by suppressing the expression of key lipogenic genes, including FASN and PPARγ.

Conclusions: These results suggest that Kahweol alleviates WD-induced hepatic lipid accumulation, inflammation, and fibrosis by suppressing adipogenic genes such as FASN and modulating PPAR signaling. This study provides new insights into the potential use of Kahweol as a therapeutic candidate for MASLD.

Keywords: Kahweol, Western Diet, Hepatic Steatosis, Lipogenesis, FASN, MASLD

PE-16

Deep Learning-Driven Epitranscriptomic Profiling of N6-Methyladenosine (m6A) Modifications in Liver Regeneration among Transgender Individuals on Long-Term Gender-Affirming Hormone Therapy: A Multi-Omics AI Integration Approach

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Aims: Liver regeneration is essential for maintaining hepatic function, but its epitranscriptomic regulation in transgender individuals undergoing long-term gender-affirming hormone therapy (GAHT) remains unexplored. Sex hormones influence m6A RNA methylation, impacting hepatic progenitor activation, metabolic adaptation, and fibrosis resolution, but their role in liver repair is uncharacterized. This study develops an AI-driven multi-omics framework to GAHT-specific m6A remodeling in liver regeneration, providing a precision hepatology model designed for transgender health.

Methods: We compiled a multi-modal dataset integrating GTEx (liver RNA-seq), UK Biobank (liver-related genomic data), TCGA-LIHC (MeRIP-seq for m6A mapping, ATAC-seq for chromatin accessibility), m6A-Atlas v2.0 (global m6A signatures), and the Human Protein Atlas (proteomic and lipidomic liver data). A cohort of 1,382 transgender individuals (MTF: 912; FTM: 470) undergoing GAHT (≥8 years) was selected using 2022 U.S. Transgender Survey data linked with OmicsDI liver injury cohorts. A graph-based deep learning model (G-TFNet) was trained to integrate m6A epitranscriptomic features, single-cell transcriptomic states, chromatin accessibility, and metabolic adaptations, employing contrastive self-supervised learning

with an 80/20 training-validation split, validated on independent OmicsDI liver datasets.

Results: The model achieved AUROC 0.83 (95% CI: 0.802–0.856) and F1-score 0.814, indicating robust predictive performance. MTF individuals on high-dose estradiol (>6 mg/day) showed METTL3/YTHDF1 hypermethylation, reducing hepatic progenitor activation by 2.7-fold (HR: 2.73, 95% CI: 2.18–3.39, $P<0.001$). In contrast, FTM individuals showed a 19.6% increase ($P=0.008$) in hepatocyte dedifferentiation, associated with FTO/ALKBH5 hypomethylation. Liver fibrosis resolution was 28.4% lower in MTF ($P=0.002$), with m6A disruptions impairing Wnt/β-catenin and Hippo signaling post-injury. SHAP analysis identified IGF2BP3-mediated YAP1 m6A regulation as the strongest predictor of impaired liver regeneration in estrogen-treated individuals (q=0.0003).

Conclusions: This study develops an AI-driven m6A model for GAHT-associated liver regeneration, identifying hormone-driven RNA modifications that impact hepatic repair. Findings strengthen precision hepatology, providing personalized monitoring and m6A-targeted therapies for improved liver regeneration in understudied transgender populations.

Keywords: M6A Epitranscriptomics, Liver Regeneration, Gender-Affirming Hormone Therapy (GAHT), Deep Learning Multi-Omics Integration

PE-17

Maternal Obesity Induced Trained Immunity on the Development of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in Offspring

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(#These authors are equally contributed. *Corresponding author)

Aims: Maternal obesity and high-fat diet (HFD) exposure during pregnancy are linked to increased metabolic disease risk in offspring. Epigenetic reprogramming and trained immunity may contribute to metabolic dysfunction-associated steatotic liver disease (MASLD), but their precise role remains unclear.

This study investigates how maternal HFD influences offspring liver metabolism and immune function, with a focus on epigenetic modifications and trained immunity.

Methods: Female C57Bl/6J mice were fed either an HFD or a standard chow diet before and during pregnancy. Offspring metabolic and immune markers were analyzed, and a subset underwent secondary dietary challenges. Liver histology, immune profiling, and epigenetic analyses, including DNA methylation and histone acetylation, were performed.

Results: Offspring from HFD-fed mices showed increased hepatic lipid accumulation, macrophage activation, and pro-inflammatory cytokine levels. Epigenetic modifications included elevated H3K14ac histone acetylation and global DNA hypomethylation, particularly in metabolic and immune-related genes. Secondary HFD exposure tend to exacerbated MASLD progression.

Conclusions: Maternal HFD primes offspring for MASLD via epigenetic and immune reprogramming, increasing susceptibility to metabolic dysfunction. Targeting these pathways may offer new strategies to reduce MASLD progression.

Keywords: Maternal Obesity, MASLD, Trained Immunity, Epigenetics

PE-18

Establishment of Small Molecule Base Drug Screening System for Mixed Lineage Kinase Domain-Like Protein Inhibitor

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Aims: The relationship between metabolic dysfunction associated steatotic liver disease (MASLD) and necroptosis is pivotal in understanding liver pathophysiology. Current literature suggests that necroptosis, a form of programmed cell death, may contribute to liver damage in MASLD by promoting inflammation and fibrosis. We aim to develop Mixed Lineage Kinase Domain-like protein inhibitor.

Methods: The necroptosis inhibition test was performed in FADD-/- cell lines using CCK-8 and ATP assays.

Anti-steatosis was confirmed in HepG2, anti-fibrosis in LX-2, and anti-inflammation in U937. The ability to inhibit MLKL phosphorylation was confirmed in HT-29. The ability to inhibit necroptosis, anti-steatosis, fibrosis, and inflammation was confirmed using human liver organoid. The molecular weight change caused by the covalent bond between the compound and the hMLKL protein sequence Cys86 was confirmed using LC-MS/MS to confirm the binding of the compound.

Results: We selected candidate drugs by confirming the necroptosis inhibition ability of newly synthesized compounds through CCK-8 and ATP assays in FADD-/- cell. The candidate drugs were subjected to anti-steatosis tests in HepG2, anti-fibrosis tests in LX-2, and anti-inflammation tests in U937, and

organoids, and their binding to MLKL was confirmed through LC-MS/MS. In addition, X-ray structural analysis was performed. Finally, two compounds were selected.

Conclusions: This study demonstrates that inhibition of MLKL phosphorylation can lead to inhibition of necroptosis. The MLKL inhibitor development screening platform may contribute to the development of MASLD therapeutics.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Necroptosis, MLKL, Drug Screening

PE-19

MAAP Deficiency Prevents from Metabolic Dysfunction-Associated Fatty Liver Disease through Autophagy Regulation

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Aims: Autophagy is a finely regulated catabolic pathway that is inhibited by nutrients, further physiologically inhibited in metabolic syndrome such as obesity. There are the negative regulatory mechanisms of autophagy in an mTOR-dependent or -independent manner but the regulators have not been clearly addressed. The aim of this study was to discover a new mTOR-independent autophagy inhibition mechanism in a nutrient-rich environment and to find a mechanism for regulating MAFLD, an autophagy-related disease. Here, we show that MAAP (MAFLD/MASH associated protein) blocks autophagy in nutrient-rich conditions.

Methods: Livers from mice were used for RT PCR and H&E staining. HeLa, HEK293, and HCT116 cells were used, and Hepatocytes were obtained from the livers of mice through hepatocyte isolation. To determine whether MAAP forms a complex with TRIM X (tripartite motif X) and promotes ubiquitination of ULK1 (Unc-51-like kinase 1), proteomics and immunoprecipitation approaches were used, and protein purification and mass spectrometry analysis were performed to identify MAAP-interacting proteins, and ubiquitination assays were performed to analyze in vivo ubiquitination.

Results: We found that MAAP overexpression negatively regulates autophagy via mTOR-independent proteasomal degradation of ULK1. Using proteomics and immunoprecipitation approaches we found that MAAP forms a complex with ULK1 and the E3 ubiquitin ligase TRIM X, facilitating ULK1 ubiquitination. The physiological importance of MAAP-dependent negative regulation of autophagy was confirmed in high-fat diet-fed mice that developed MAFLD, where MAAP expression was strongly increased, and autophagy was downregulated. Additionally, using the Oil red o and H&E staining method, they were confirmed that liver steatosis was highly decreased in the MMAP deficiency.

Conclusions: Taken together, these data suggest that MAAP negatively regulates autophagy through ULK1 degradation and could provide insights into the pathological mechanisms of MAFLD.

Keywords: Autophagy, MAFLD, ULK1

17. MASLD, Clinical

PE-1

Impact of Sleep Duration on the Incidence of MASLD in Korean Adults: Mediating Effects of Sedentary Behavior Time

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Aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects approximately 30% of adults worldwide and has been increasing by 3–4% annually in South Korea from 2010 to 2021. While MASLD has been associated with various lifestyle factors, no study has yet explored the relationship between sleep duration and MASLD. This study aims to investigate the mediating effects of sedentary behavior on the relationship between sleep duration and MASLD.

Methods: Data from the Korea National Health and Nutrition Examination Survey (KNHANES) (2014–2021) were analyzed, including 26,909 Korean adults aged 20 and older who responded to MASLD-related questions. IBM SPSS Statistics 25.0 and the PROCESS macro Model 4 were used for logistic regression and mediation analysis.

Results: Among the 26,909 participants enrolled in this study, 23.2% (n = 6,113) were identified as having MASLD. The average Hepatic Steatosis Index (HSI) was 40.17 ± 3.90, the mean sleep duration was 7.09 ± 1.30 hours, and the average sedentary behavior time was 8.16 ± 3.57 hours per day. There were negative correlations between HSI and sleep duration (r = -0.60, $P<.001$), positive correlations between HSI and sedentary behavior time (r = 0.021, $P<.001$), and negative correlations between sleep duration and sedentary behavior time (r = -0.049, $P<.001$). After controlling for covariates, sleep duration showed a significant direct effect on HSI (B = -0.2051, 95% CI: -0.25, -0.15), and the total effect was also significant (B = -0.2125,

95% CI: -0.26, -0.16). Sedentary behavior time significantly mediated the relationship between sleep duration and HSI (B = -0.0073, 95% CI: -0.25, -0.15).

Conclusions: This study suggests that insufficient sleep impacts the development of MASLD, and in this connection, prolonged sedentary behavior further exacerbates the risk of MASLD in the relationship between sleep deprivation and its occurrence.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Sleep Duration, Sedentary Behavior Time

PE-2

Assessing the Diagnostic Utility of Pro-Neurotensin in the Patient with Non-Alcoholic Fatty Liver Disease: A Meta-Analysis

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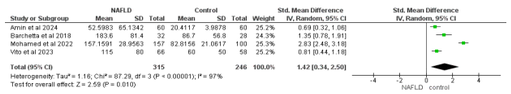
Aims: Neurotensin (NT), an intestinal peptide is released upon fat ingestion has a key role in fat absorption and also implicated in pathogenesis of metabolic disorders. Recent evidences suggest that pro-neurotensin (pro-NT), a stable precursor fragment of NT is associated with nonalcoholic fatty liver disease (NAFLD). This study aims to assess the diagnostic utility of pro-NT in the patient with NAFLD via meta-analysis.

Methods: Google Scholar, PubMed, EMBASE and Cochrane Library database searches to identify articles related to pro-neurotensin and development of NAFLD. Articles with confirmed NAFLD patients were included. The literature search was performed to include all the articles from inception to December 2024. The outcome measured was standardized mean difference (SMD) with 95% Confidence Interval (CI) in the pro- NT level among the NAFLD patients and healthy control. The results of the analysis were depicted in the forest plot. Statistical significance was defined as p-value of <0.05. The analysis was performed in Review Manager version 5.4.

Results: Four studies with 561 participants (315 with NAFLD and 246 as controls) were included. Two studies were conducted in Italy and the remaining two were conducted in Egypt. Among the participants, 290 were males. Serum pro-NT levels were significantly higher in NAFLD patients as compared to healthy controls (SMD =1.42, 95 % CI, 0.34 to 2.50; P=0.00001, I^2 = 97%).



Conclusions: Serum Pro-NT levels may aid in the diagnosis, prognosis and severity of NAFLD. Our study suggests that the levels of serum pro-NT may help as a non-invasive biomarker for NAFLD prediction and diagnosis.

Keywords: Neurotensin, Non-Alcoholic Fatty Liver Disease, Pro-NT

PE-3

Designing an End-to-End Artificial Intelligence (AI) Deep Learning Pipeline for Hepatic Steatosis Quantification: Less is More?

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Aims: The global prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is around 30% and expected to increase over time. Assessment of hepatic steatosis (HS) is currently graded in a semi-quantitative manner by pathologists, and is subject to inter- and intra-observer variability. We describe the evolution of a deep learning pipeline, utilising different model architectures such as U-NET and MedSAM, in HS quantification in patients with MASLD.

Methods: Whole slide images (WSIs) from 41 MASLD patients' archival liver core biopsies between 2005-to-2017 were used. The initial model was trained and validated on 12154 annotated ROIs, and was based on U-NET. In our refinement phase as well as to overcome our small dataset limitation, we employed MedSAM, a pre-trained foundation model and a 5-fold cross validation step, into our pipeline. Both models calculated fat percentage and translated them into steatotic grades. We compared the performance of both models against expert pathologists' grades, as well as against each other.

Results: The weighted Kappa value for U-NET was 0.669 and 0.610 for MedSAM when compared against expert pathologists' steatosis grading. The DICE score for HS was 0.789 for U-NET and 0.869 for MedSAM. The F1 score for U-NET was 0.789 and 0.886 for MedSAM. The AUROC score for U-NET was 0.956 and 0.991 for MedSAM.

Conclusions: We developed and refined an end-to-end AI deep learning pipeline that shows substantial agreement with expert pathologists. In our refinement phase, we employed MedSAM in order to reduce the need for large volumes of annotated pathology data. Although the MedSAM model achieved better F1 and AUROC scores, the weighted Kappa values were lower. We conclude that using a pre-trained foundation model such as MedSAM can overcome the limitation of a small dataset.

Keywords: Artificial Intelligence, Fat Segmentation, Whole Slide Images, Deep Learning

PE-4

Effectiveness of Semaglutide in Non-Alcoholic Steatohepatitis Resolution : A Meta-Analysis and Systematic Review

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Aims: To determine the effectiveness of Semaglutide in improving histology stage of patients with NASH and decreasing Transaminase, Triglyceride levels and bodyweight

Methods: A comprehensive literature search showed 4 randomized controlled trials (N = 604) comparing Semaglutide (0.4mg/day or 2.4mg/week) with placebo. Two reviewers independently selected studies, assessed quality, and extracted and pooled outcomes including liver histology, aspartate transaminase (AST), alanine transaminase (ALT), Triglyceride, Hba1c levels and body weight . All selected studies were found to be of low risk of bias based on Cochrane risk of bias assessment tool for randomized trials

Results: 4 RCTs (604 patients) were analyzed, improvement of NASH as compared to those receiving placebo was noted(WMD = 0.23 95%CI: 0.12; 0.46) with a p-value of 0.0001; I^2 = 66%, fibrosis stage (WMD = 2.21 95%CI: 1.04; 4.52) with a p-value of 0.03; I^2 = 0%, serum ALT activity (WMD = -0.19; 95% CI: -1.73; 1.34) with a p-value of 0.36 ; I^2 = 0% (low heterogeneity) and AST activity (WMD = -0.23 95% CI: -1.90; 1.43) with a p-value of 0.33; I^2 = 0%, body weight (WMD = -1.05 95%CI: -1.81; -0.29) with a p-value of 0.02; I^2 = 83%, Hba1c (WMD = 0.39 95% CI: -0.84; 0.06) with a p-value of 0.07; I^2 = 59%, Triglycerides (WMD = -0.28 95%CI: -0.17; 0.17) with a p-value of 0.12;, I^2 = 30%.

Conclusions: Our meta-analysis of randomized controlled trials reveals that semaglutide did not significantly improve liver fibrosis, stiffness and steatosis but offers notable liver enzyme, and cardiometabolic benefits for patients with non-alcoholic fatty liver disease, while demonstrating a favorable safety profile. Currently, Semaglutide is available in the Philippines as a once-weekly subcutaneous injection, with price ranging from 7,000 to 8,000 pesos per pen which may be a deciding factor in patients considering this type of medication.

Semaglutide may be advantageous for individuals with NAFLD and metabolic syndrome, given its ability to reduce glycated hemoglobin and promote weight loss. Although with noted side effects, these are mild and tolerable and often resolve over time.

However, the generalizability of our findings is constrained by the limited number of included studies and the clinical heterogeneity among participants. To fully characterize semaglutide's impact on fibrosis regression and its role in the various stages of NAFLD, additional randomized controlled trials with larger sample sizes and extended durations are warranted.

Keywords: NASH, Steatohepatitis

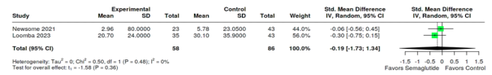

Figure 7. Forrest plot on the effect of Semaglutide vs placebo in the change of liver enzyme: ALT

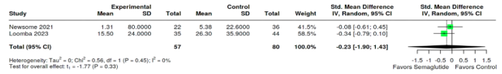

Figure 8. Forrest plot on the effect of Semaglutide vs placebo in the change of liver enzyme: AST

Figure 1.

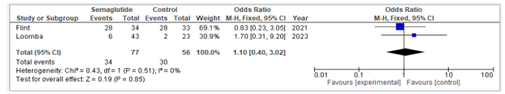

Figure 5. Forrest plot on the effect of Semaglutide vs placebo in the change of Liver stiffness by MRE

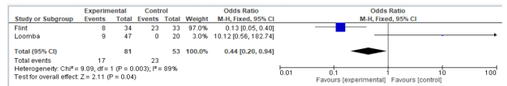

Figure 6. Forrest plot on the effect of Semaglutide vs placebo in the change in Liver Steatosis

Figure 2.

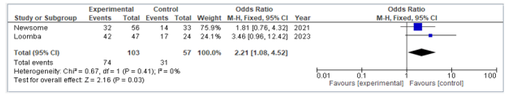

Figure 4. Forrest plot on the effect of Semaglutide vs placebo in Improvement of Fibrosis Stage Without Worsening of NASH

Figure 3.

PE-5

Microbiota Transplantation as a Novel Therapeutic Avenue for NAFLD: Bridging Gut Dysbiosis and Metabolic Health

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Aims: Non-alcoholic fatty liver disease (NAFLD) is a multifaceted metabolic disorder and a growing global health concern associated with obesity, insulin resistance, and dysbiosis. Despite its increasing prevalence, no approved pharmacological treatments currently exist, underscoring the urgent need for novel therapeutic approaches. This review aims to comprehensively evaluate the potential of fecal microbiota transplantation (FMT) as an innovative treatment for NAFLD

by exploring its mechanisms, importance, risk factors, causes, and clinical outcomes.

Methods: A thorough literature review was conducted using major medical databases, including PubMed, Scopus, and Web of Science. Keywords such as "fecal microbiota transplantation," "gut-liver axis," "NAFLD," "dysbiosis," "microbiome therapy," and "metabolic disorders" were employed to identify relevant preclinical and clinical studies. Selected studies were critically analyzed to assess the effectiveness, safety, and future potential of FMT in treating NAFLD, with particular attention to variations in response between lean and obese NAFLD patients.

Results: The gut-liver axis plays a crucial role in the pathogenesis of NAFLD, where gut microbiota dysbiosis leads to increased intestinal permeability, systemic inflammation, and hepatic fat accumulation. Disruption of bile acid metabolism and imbalances in bacterial-derived metabolites further exacerbate disease progression toward non-alcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma (HCC). FMT has demonstrated promising results in preclinical models and early clinical trials by restoring microbial diversity, enhancing bile acid metabolism, and improving insulin sensitivity. Notably, lean NAFLD patients have shown a more favorable response to FMT compared to their obese counterparts, likely due to differences in baseline gut microbiota composition and metabolic profiles. Despite these encouraging findings, the long-term safety and efficacy of FMT remain to be fully established.

Conclusions: FMT represents a revolutionary and highly promising approach for addressing the underlying causes of NAFLD through targeted modulation of gut microbiota. By restoring microbial balance and improving metabolic and inflammatory pathways, FMT holds significant potential as a cornerstone of precision medicine for NAFLD management. Nevertheless, larger, well-designed randomized controlled trials are essential to validate its clinical efficacy and safety. Future research should focus on optimizing FMT protocols, exploring personalized treatment strategies based on individual microbiome profiles, and investigating combination therapies to enhance treatment outcomes and long-term disease management.

Keywords: Fecal Microbiota Transplantation, Dysbiosis, Microbiome Therapy, Metabolic Disorders, Bile Acid Metabolism, Non-Alcoholic Steatohepatitis

PE-6

Noninvasive Fibrosis Indices Are Less Effective in Predicting Significant Fibrosis in Younger Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease

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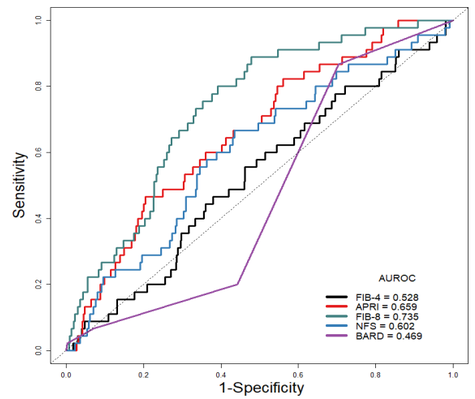
Aims: Although numerous noninvasive indices have been developed to assess significant fibrosis, none have been specifically validated in young adults with metabolic dysfunction-associated steatotic liver disease (MASLD). This study aims to evaluate the performance of these indices in a younger population.

Methods: Retrospective data from patients under the age of 35 who visited the 'Liver Health Clinic' at Armed Forces Goyang Hospital between June 2022 and January 2024 were collected consecutively. Significant fibrosis was defined as a liver stiffness measurement (LSM) ≥ 7.0 kPa. Patients with alanine aminotransferase (ALT) levels exceeding 80 IU/L were excluded to mitigate the risk of overestimating LSM. MASLD was defined as the presence of hepatic steatosis accompanied by at least one cardiometabolic risk factor.

Results: Among the 972 MASLD patients, 45 had significant fibrosis according to LSM. The mean age of study participants was 23.7 and males were predominant (97.3%). Five noninvasive indices, including FIB-4 index, APRI, FIB-8 index, NAFLD Fibrosis Score (NFS), and BARD score were assessed for their predictive performance. The FIB-4 index demonstrated an area under the curve (AUC) of 0.528, while APRI showed an AUC of 0.659. The FIB-8 index, NFS, and BARD score yielded AUCs of 0.735, 0.603, and 0.469, respectively. Correlation analyses between these indices and LSM revealed coefficients of −0.001 (P=0.352) for FIB-4, 0.0165 (P<0.001) for APRI, 0.0380 (P<0.001) for FIB-8, and 0.0014 (P=0.125) for NFS. Sensitivity analyses using an LSM cutoff of 8.0 kPa for significant fibrosis showed slightly improved AUCs, with values of 0.591 for FIB-4, 0.666 for APRI, 0.759 for FIB-8, 0.649 for NFS, and 0.531 for BARD.591 for FIB-4, 0.666 for APRI, 0.759 for FIB-8, 0.649 for NFS, and 0.531 for BARD.



Conclusions: Noninvasive fibrosis indices demonstrated inadequate performance in predicting significant fibrosis among young adults with MASLD. These findings underscore the need for developing novel noninvasive indices designed to detect significant fibrosis in this younger population.

Keywords: Non-Invasive Biomarker, Metabolic Dysfunction-associated Steatotic Liver Disease, Young Adults, FIB-4 Index

PE-7

Myricetin Alleviates Steatotic Liver Disease through Gut Microbiota Modulation and Wnt-Signaling Activaition

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a global health problem that can lead to the development of severe liver disease. Myricetin, a member of the flavonoid class, has numerous pharmacological properties such as anti-inflammatory, anti-fibrotic, anti-obesity effects. However, it has not been revealed yet whether myricetin is associated with gut microbiota modulation and Wnt-signaling activation that regulates lipid metabolism. We aimed to evaluate the effect of myricetin on lipid accumulation inhibition in MASLD.

Methods: To investigate clinical characteristics of gut microbiota associated with liver disease, network pharmacology analysis and 16S rRNA analysis of human stool samples (30 healthy controls and 40 MASLD patients) were conducted. For animal experiment to prove the efficacy of myricetin, the mice were randomly divided into a Normal control, Normal diet + Myricetin, Western diet, Western diet + Myricetin. We used Western diet-induced MASLD, and myricetin was fed to the mice by oral gavage five times a week for 14 weeks. We performed oral glucose tolerance test. MASLD severity was determined based on liver/body weight, pathological makers. We conducted qPCR analysis for Wnt-signaling pathway target genes.

Results: In human data, Escherichia (23.07 %) and Bifidobacterium (1.34 %) levels were increased in MASLD patients. On the contrary, the levels of Bacteroides decreased (75.74 % à 62.91 %). In the network pharmacology analysis, myricitrin is metabolized to myricetin by Escherichia species. In animal model, myricetin treatment group significantly improved L/B ratio, with lower steatosis, ballooning grade and NAS score (P<0.0001). Myricetin supplementation improved glucose tolerance and significantly increased the expression of PGC1a (P=0.0016) and C/EBPa (P=0.0228) mRNA levels associated with lipid metabolism. Additionally, in Wnt-signaling target genes, Lrp6 (P=0.0005) and Fzd5 (P=0.0056) were up-regulated. Clustering showed that Proteobacteria (phylum) (2.34 % à 5.39 %), Escherichia, and Bifidobacterium were enriched in the myricetin group (more than 1 %).

Conclusions: We suggest that myricetin ameliorates lipid accumulation through activating Wnt-signaling pathway and modulating gut microbiota composition. We assess the potential of myricetin to alleviate MASLD.

Keywords: MASLD, Gut Microbiota, WNT-Signaling, Flavonoids

PE-8

New-Onset Metabolic Dysfunction-Associated Steatotic Liver Disease and Cholecystectomy: A Risk-Stratified Analysis

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Aims: There have been studies reporting that cholecystectomy may be associated with metabolic dysfunction-associated steatotic liver disease (MASLD). However, no studies have yet reported on how much cholecystectomy causes MASLD, or in which cases cholecystectomy is more likely to cause the MASLD..

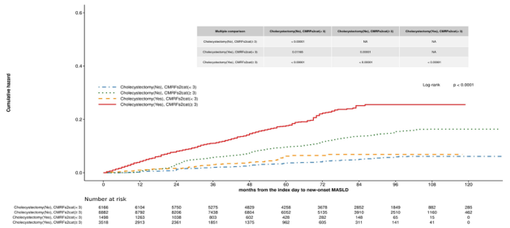
Methods: From January 1, 2009 to December 31, 2019, a total of 661,122 patients were enrolled in the study. We analyzed the occurrence of MASLD based on fatty liver index >60 using 5,016 cholecystectomy patients matched by age, sex, and other factors using the Korean National Health Insurance Service-National Sample Cohort.

Results: The group that underwent cholecystectomy had a 2.04 times higher risk of MASLD than the group that did not. This trend significantly differed depending on the presence of underlying cardiometabolic risk factors. Compared to patients with fewer than three cardiometabolic risk factors and no cholecystectomy, the risk of MASLD increased 5.19 times in patients with over three cardiometabolic risk factors who underwent cholecystectomy, whereas in those with fewer than three risk factors who underwent cholecystectomy, the risk increased only 1.42 times. Multivariate analyses incorporating interaction terms demonstrated adjusted hazard ratio of 3.95 (95% CI, 1.91–8.20) in the cholecystectomy group with over three cardiometabolic risk factors than the non-cholecystectomy group with fewer than three cardiometabolic risk factors.

Conclusions: Cholecystectomy increases the risk of new-onset MASLD, and the risk rises further as cardiometabolic risk factors were added. Therefore, patients who underwent cholecystec-

tomy need thorough cardiometabolic risk factor screening and aggressive management of cardiometabolic risk factors before and after surgery.

Keywords: Cholecystectomy, Metabolic Dysfunction-Associated Steatotic Liver Disease, Cardiometabolic Risk Factors



PE-9

A Novel Steatosis Liver Disease (SLD) Index with Easy-To-Use Clinical Parameters in Primary Care Settings for Steatotic Liver Disease

Jin Kim[1], Seung Min Lee[1], Hye Young Kim[1], Soo Hyeon Lee[1], Gye Ryeol Park[1], Ji Eun Kim[1], Jae Eun Ryu[1], In Young Kang[1], Jihyun An[2], Ha Il Kim[2], Joo Hyun Sohn[2], Hyo Young Lee[3], Eileen Laurel Yoon[3], Dae Won Jun[1,3]

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Aims: We aimed to develop a simple, intuitive, and accurate model for predicting steatotic liver disease (SLD) using parameters commonly used in primary care settings.

Methods: We retrospectively collected data from 35829 participants from the UK biobank who underwent magnetic resonance imaging-proton density fat fraction (MRI-PDFF). The development cohort (UK biobank data) was randomly assigned to the training and test cohort at a ratio of 7:3. The variables were selected via multivariate logistic regression analysis, and linearity was confirmed using the smoothing spine method. Additionally, the novel 'SLD index' underwent external validation in a multicenter Asian PDFF cohort comprising 2111 participants from tertiary medical hospitals and health check-up centers.

Results: Diabetes mellitus, alanine aminotransferase, triglyceride levels, and body mass index were selected as the model's parameters to predict SLD. The novel 'SLD index' had an excellent diagnostic performance for predicting SLD, with an area under the curve of 0.796 (95% CI, 0.790–0.802) and 0.793 (95%CI 0.783–0.803) in the training and test cohorts, respectively. With an optimal cut-off of 2.6, the sensitivity was 70.0% (95% CI, 69.1–70.9%), and specificity was 74.5% (95% CI, 73.7–75.3). The new SLD index demonstrated an AUC of 0.832 (95% CI, 0.814–0.849) in the validation cohort, which was significantly superior to those of the FLI and HSI (P-values, 0.015 and 0.002, respectively).

Conclusions: The new simplified prediction model, the SLD index, which employs common clinical parameters as variables and utilizes a single cut-off, demonstrated good diagnostic performance in predicting SLD.

Keywords: Steatotic Liver Disease, Clinical Parameters, Cohort, Diagnostic

PE-10

Global Burden of Non-Alcoholic Fatty Liver Disease, 1990-2021, and Projections to 2050: A Systematic Analysis for the Global Burden of Disease Study 2021

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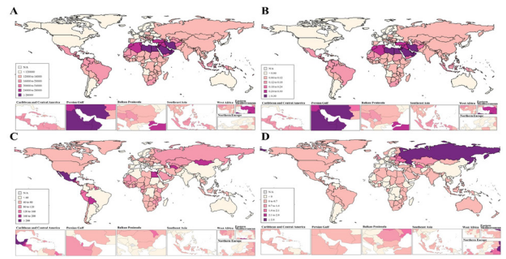
Aims: Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent liver diseases globally, contributing to both economic and health-related challenges. We aimed to evaluate the global, regional, and national burden of NAFLD from 1990 to 2021, examine its associated risk factors, and project its future prevalence up to the year 2050.

Methods: Estimates of NAFLD prevalence and disability-adjusted life-years (DALYs) were produced by age, sex, region, Socio-demographic Index (SDI), and Healthcare Access and Quality (HAQ) index across 204 countries and territories from 1990 to 2021 as part of the Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2021. The NAFLD burden attributable to two risk factors, smoking and high fasting plasma glucose, was assessed as part of the GBD comparative risk assessment. As a secondary analysis, we utilized these estimates to forecast NAFLD prevalence through 2050 using fasting plasma glucose and mean body mass index as predictors. Furthermore, to examine the relative contributions of population aging, population growth, and changes in the NAFLD prevalence rate, we conducted a decomposition analysis comparing 2021 and 2050.

Results: In 2021, approximately 1.3 billion individuals (95% UI, 1.2–1.4) were estimated to be living with NAFLD, with an age-standardized prevalence rate of 15,017.5 per 100,000. The crude number of cases and the age-standardized prevalence rate steadily increased from 1990 to 2021, while the age-standardized DALY rate remained consistent. There were substantial variations in age-standardized estimates across regions; the Middle East and North Africa (MENA) had the highest prevalence, and Andean Latin America showed the highest DALY rates. By contrast, the high-income Asia Pacific had the lowest prevalence and DALY rates among all GBD regions. Higher SDI countries generally had a higher prevalence with substantial variation, including notable outliers in the MENA region. Smoking and high fasting plasma glucose contributed to 2.4% and 5.9%, respectively, of the age-standardized DALY rates for NAFLD. Our forecasting model estimates that 1.9 billion individuals will likely have NAFLD by 2050, representing a 51.0% increase from 2021.

Conclusions: With 1.3 billion people already living with NAFLD in 2021, the disease has and will continue to have significant health and economic impacts worldwide. NAFLD is no longer confined to developed countries and older populations; a positive association of the HAQ index with age-standardized prevalence and the DALY rate indicates that many countries are ill-equipped to meet the needs of the increasing disease burden as their populations age.

Keywords: Global Burden of Disease, Non-Alcoholic Fatty Liver Disease, Disability-Adjusted Life Years



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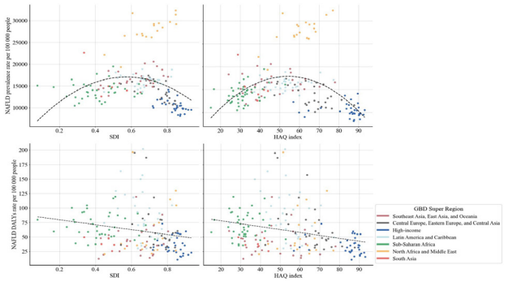

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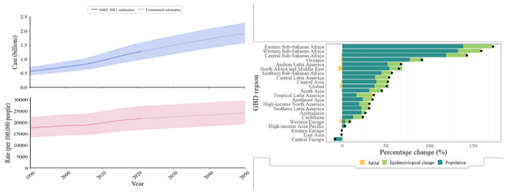

Figure 3.

PE-11

The Characteristics of Metabolic Dysfunction Associated Steatotic Liver Disease in Young College Students in Taiwan

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Aims: The features of metabolic dysfunction associated steatotic liver disease (MASLD) remains uncertain in young adult population. We aimed to investigate the risks of MASLD and disease severity in young college students.

Methods: We prospectively enrolled the first-year students, aged >18 years old, from Kaohsiung Medical University, Kaohsiung, Taiwan. Demographics, biochemistry including liver, renal function, blood glucose, and lipid profiles were collected during their health checkup. We also perform the elastography for assessment of hepatic steatosis and fibrosis. The primary endpoint was the prevalence and disease severity of MASLD in this young adult population.

Results: A total of 621 college freshmen were enrolled (mean age of 19.0 ± 1.4 years, 61% females). The mean body mass index (BMI) was 21.7 ± 3.8 kg/m^2. The prevalence of overweight and obesity were 27.6%/, and 14.8%, respectively. Male students had significantly higher BMI, ALT, fasting glucose, and triglycerides, but lower T-Chol, HDL-C levels than the females. The prevalence of elevated ALT level (>40 U/L) was 6.9%. The overall prevalence of MASLD was 13.5% and male students had a significantly higher risk of MASLD than females (19.0% vs. 10.0%, *P*=0.002). A total of 51.4 % of students had at least one cardiometabolic risk factor (CMRF) and male students had a significantly high proportion of carrying at least one CMRF (61.2% vs. 45.1%, p <0.001). The mean value of controlled attenuation parameter (CAP) was 199 ± 43 dB/m, and 15.0% of them had a CAP level> 238 dB/m. The mean liver stiffness was 4.6 ± 1.1 kPa and two (0.3%) students had liver stiffness> 8 kPa. Male students also had a significantly higher CAP and liver stiffness values than their female counterparts.

Conclusions: We observed a high risk of metabolic dysfunction in the first-year college students, especially male students. The findings suggest that lifestyle modifications could be implemented in the young population in order to reduce MASLD risk.

Keywords: Metabolic Dysfunction Associated Steatotic Liver Disease, Young Adults, Disease Severity, Risk Stratification

PE-12

Efficacy and Safety of Statins for Nonalcoholic Fatty Liver Diseases and Metabolic Dysfunction-Associated Fatty Liver Diseases: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Aims: Nonalcoholic fatty liver diseases (NAFLD) and metabolic dysfunction-associated fatty liver diseases (MAFLD) are closely associated with metabolic syndrome, including obesity, dyslipidemia, and insulin resistance (IR). Thus, stains may be considered for the management of NAFLD/MAFLD. However, its efficacy and safety remain unclear in NAFLD/MAFLD patients.

Methods: The PubMed, EMBASE, and Cochrane library databases were searched to identify randomized controlled trials (RCTs) evaluating the efficacy and/or safety of statins in NAFLD/MAFLD patients. Risk ratios (RRs) and weight mean differences (WMDs) with their 95% confidence intervals (CIs) were calculated. Subgroup analyses were performed.

Results: Overall, seven studies involving 993 patients with NAFLD/MAFLD were included. Statins were significantly associated with reductions in alanine aminotransferase (ALT, WMD=-9.76 U/L, 95%CI: -17.28, -2.24, P=0.010), aspartate aminotransferase (AST, WMD=-4.46 U/L, 95%CI: -9.03, 0.11, *P*=0.060), gamma-glutamyl-transpeptidase (GGT, WMD=-10.18 U/L, 95%CI: -13.65, -6.70, *P*<0.001), low-density lipoprotein (LDL, WMD=-0.86 mmol/L, 95%CI: -1.06, -0.66, *P*<0.001), total cholesterol (TC, WMD=-0.88 mmol/L, 95%CI: -1.14, -0.61, *P*<0.001), and triglyceride (TG, WMD=-0.32 U/L, 95%CI: -0.45, -0.19, *P*<0.001) levels. Additionally, statins did not increase the risk of myalgia (RR=0.96, 95%CI: 0.10, 9.00, *P*=0.970). In subgroup analyses of male patients, patients with age ≤50 years, or studies where no medication was given in control group, statins significantly decreased the level of liver enzymes, especially ALT and AST levels.

Conclusions: Statins could improve liver function and lipid profiles in NAFLD/MAFLD patients, without any increase in the risk of myalgia. It seems that statins should be recommended for the management of NAFLD/MAFLD.

Keywords: Statins, Nonalcoholic Fatty Liver Diseases, Metabolic Dysfunction-Associated Fatty Liver Diseases, Efficacy

PE-13

Exploring Significance of a Hypothetical Drug in View of Cost-effectiveness its Initial and Durable Efficacy in Metabolic-Associated Steatotic Liver Disease

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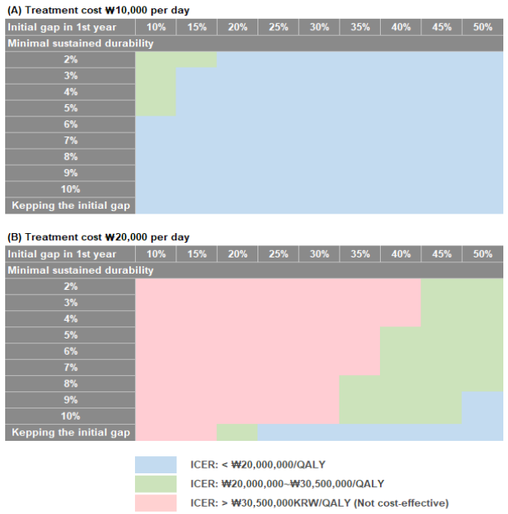
Aims: Although the first metabolic dysfunction-associated steatotic liver disease (MASLD) drug has shown a significant histological improvement in phase 3 trials, the small effect size in fibrosis regression is still unsatisfactory. This study aims to identify the minimum limit of both the initial and durable efficacy for a drug to be cost-effective.

Methods: A Markov model was developed to simulate MASLD progression, incorporating liver-related and cardiovascular events, and comparing costs and quality-adjusted life-years (QALYs) between 'Treatment with hypothetical Drug X' and 'No treatment.' The treatment effect on hepatic fibrosis was assumed as: 1) one-stage regression with a 25% greater effect than no treatment in year one; 2) effect waning by 50% annually until reaching a 2% minimum sustained durability. Incremental cost-effectiveness ratios (ICERs) were calculated over 20 years, assessing various fibrosis regression effects.

Results: In the base-case analysis, at the daily treatment cost of ₩10,000, the ICER was calculated to ₩15,073,177/QALY – below the ICER threshold of ₩3,050,000/QALY in Korea – which indicates that Drug X treatment is cost-effective. Sensitivity analyses identified the initial gap of effect size and sustained durable response in regression rate, and baseline fibrosis stage distribution were major key factors influencing cost-effectiveness of Drug X. In two-way sensitivity analyses, if the initial fibrosis regression gap was more than 10%, drug treatment was cost effective regardless of the size of sustained durability (Table 1). For this treatment to be cost-effective at double the price (₩20,000/day), it should achieve an initial fibrosis regression gap of at least 20% and remain constant in subsequent years, or achieve an initial gap of at least 40% and remain sustained durability with a gap of at least 5%.

Conclusions: Both the initial histologic response rate and the effect size of sustained durability of the drug are crucial for achieving cost-effectiveness in MASLD treatment.

Keywords: Metabolic Associated Steatotic Liver Disease, Cost Effectiveness, Efficacy



PE-14

Impact of Breast Cancer and Hormone Therapy on Liver Disease Progression in Patients with MASLD

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Aims: This prospective study aimed to assess the progression of metabolic dysfunction-associated steatotic liver disease (MASLD) among breast cancer (BC) patients compared to female patients without BC.

Methods: MASLD patients with BC who underwent surgery were prospectively enrolled at Ewha Womans University Mokdong Hospital between August 2018 and December 2022. Data from female patients without BC were retrospectively collected during the same period. The primary outcome was the relative change in hepatic steatosis, assessed using the controlled attenuation parameter (CAP) via vibration-controlled transient elastography (VCTE), from baseline to year 2.

Results: A total of 339 patients with BC and 2,200 patients without BC were included in the study. At baseline, the BC group had lower liver stiffness (LS) (4.7 kPa vs. 7.3 kPa) and CAP values (288 dB/m vs. 299 dB/m) compared to the non-BC group. At two years after the initial VCTE measurement, the CAP value increased in the BC group but decreased in the non-BC group (relative change: +7.6% vs. -4.1%; *P*<0.001). The relative change in LS value was similar between the two groups (+1.4% vs. -0.01%; *P*=0.119). In subgroup analysis, BC patients who received hormone therapy exhibited significant increases in both LS (+2.8% vs. -0.1%; *P*=0.039) and CAP (+7.3% vs. -4.1%; *P*<0.001) at year 2 compared to the non-BC group. Conversely, in BC patients who did not receive hormone therapy, the CAP value significantly increased (+9.9% vs. -4.1%; *P*<0.001), whereas the relative change in LS were not significantly different (-4.4% vs. -0.1%; *P*=0.064) compared to the non-BC group.

Conclusions: BC patients with MASLD experienced a significant increase in hepatic steatosis, whereas non-BC patients showed a reduction. Notably, those receiving hormone therapy exhibited a significant increase in both LS and CAP values, suggesting a potential impact of breast cancer and its treatments on MASLD progression.

Keywords: MASLD, Breast Cancer, Hormone Therapy

PE-15

Steatotic Liver Disease Predicts Lower Likelihood of LDLR Gene Mutations in Young Patients with Suspected Familial Hypercholesterolemia

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Aims: Familial hypercholesterolemia (FH) is an inherited disorder primarily caused by mutations in the low-density lipoprotein receptor (LDLR) gene. Early identification and appropriate management are essential for improving patient outcomes. Steatotic liver disease (SLD) is frequently associated with various metabolic dysfunctions, including dyslipidemia. In this study, we aimed to investigate the relationship between SLD and LDLR mutations in young patients suspected of having FH.

Methods: We retrospectively reviewed patients who underwent LDLR genetic testing for suspected FH at the Armed Forces Goyang Hospital between January 2022 and July 2024. SLD was defined as a controlled attenuation parameter (CAP) score of ≥238 dB/m. Relevant clinical, anthropometric, and laboratory data were collected at the time of genetic testing.

Results: A total of 111 patients underwent LDLR genetic testing, of whom 26 (23.4%) tested positive for LDLR mutations. Most were male (99.1%), with a mean age of 21.6 years. The proportion of impaired fasting glucose (IFG) was significantly lower in the mutation-positive group than in the mutation-negative group (*P*<0.05). The CAP score tended to be

lower in the mutation-positive group (P=0.085), and the prevalence of SLD was also lower in the mutation-positive group (P=0.025). In logistic regression analysis, the presence of SLD and IFG were each associated with a lower likelihood of having an LDLR mutation (P=0.030 and P=0.033, respectively). Furthermore, the CAP score demonstrated an inverse correlation with the Dutch Lipid Clinic Network score (r = −0.18).

Conclusions: The presence of hepatic steatosis, as indicated by a CAP score ≥238 dB/m, correlated with a decreased likelihood of carrying LDLR mutations in young patients with suspected FH. Evaluating hepatic steatosis may therefore serve as a supplementary guide for presuming FH in this population.

Keywords: Metabolic Dysfunction -Associated Steatotic Liver Disease, Familial Hypercholesterolemia, Controlled Attenuation Parameter

PE-16

A Randomized Controlled Trial to Evaluate the Effect of Vitamin D Supplementation on Nonalcoholic Fatty Liver Disease in Pediatric Patients

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Aims: The incidence of Nonalcoholic fatty liver disease (NAFLD) has been steadily rising in pediatric age group and is often associated with metabolic dysfunction and obesity. Recent evidence has proven efficacy of Vitamin D in improving liver health by reducing inflammation. Hence, this randomized controlled trial (RCT) was planned to evaluate the efficacy of vitamin D supplementation in children with NAFLD.

Methods: A placebo controlled RCT was conducted for a duration of 12 weeks at a tertiary care hospital. Children aged 8-16 years, diagnosed with NAFLD were randomly divided into two groups. Intervention group received 2,000 IU/day of vitamin D3 and the children in control group were given placebo for the study duration. The outcomes were measured at baseline and after 12 weeks. They included liver fat percentage, liver enzymes and C-reactive protein. Any changes in body mass index were also reported. Relevant statistical analysis was conducted and P<0.05 was considered as significant.

Results: Total 80 participants were recruited in the study and divided into 40 in each group. There was a significant reduction in liver fat percentage in intervention group as compared to control group (-14% vs -3%, P<0.01). There was a significant 18% reduction in ALT in intervention group compared to 6% in control group (P=0.03). There was 26% reduction in CRP levels in intervention group which did not reduce in control group (P<0.01). Both the groups reported no significant changes in body mass index of participants.

Conclusions: Thus, vitamin D supplementation was effective in improving inflammation, liver fat content and liver enzymes in pediatric NAFLD patients. Future studies with larger sample size must be conducted to further elucidate the adjunctive role of vitamin D in pediatric NAFLD.

Keywords: Cholecalciferol, Metabolic Dysfunction-Associated Steatotic Liver Disease

PE-17

Impact of Thyroid Hormone Replacement on MASLD Progression in Hypothyroid Patients: A Hospital-Based Cohort Study in Chennai, India

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Aims: 1) To analyze the effect of thyroid hormone replacement on MASLD progression in hypothyroid patients over six months

2) To compare disease severity before and after treatment

Methods: A hospital-based cohort study was conducted at ACS Medical College and Hospital, Chennai, from January 2024 to January 2025, enrolling 300 hypothyroid patients based on inclusion criteria. Baseline assessments included TSH, liver function tests, lipid profile, platelet count, and FibroScan before initiating thyroid hormone replacement therapy for six months. Disease progression was evaluated using the Aspartate Aminotransferase to Platelet Ratio Index (APRI) score at baseline and follow-up. A Paired T-test was done to analyse the statistical difference. A p-value (<0.05) was considered significant. Data were analysed using SPSS 25.0 software

Results: Thyroid hormone replacement therapy led to a significant reduction in TSH levels, APRI scores, and AST levels, along with a notable increase in platelet count, suggesting an improvement in liver function and a potential slowdown in MASLD progression.

All parameters showed statistically significant improvement post-treatment (P<0.05).

Conclusions: Thyroid hormone replacement treatment improves MASLD markers in hypothyroid patients, guiding clinicians in optimizing treatment to mitigate disease progression.

Table 7: Association between Before and After Treatment

Parameters	Before Treatment	After Treatment	P-value
TSH	10.23 ± 3.76	5.33 ± 2.85	0.01*
AST	64.39 ± 48.92	35.07 ± 22.05	0.01*
APRI	1.06 ± 0.58	0.39 ± 0.40	0.01*
Platelet Count	122.43 ± 115.80	272.03 ± 164.33	0.01*

*P value <0.05 is significant.

Table 6: Distribution of subjects according to their APRI Score Category Before and After Treatment

APRI Score	Before		After	
	Frequency	Percentage	Frequency	Percentage
>1.5	86	28.7	16	5.3
0.5 – 1.5	131	43.7	33	11.0
<0.5	83	27.7	251	83.7
Total	300	100.0	300	100.0

Keywords: APRI- Aspartate Aminotransferase to Platelet Ratio Index, MASLD- Metabolic Dysfunction Associated Steatotic Liver Disease, Hypothyroidism, LIPID

PE-18

Unraveling Platelet Dynamics in MASLD: A Silent Catalyst in the March toward Cirrhosis

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Aims: MASLD is a growing global health concern, affecting nearly one-third of the population and increasing cirrhosis risk. While MASH is well studied, platelet involvement remains unclear. Thyroid hormones regulate lipid metabolism, insulin sensitivity, and inflammation. Their dysfunction promotes platelet activation and thrombosis, accelerating fibrosis. This study examines platelet activation, thyroid dysfunction, and MASLD severity in cirrhosis progression.

Methods: A retrospective analysis of 200 samples collected from ACS Medical College and Hospital was conducted. The MASLD Severity Index (MSI) was calculated using AST, ALT, Triglycerides, HDL, TSH, and FT4 levels. Participants were categorized into two groups based on MSI (<30 and >30). Statistical analysis was performed using SPSS 20 to identify significant correlations between metabolic and hematological parameters.

Results: The MSI >30 group exhibited significant increases in Fasting glucose (P<0.05), T3, T4 (P<0.01), TSH (P<0.01), TGL (P<0.01), VLDL (P<0.01), AST/ALT ratio (P<0.05), TDRI (P<0.05), TFMI (P<0.05), HIMI (P<0.05), TyG (P<0.05), and MRS (P<0.05) and elevated AST/ALT ratio (P<0.05) and TGL/HDL ratio (P<0.01) indicate progressive hepatic damage and worsening lipid metabolism, further potentiating fibrotic transformation, while Platelet count (P<0.05) was significantly reduced. Thyroid dysfunction was associated with increased platelet activation and a hypercoagulable state, exacerbating fibrosis.

Conclusions: This study links MASLD severity, metabolic dysfunction, and a prothrombotic state, worsened by thyroid abnormalities. The MASLD Severity Index (MSI) correlates with fasting glucose, bilirubin, AST, ALT, ALP, hemoglobin, platelets, and thyroid dysfunction markers (TSH, FT4, TDRI, TFMI, HIMI), indicating hepatic stress, inflammation, and coagulation dysfunction. Elevated TSH and reduced FT4 drive lipid dysregulation, insulin resistance, and platelet activation, increasing triglycerides, VLDL, AST, ALT, and the TGL/HDL ratio, leading to fibrosis and endothelial dysfunction. Despite lower platelet counts, increased adhesion suggests a hypercoagulable state, microthrombosis, and hepatocellular injury. Thyroid dysfunction and insulin resistance drive MASLD-related thrombosis, fibrosis, and cirrhosis, necessitating targeted metabolic and hematological interventions.

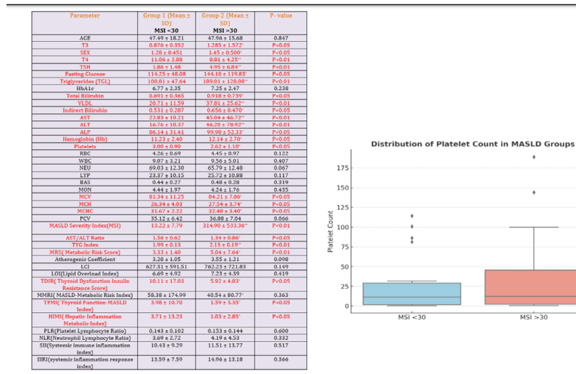

Figure 1.

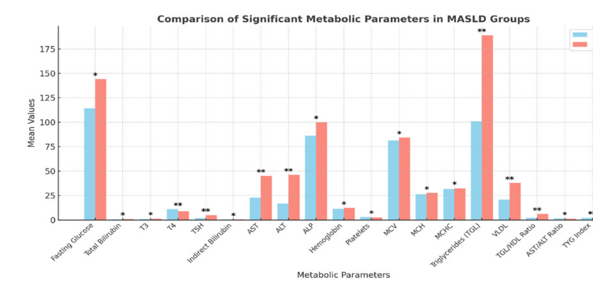

Figure 2.

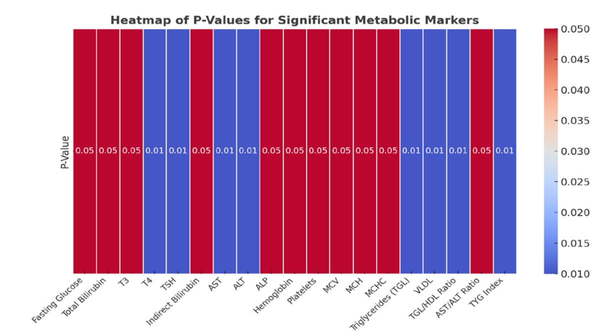

Figure 3.

Keywords: MASLD Severity Index (MSI), Thyroid Dysfunction And Insulin Resistance, Platelet Activation and Thrombosis, Fibrosis Progression and Cirrhosis Risk

PE-19

A Prospective Observational Study to Evaluate the Efficacy and Safety of Obeticholic Acid in Patients with Advanced Liver Fibrosis due to Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: Obeticholic Acid is a recently approved Farnesoid X Receptor (FXR) agonist which is used for primary biliary cholangitis. This study was conducted to investigate the efficacy and safety of this drug in patients with advanced liver fibrosis due to metabolic dysfunction-associated steatotic liver disease (MASLD).

Methods: This was a prospective observational study carried out over a duration of one and half years at a tertiary care hospital in India. Patients with MASLD and biopsy confirmed advanced fibrosis (stage F2-F3) were included in the study. The patients were given Obeticholic Acid 10 mg daily (titrated to 25 mg) for 12 months. The primary outcome of fibrosis regression was assessed using transient elastography and serum biomarkers with Enhanced Liver Fibrosis (ELF) score and Fibrosis-4 (FIB-4) index. Secondary outcomes included adverse events, improvement in metabolic parameters and liver enzymes. Relevant statistical tests were used and $P<0.05$ was considered significant.

Results: Total 180 patients with advanced liver fibrosis due to MASLD were recruited in the study. The average age of the patients was 51.63 ± 2.71 years. At the end of 12-month treatment period, there was evidence of one-stage regression in fibrosis in 41% patients on transient elastography ($P<0.001$). There was significant reduction in liver stiffness of 3.1kPa. There was significant improvement in ELF score and FIB-4 index ($P<0.05$). ALT decreased by 34% and AST decreased by 27% ($P<0.005$). Lipid profile and insulin resistance also improved but it was not statistically significant. The most common adverse event was pruritus which was observed in 22% patients and required dose reduction in 9% cases. No serious or life-threatening adverse events were reported.

Conclusions: Obeticholic Acid is a novel Farnesoid X Receptor (FXR) agonist agent which shows significant activity in fibrosis regression and improving metabolic profile in patients with MASLD. Further studies must be conducted with larger sample size and to evaluate long term safety of the drug.

Keywords: FXR Agonist, Fibrosis Regression, Pharmacotherapy

PE-20

Ultrasound Elastography in Fatty Liver vs.Normal Controls: A Retrospective Study

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Millennium Seoul IM Clinic

Aims: Metabolic associated statohepatic liver disease (MASLD) is increasing with lifestyle changes, making early detection of fibrosis crucial. In primary care settings where Fibroscan is unavailable, ultrasound elastography offers a cost-effective alternative for assessing liver stiffness.

Methods: Between January and December 2024, 20 patients from a primary care clinic underwent abdominal ultrasound. Ten patients with fatty liver findings (fatty liver group) were compared with 10 patients with normal liver appearances (control group). Baseline characteristics (mean age ~52 years, 60% female, weight 65±7 kg, AST 35±8 IU/L, ALT 38±9 IU/L) showed no significant differences between the groups. All patients underwent both B-mode ultrasound and elastography using the same device.

Results: The fatty liver group exhibited a mean stiffness of 4.5 kPa compared to 3.2 kPa in controls. Although the difference was not statistically significant ($p > 0.05$), a trend toward higher liver stiffness that correlated with the severity of fatty liver findings was observed.

Variable	Fatty Liver Group (n = 10)	Control Group (n = 10)
Age (years)	54 ± 8	50 ± 7
Gender (Female %)	60%	60%
Weight (kg)	68 ± 7	65 ± 8
BMI (kg/m²)	26.3 ± 2.1	25.1 ± 2.0
Hypertension (%)	30%	20%
Diabetes (%)	20%	10%

Table 1. Baseline Characteristics

Parameter	Fatty Liver Group (n = 10)	Control Group (n = 10)
Liver Stiffness (kPa)	4.5 ± 0.8	3.2 ± 0.7
AST (IU/L)	35 ± 7	32 ± 6
ALT (IU/L)	38 ± 8	34 ± 7
Albumin (g/dL)	4.1 ± 0.3	4.3 ± 0.2

Table 2. Liver Stiffness and Laboratory Measurements

Conclusions: These findings suggest that ultrasound elastography may help assess MASLD in primary care, even though the results were not statistically significant. Further large-scale prospective studies are warranted to confirm these trends and validate the clinical applicability of elastography in evaluating MASLD.

Keywords: Ultrasound Elastography, MASLD, Liver Stiffness

PE-21

Risk of Major Adverse Liver Outcomes in Patients with Metabolic Dysfunction-Associated Steatohepatitis: A Large Population-Based Retrospective Cohort Study

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Aims: Patients with metabolic dysfunction-associated steatohepatitis (MASH) are at increased risk for major adverse liver outcomes (MALO). However, research on the magnitude of this association in real-world settings is scarce. This study aimed to determine the extent to which patients with MASH have an increased risk for MALO compared to patients without MASH.

Methods: In this retrospective cohort study using Optum's de-identified Clinformatics® Data Mart Database, patients (≥18 years) with MASH were identified and matched with patients without MASH. MALO was defined as any evidence of cirrhosis, hepatocellular carcinoma (HCC), or liver transplant (LT). Kaplan-Meier survival rates were estimated, and the risk of MALO was analyzed using a Fine and Gray model accounting for competing risk of death. Subgroup analyses were conducted stratified by type 2 diabetes status and age group.

Results: In the matched cohort (n=26,301 pairs), patients had a mean age of 59.0 years, with 56.3% being female. Over the follow-up period, MALO occurred more frequently in patients with MASH (116.8 vs. 15.5 events per 1,000 person-years; IRR=7.55, 95% CI: 7.00-8.15). Patients with MASH also had significantly higher rates of cirrhosis (IRR: 7.85; 95% CI: 7.26-8.49), HCC (5.07; 3.94-6.51), and LT (18.42; 7.53-45.09). After adjusting for baseline confounders, the risk for MALO remained significantly higher (adjusted HR: 6.78; 95% CI: 6.27-7.34) among patients with MASH). Results were similar in the subgroup analyses.

Conclusions: Patients with MASH demonstrated a sevenfold higher risk for MALO than those without MASH. This highlights the significant clinical burden of MASH, underscoring the need for enhanced early detection and therapeutic strategies.

Keywords: MASH, NASH, MASLD, NAFLD, Metabolic

PE-22

Cardiovascular Disease Burden in Patients with and without Metabolic Dysfunction-Associated Steatohepatitis: Data from the unCoVer-MASH Longitudinal Cohort Study

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Aims: Metabolic dysfunction-associated steatohepatitis (MASH) is linked to increased cardiovascular (CV) disease (CVD) risk, but many aspects of CVD burden in MASH patients remain unknown. This study aimed to assess CVD burden in patients with and without MASH.

Methods: Patients with MASH were identified using the International Classification of Diseases code for non-alcoholic steatohepatitis (K75.81) from October 2015–June 2022, using data from a federated network (TriNetX). Exclusion criteria included viral hepatitis, alcohol use disorder, chronic liver diseases other than MASH, cirrhosis, decompensated MASH, hepatocellular carcinoma, and human immunodeficiency virus. Patients with MASH were matched 1:1 to patients without MASH based on demographics. Outcomes were CVD prevalence and risk of CV events during follow-up amongst patients with no history of respective CV events at baseline. Cumulative incidence was plotted using Aalen-Johansen curves after adjusting for competing risk of non-CV death. Incidence rate (IR) and hazard ratios (HR) were calculated using Cox proportional hazard models.

Results: In total, 9,642 patients (4,821 with MASH; 4,821 without MASH) were included. Mean age was 50.8 years, and 58.5% were women. Compared with those without MASH, more patients with MASH had hypertension, hyperlipidaemia, obesity, type 2 diabetes, and chronic kidney disease at baseline. Prevalence of any CVD was higher in patients with MASH than without MASH (23% vs 12%), as was risk of any CV event (IR: 11.1 vs 4.5 per 100 person-years; adjusted HR: 2.27, $P<0.0001$). Similar results were seen for individual CV events, namely ischaemic heart disease), cerebrovascular disease, atherosclerosis, and heart failure .

Conclusions: CVD prevalence at baseline and risk of CV events during follow-up were significantly higher in patients with non-cirrhotic MASH compared with matched controls without MASH in a real world cohort.. These data provide additional evidence of the association between MASH and CVD.

Keywords: MASH, NASH, MASLD, NAFLD, Metabolic, Cardiovascular

PE-23

Phase 3 ESSENCE Trial of Semaglutide 2.4 MG in Participants with Non-Cirrhotic Non-Alcoholic Steatohepatitis: Baseline Characteristics, Impact of New Metabolic Dysfunction-Associated Steatotic Liver Disease Criteria and Non-invasive Tests

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[*]Presenting on behalf of the authors, [1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Korea; [2]National Institute for Health Research, Birmingham Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust and Centre for Liver and Gastrointestinal Research, Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK; [3]Institute of Hepatology, Faculty of Life Sciences and Medicine, King's College London and King's College Hospital, London, UK; [4]Department of Medical Sciences, University of Turin, Turin, Italy; [5]Sorbonne Université, Institute for Cardiometabolism and Nutrition, Hospital Pitié-Salpêtrière, INSERM UMRS 1138 CRC, Paris, France; [6]Department of Medicine, University of Chicago, Chicago, IL, USA; [7]Department of Endocrinology and Diabetology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany; [8]German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Germany; [9]Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany; [10]Novo Nordisk A/S, Copenhagen, Denmark; [11]Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, VCU School of Medicine, Richmond, VA, USA

Aims: This study reports the baseline characteristics of participants in the Phase 3 ESSENCE trial (NCT04822181) of semaglutide for non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH).

Methods: 800 participants with MASH and fibrosis stages 2/3 (F2/F3) were randomised 2:1 to receive semaglutide 2.4 mg subcutaneous once weekly (OW) or placebo OW added to standard of care. The primary endpoints at 72 weeks are resolution of steatohepatitis and no worsening of liver fibrosis, and improvement in liver fibrosis and no worsening of steatohepatitis. Inclusion criteria were histological presence of steatohepatitis stages F2/F3 and a non-alcoholic fatty liver disease activity score (NAS) of ≥ 4.

Results: 800 participants (250 F2; 550 F3) were randomised. Mean age was 56 years; 57.1% were female; ≥ 99% had ≥ 1 cardiometabolic risk factor(s). Mean NAS was 5.05, higher in F3 versus F2 (5.11 vs 4.92). Participants with higher NAS had more cardiometabolic risk factors (52.9% with NAS ≥ 5 vs 45.3% with NAS 4). A greater proportion of participants with F3 had all five cardiometabolic risk factors versus F2 (52.9% vs 44.8%). Although cardiometabolic comorbidities were highly prevalent, 44.5% did not have type 2 diabetes (T2D), and 27.3% did not have obesity. Normal liver transaminases were observed in 26.3% of participants. Mean FibroScan liver stiffness was 12.8 kPa, with values of < 8 kPa in 15.3% of participants. Mean enhanced liver fibrosis (ELF) score was 10.0, with 43.5% having an ELF score of < 9.8. Overall, 8.8% and 9.0% of participants with/without T2D did not meet any non-invasive criteria: Fibrosis-4 index ≥ 1.3, vibration-controlled transient elastography ≥ 8.1, or ELF ≥ 9.8, and more participants with F2 did not meet these criteria versus F3.

Conclusions: The ESSENCE baseline population includes participants with significant fibrosis (F2 and F3) and approximately 91% had ≥ 1 positive diagnostic non-invasive test. Cardiometabolic risk factors were found in ≥ 99% of participants, increasing with higher NAS and fibrosis stages.

Keywords: MASH, NASH, MASLD, NAFLD, Metabolic

PE-24

Metabolic Dysfunction-Associated Steatotic Liver Disease and the Risk of Cardiovascular Disease: Results from Two Independent Nationwide Cohort Studies

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Aims: There is a lack of evidence on whether metabolic dysfunction-associated steatotic liver disease (MASLD) is associated with an increased risk of cardiovascular disease (CVD) or whether it outperforms metabolic dysfunction-associated fatty liver disease (MAFLD) in predicting CVD risk. This study aimed to compare the incidence of CVD according to MASLD and/or MAFLD status using two independent nationwide cohorts.

Methods: A population-based cohort was established using data from the general health screening program provided by the National Health Insurance Service (NHIS) of Korea in 2009. In parallel, we also utilized UK Biobank phenotype data, which is a population-based prospective cohort consisting of UK residents enrolled between 2006 and 2010. Hepatic steatosis was identified using a fatty liver index greater than 30. The primary outcome was the incidence of composite CVD events, which included myocardial infarction, ischemic stroke, heart failure, and CVD-related death.

Results: A total of 7,198,643 patients were included in the Korean NHIS, and they were categorized as MASLD (*n*=2,056,609) or MAFLD (*n*=2,388,436). Patients with MASLD or MAFLD had a higher risk of CVD compared to the control group (MASLD: subdistribution hazard ratio [SHR]=1.43, 95% confidence interval [95% CI]=1.42–1.44, *P*<0.001; MAFLD: SHR=1.42, 95% CI=1.40–1.43, *P*<0.001). Patients satisfying both MASLD and MAFLD criteria showed a significantly higher risk of CVD (SHR=1.44, 95% CI=1.42–1.45, *P*<0.001), followed by those with MASLD only (SHR=1.28, 95% CI=1.26–1.31, *P*<0.001) and MAFLD only (SHR=1.14, 95% CI=1.07–1.21, *P*<0.001). Similar results were reproduced in the UK biobank cohort (*n*=485,895), where MASLD was associated with a greater risk of CVD compared to the control group (SHR=1.65, 95% CI=1.60–1.71, *P*<0.001).

Conclusions: Patients with MASLD had a higher risk of CVD compared to those without steatotic liver disease. Using both MASLD and MAFLD criteria, patients at higher risk for CVD may be appropriately identified.

Keywords: Fatty Liver, Cardiovascular Risk, Nationwide Cohort, UK Biobank

PE-25

Risk of Pyogenic Liver Abscess and its Clinical Complications in Metabolic Dysfunction-Associated Steatotic Liver Disease: A Nationwide Cohort Study

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Aims: Pyogenic liver abscess (PLA) is a severe infectious disease with significant morbidity and mortality. This study investigated the association between metabolic dysfunction-associated liver disease (MASLD) and PLA incidence, as well as the risk of PLA complications.

Methods: We analyzed data from 2,951,003 adults aged 40–64 years who underwent health examinations between 2009 and 2010, as recorded in the Korean National Health Insurance Service database. Hepatic steatosis was defined as a fatty liver index ≥30, and MASLD was identified based on established criteria. Cox proportional hazards models were used to assess the risk of PLA and its complications. Additionally, changes in MASLD status over a four-year follow-up period were evaluated for their impact on PLA risk.

Results: Over a median follow-up of 13 years (IQR 13–14), PLA occurred in 3,152 individuals with MASLD (N=881,466) and 3,169 individuals without any SLD (N=1,797,978). The incidence rate of PLA was 27.2 vs. 13.3 per 100,000 person-years in the MASLD and non-SLD group, respectively. MASLD was significantly associated with an increased risk of PLA (HR: 1.53, 95% CI: 1.45–1.61) and its complications (HR: 1.72, 95% CI: 1.27–2.33) compared to non-SLD. In the 4-year follow-up analysis, individuals with persistent MASLD had the highest risk of PLA (HR: 1.61, 95% CI: 1.39–1.74), followed by those who MASLD regressed to non-SLD (HR: 1.38, 95% CI: 1.23–1.53) and who developed MASLD during follow-up (HR: 1.27, 95% CI: 1.13–1.43) compared to individuals without any SLD at both baseline and follow-up. Other SLD categories, including MetALD, MASLD with other combined etiologies, and the ALD group, also showed a higher risk of PLA compared to the non-SLD group.

Conclusions: MASLD was significantly associated with an increased risk of PLA and its complications, with the highest risk observed in individuals with persistent MASLD.

Keywords: MASLD, Pyogenic Liver Abscess

PE-26

Prevalence and Trends of Metabolic Syndrome among Chronic Viral Hepatitis Patients in Korea: A KNHANES 2013-2022 Analysis

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Aims: As treatments for chronic viral hepatitis have advanced, identifying and managing concurrent metabolic dysfunction-associated steatotic liver disease in these patients has become increasingly crucial. This study utilizes data from the Korea National Health and Nutrition Examination Survey (KNHANES) from 2013 to 2022 to examine trends in the prevalence of metabolic syndrome among patients with viral hepatitis over the past decade.

Methods: Data from KNHANES spanning 2013 to 2022 were analyzed. Patients with chronic hepatitis B (CHB) were identified through self-reported illness or a positive HBsAg test, and those with chronic hepatitis C (CHC) through self-reported illness or a positive anti-HCV test. Cases were matched 1:1 by age (± 5 years), gender, and primary sampling units (variable psu), as well as variance estimation strata (variable ksatrata).

Results: A total of 1107 CHB and 318 CHC patients were identified. The average age of CHB patients increased from 48.4 years in 2013 to 58.1 years in 2021, with the prevalence of metabolic syndrome also rising from 21.4% in 2013 to 38.8% in 2021 (p for trend = 0.015). However, when adjusted for age,

gender, and stratification variables, the prevalence was not significantly higher than in the control group (32.2% vs. 36.0%, *P*=0.05). CHC patients showed a similar age progression and an increasing trend in metabolic syndrome prevalence from 22.2% in 2013 to 48.6% in 2021 (p for trend = 0.252), with no significant difference from controls after adjustment (*P*=0.575).

Conclusions: This study indicates that while chronic viral hepatitis patients in Korea are aging and experiencing increased metabolic syndrome, the prevalence does not exceed that of the general population when adjusted for demographic factors.

Keywords: Metabolic Syndrome, Chronic Hepatitis B, Chronic Hepatitis C, Prevalence

PE-27

Association of Metabolic Dysfunction-Associated Steatotic Liver Disease and Subclinical Coronary Atherosclerosis: Observation Cohort Study

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Aims: Previous population-based studies have demonstrated differences in cardiovascular events according to the new classification of steatotic liver disease (SLD). However, detailed data on coronary artery status have not been presented. Therefore, we aimed to investigate the association between SLD classifications and coronary artery status using findings from coronary computed tomography angiography (CCTA).

Methods: We analyzed 8,622 asymptomatic individuals without coronary artery disease (CAD) who underwent both abdominal ultrasonography and CCTA. Study participants were divided into four groups: 934 in the no SLD without cardiometabolic (CM) criteria group, 4,811 in the no SLD with CM criteria group, 2,494 in the metabolic dysfunction-associated steatotic liver disease (MASLD) group, and 252 in the MASLD with increased alcohol intake (Met-ALD) group. Obstructive CAD was defined as coronary arterial stenosis ≥50%.

Results: Compared with the no SLD without CM group, the no SLD with CM, MASLD, and Met-ALD groups were significantly associated with any coronary plaque (multivariable-adjusted OR 2.05 [95% CI 1.67–2.52], 2.71 [2.18–3.35], and 2.36 [1.69–3.31], respectively); calcified plaques (1.97 [1.59–2.43], 2.54 [2.04–3.16], and 2.10 [1.49–2.96], respectively); non-calcified plaques (2.04 [1.28–3.25], 2.42 [1.51–3.89], and 3.26 [1.73–6.13], respectively); and obstructive CAD (2.57 [1.53–4.32], 3.64 [2.15–6.16], and 3.51 [1.73–7.10], respectively) (p for all <0.05). In addition, the inverse probability of treatment weighting (IPTW) analyses showed similar ORs for coronary plaques and obstructive CAD. Additionally, higher steatosis-associated fibrosis estimator (SAFE) was strongly associated with all atherosclerotic plaques and obstructive CAD. This association remained significant across adjusted and IPTW analyses.

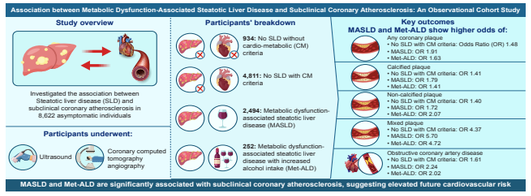
Conclusions: Subtypes of SLD had significant, yet different strengths of associations with subclinical coronary atherosclerosis.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, MET-ALD, Computed Tomography Angiography

Table 1. Baseline characteristics in study population

	No SLD without CM criteria (n=934)	No SLD with CM criteria (n=4,811)	MASLD (n=2,494)	Met-ALD (n=252)	p-value
Age, years old, mean ± SD	51.0 ± 8.1	54.2 ± 8.1	54.1 ± 7.9	51.9 ± 7.0	<0.001
Male sex, no. (%)	430 (46.0%)	2,930 (60.9%)	1,826 (73.2%)	218 (86.5%)	<0.001
Body mass index, kg/m^2, mean ± SD	20.7 ± 1.5	23.8 ± 2.4	25.9 ± 2.8	25.7 ± 2.7	<0.001
Waist circumference (cm), male	78.5 ± 4.6	85.7 ± 6.2	90.7 ± 6.8	90.1 ± 6.5	<0.001
Waist circumference (cm), female	74.2 ± 4.0	82.7 ± 6.7	88.1 ± 7.6	88.4 ± 8.5	<0.001
Systolic blood pressure, mmHg, mean ± SD	113.4 ± 10.1	125.0 ± 13.8	128.2 ± 13.1	126.8 ± 12.1	<0.001
Diastolic blood pressure, mmHg, mean ± SD	71.7 ± 7.6	78.4 ± 9.4	80.3 ± 8.9	80.7 ± 8.9	<0.001
Hypertension, no. (%)	0 (0%)	1,621 33.7%)	1,064 (42.7%)	115 (45.6%)	<0.001
Anti-hypertensive agent, no. (%)	0 (0%)	982 (21.4%)	659 (26.4%)	78 (31.0%)	<0.001
Diabetes mellitus, no. (%)	0 (0%)	470 (9.8%)	531 (21.3%)	46 (18.3%)	<0.001
Glucose lowering agent, no. (%)	0 (0%)	316 (6.6%)	315 (12.6%)	24 (9.5%)	<0.001
Lipid-lowering agent use, no. (%)	0 (0%)	312 (6.5%)	216 (8.7%)	20 (7.9%)	<0.001
Obesity[a], no. (%)	0 (0%)	1,375 (28.6%)	1,498 (60.1%)	141 (56.0%)	<0.001
Family history of CAD[b], no. (%)	97 (10.4%)	428 (8.9%)	224 (9.0%)	18 (7.1%)	0.280
Alcohol intake[c], no. (%)					<0.001
None	384 (41.1%)	1,708 (35.5%)	925 (37.1%)	0 (0%)	
Mild	373 (39.9%)	2,122 (44.1%)	1,569 (62.9%)	0 (0%)	
Moderate	65 (7.0%)	336 (7.0%)	0 (0%)	252 (100%)	
Heavy	112 (12.0%)	645 (13.4%)	0 (0%)	0 (0%)	
Tobacco use, (n, %)					<0.001
Never	587 (62.9%)	2,435 (50.6%)	985 (39.5%)	62 (24.6%)	
Past	198 (21.2%)	1,393 (28.95%)	885 (35.5%)	111 (44.1%)	
Current	149 (16.0%)	983 (20.4%)	624 (25.0%)	79 (31.4%)	
Physical activity[d]					
Moderate intensity (day)	1.5 ± 1.7	1.8 ± 1.8	1.4 ± 1.7	1.4 ± 1.5	<0.001
High intensity (day)	1.2 ± 1.5	1.4 ± 1.7	1.1 ± 1.4	1.2 ± 1.3	<0.001
Current marital status, yes, no. (%)	841 (90.0%)	4,287 (89.1%)	2,250 (90.2%)	231 (91.7%)	0.342
Monthly income (Korean won)					0.002
< 2 million	51 (5.5%)	378 (7.9%)	152 (6.1%)	12 (4.8%)	
2 - 4 million	166 (17.8%)	914 (19.0%)	448 (18.0%)	39 (15.5%)	
4 - 6 million	201 (21.5%)	997 (20.7%)	524 (21.0%)	71 (28.2%)	
≥ 6 million	457 (48.9%)	2,187 (45.5%)	1,217 (48.8%)	122 (48.4%)	
Unknown	59 (6.3%)	335 (7.0%)	153 (6.1%)	8 (3.2%)	
Fasting blood glucose, mg/dL, mean ± SD	83.7 ± 9.4	94.1 ± 18.9	103.3 ± 26.8	102.9 ± 24.0	<0.001
Glycated hemoglobin, %, mean ± SD	5.3 ± 0.2	5.6 ± 0.6	6.0 ± 1.0	5.9 ± 0.9	<0.001
Total cholesterol, mg/dL, mean ± SD	189.6 ± 34.6	188.6 ± 36.1	195.0 ± 37.7	199.0 ± 37.8	<0.001
LDL-cholesterol, mg/dL, mean ± SD	121.6 ±32.9	125.3 ± 33.4	132.4 ± 34.7	133.4 ± 36.3	<0.001
HDL-cholesterol, mg/dL, mean ± SD	64.8 ± 14.9	54.3 ± 14.9	47.1 ± 12.1	47.4 ± 10.7	<0.001
Triglyceride, mg/dL, mean ± SD	71.2 ± 27.1	103.4 ± 60.9	148.5 ± 95.3	158.6 ± 101.5	<0.001
Creatinine, mg/dL, mean ± SD	0.8 ± 0.2	0.8 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	<0.001
AST, IU/L, mean ± SD	22.2 ± 10.9	23.4 ± 11.0	28.1 ± 15.6	29.6 ± 18.7	<0.001
ALT, IU/L, mean ± SD	19.5 ± 15.4	23.3 ± 14.3	35.3 ± 23.3	36.9 ± 25.3	<0.001
ALT > upper normal limit, no. (%)	420 (45.0%)	2,004 (41.7%)	1,053 (42.2%)	109 (43.3%)	0.266
NFS	-2.4 ± 0.9	-2.1 ± 1.0	-2.2 ± 1.0	-2.3 ± 1.0	<0.001
NFS ≥ -1.455, no. (%)	128 (13.7%)	1,158 (24.1%)	564 (22.6%)	51 (20.24%)	<0.001
NFS < -1.455, no. (%)	806 (86.3%)	3,653 (75.9%)	1,930 (77.4%)	201 (79.8%)	
SAFE score, mean ± SD	37.9 ± 36.8	50.1 ± 41.8	53.9 ± 45.1	47.1 ± 43.6	<0.001
SAFE score <0, no. (%)	130 (13.9%)	461 (9.6%)	226 (9.1%)	30 (11.9%)	<0.001
0 ≤ SAFE < 100, no. (%)	758 (81.2%)	3,820 (79.4%)	1,905 (76.4%)	190 (75.4%)	
SAFE score ≥100, no. (%)	46 (4.9%)	530 (11.0%)	363 (14.6%)	32 (12.7%)	

Values are presented as mean±standard deviation or number (%).
[a]Defined as a body mass index ≥25 kg/m^2.
[b]Defined as family history of coronary artery disease in a first-degree relative of any age.
[c]Alcohol intake was categorized according to the criteria specified by diagnostic criteria for new SLD classification, based on the calculated average daily intake expressed in grams.
[d]Physical activity was assessed using the validated Korean version of the self-administered International Physical Activity Questionnaire, focusing on activities over the past seven day.
SLD, steatotic liver disease; CM, cardiometabolic; MASLD, metabolic dysfunction-associated steatotic liver disease; Met-ALD, metabolic dysfunction-associated alcoholic liver disease; SD, standard deviation; LDL, low density lipoprotein; HDL, high density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; NFS, non-alcoholic fatty liver disease fibrosis score; SAFE score, steatosis-associated fibrosis estimator score; HSI, hepatic steatosis index.



PE-28

Improved Decision-Making in Advanced Fibrosis Assessment through the Incorporation of PNPLA3 and TM6SF2 Genetic Information into Existing Non-Invasive Test Scores

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Aims: Genetic information is not yet used for the clinical diagnosis of advanced fibrosis in patients with metabolic dysfunction-associated steatotic liver disease (MASLD). Here we investigated whether incorporating genetic information regarding *PNPLA3* and *TM6SF2* into existing non-invasive fibrosis scoring systems could enhance the predictive accuracy, particularly in terms of reducing indeterminate diagnostic zones.

Methods: Data were collected from a cohort of 573 patients with biopsy-proven MASLD. All participants underwent liver stiffness measurement (LSM), serum marker analysis, and genotyping for *PNPLA3* (rs738409), *TM6SF2* (rs58542926), and other relevant SNPs. We evaluated the benefit of adding genetic information to existing non-invasive tests (NITs) —including the Agile 3+, Fibrosis-4 (FIB-4) index, and NAFLD fibrosis score (NFS).

Results: Decision curve analysis (DCA) was performed to determine the net benefit of adding genetic information, and we analyzed its impact on reducing indeterminate zones. Integrating genotype data into existing NITs improved their diagnostic performance, as demonstrated by higher net benefits compared to models without genetic information. The net benefit at a 30% threshold increased from 18.7 to 19.0 per 100 patients with genotypes for Agile 3+, increased from 12.7 to 13.7 for the NFS, and increased from 9.2 to 12.1 for FIB-4.

Conclusions: Incorporating genetic data into NITs for MASLD enhanced their predictive accuracy. Addition of genetic data particularly reduced indeterminate zones, thereby offering a more reliable tool for identifying patients at risk for advanced fibrosis. The proposed approach may improve clinical decision-making and outcomes.

Keywords: MASLD, Genotype, NIT, DCR

PE-29

Metabolic Dysfunction Associated Steatotic Liver Disease: Trivandrum Cohort 3

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Aims: To evaluate the prevalence and risk factors for Metabolic dysfunction Associated Steatotic Liver Disease in South India, Kerala

Methods: Between May 2022 to September 2023, 2846 participants (Male 47.2 % and females 52.8%) were recruited through multistage cluster sampling across the whole population of Trivandrum, within the state of Kerala, South India. Data (gender, level of education, work status, marital status and religion, history of tobacco smoking/chewing and alcohol intake, height in centimetres, weight in Kg, waist circumference in cm) were collected from all inhabitants of randomly selected households over the age of 25. Liver stiffness and fat content were evaluated by Fibrotouch (FT; FibroTouch-FT5000, iLivTouch series, Wuxi Hisky Medical Technologies, China). Categorical data are presented as numbers (percentage) and continuous data as mean (SD) for normally distributed data and medians (range) for non-parametric data. Univariate and multivariate analysis to compare characteristics of the cohort with/without MASLD (using the definition laid down by EASL) was undertaken and Odds ratio with 95% confidence intervals were computed .

Results: The MASLD prevalence within this population was 65.8% (95% CI 64-67.52 %%). Mean age was 51.71 years. Median Stiffness of liver >10.2 was seen in 20.5% in MASLD compared to those without MASLD (13.2%: *P*<0.001) . Table 1 and 2 denote the variables and the risk association.

Conclusions: MASLD is prevalent in 66% of general population and the main risk factors are obesity, diabetes and metabolic syndrome. Population based life style interventions are needed

Keywords: Metabolic Dysfunction Associated Steatotic Liver Disease, Trivandrum Cohort 3, Risk Facrors, Prevalence of MASLD

Table 1. Characteristics of those with or without MASLD

	MASLD				
	No (n=974)	Yes (n=1872)	Mean	sd	P value
	Mean	sd			
AGE	50.2	14.7	51.7	12.3	0.003
Median stiffness kPa	7.8	4.5	8.6	4.0	<0.001
UPA Median	199.6	60.9	294.0	29.1	<0.001
Body Fat (%)	29.2	16.0	32.9	12.0	<0.001
Body fat wt	19.4	11.9	22.6	7.5	<0.001
Skeletal muscle (%)	38.1	6.2	36.3	5.7	<0.001
Muscle weight	34.6	11.5	39.7	12.0	<0.001
Muscle (%)	66.9	8.9	62.8	8.4	<0.001
Muscle wt(kg)	43.3	9.3	44.6	9.1	0.080
Visceral fat %	10.0	6.9	11.9	6.1	<0.001
Waist circumference in cm	91.4	10.5	98.1	9.7	<0.001
BMI	24.4	4.2	27.5	4.1	<0.001
Fasting glucose mg/dl	124.2	51.4	145.6	68.6	<0.001
Systolic BP mm Hg	127.0	15.7	131.9	17.3	<0.001
Diastolic BP mm Hg	81.5	8.5	84.1	9.7	<0.001

Table 2. Risk factors for MASLD

		MASLD			
		No	Yes	OR (univariable)	OR (multivariable)
Sex	Male	468 (34.9)	874 (65.1)	-	-
	Female	506 (33.6)	998 (66.4)	1.06 (0.90-1.23, p=0.490)	1.10 (0.94-1.29, p=0.241)
Past Covid infection	No	681 (34.3)	1305 (65.7)	-	-
	Yes	293 (34.1)	567 (65.9)	1.01 (0.85-1.20, p=0.909)	1.02 (0.86-1.21, p=0.846)
Hypothyroid	No	880 (34.8)	1646 (65.2)	-	-
	Yes	94 (29.4)	226 (70.6)	1.29 (1.00-1.66, p=0.053)	1.24 (0.96-1.62, p=0.102)
B Asthma	No	919 (34.2)	1766 (65.8)	-	-
	Yes	55 (34.2)	106 (65.8)	1.00 (0.72-1.41, p=0.986)	1.03 (0.74-1.46, p=0.858)
CAD	No	915 (33.9)	1788 (66.1)	-	-
	Yes	59 (41.3)	84 (58.7)	0.73 (0.52-1.03, p=0.070)	0.72 (0.51-1.02, p=0.064)
Medial Stiffness kPa	<10.2	845 (36.2)	1489 (63.8)	-	-
	>10.2	129 (25.2)	383 (74.8)	1.68 (1.36-2.10, p<0.001)	1.71 (1.38-2.14, p<0.001)

PE-30

GLP-1 Receptor Agonists for the Treatment of MASLD: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), has become a major global health concern due to its increasing prevalence and association with metabolic syndrome. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), initially developed for type 2 diabetes and obesity, have shown potential in improving hepatic steatosis and metabolic parameters in MASLD patients. This systematic review and meta-analysis aimed to assess the efficacy and safety of GLP-1 RAs in patients with MASLD based on evidence from randomized controlled trials (RCTs).

Methods: A comprehensive search was conducted following PRISMA guidelines across PubMed, Web of Science, and Scopus databases from inception through January 2025. RCTs evaluating GLP-1 RAs in adult patients with biopsy-proven or imaging-diagnosed MASLD were included. Primary outcomes were liver fat content reduction (measured by MRI-PDFF), resolution of steatohepatitis without worsening fibrosis, and fibrosis improvement without worsening NASH. Secondary outcomes included changes in weight, glycemic control, and adverse events. Study quality was assessed using the Cochrane Risk of Bias tool.

Results: A total of 18 RCTs comprising 4,752 patients were included. GLP-1 RAs significantly reduced hepatic fat content (mean difference: -5.78%; 95% CI: -7.14 to -4.42; *P*<0.001) and achieved higher rates of NASH resolution without fibrosis worsening compared to placebo (RR: 2.45; 95% CI: 1.85 to 3.24). Improvement in fibrosis by at least one stage was also more common in the GLP-1 RA group (RR: 1.62; 95% CI: 1.15 to 2.28). Significant reductions in body weight (mean difference: -7.24 kg) and HbA1c were observed. The most common adverse events were gastrointestinal (nausea and vomiting), but they were generally mild to moderate in severity.

Conclusions: GLP-1 receptor agonists are effective and safe for improving histological and metabolic outcomes in MASLD. They offer a promising pharmacological option for this population, particularly in patients with obesity or type 2 diabetes. Further long-term studies are needed to confirm their impact on fibrosis progression and cardiovascular outcomes.

Keywords: MASLD, GLP-1 Receptor Agonists, NASH, Randomized Controlled Trials

PE-31

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Depression as a Risk Factor in a Population Cohort in S India (Cohort 1)

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Aims: To evaluate depression as a major risk factor for METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD

Methods: Population cohort with a nested case control design in Trivandrum, S India. We noted demographic, clinical, and biochemical and Metabolic Associated Steatotic Liver Disease (MASLD) in 2,161 individuals. Duke Anxiety-Depression Scale (DUKE-AD), a 7 item scale was used. Univariate and multivariate models with odds ratios (ORs) and 95% confidence intervals (CIs) were done using "jamovi 2.5.3"

Results: Among 2,161 subjects, 59.4% were females; urban domicile was 53.8%. Education was up to the 10th grade in 64.3% and marital status was in 91.1%. BMI was 37.0% overweight and 13.7% are obese. 42.9% had hypertension and 25.5% had diabetes mellitus. 45.7% had higher waist circumference and metabolic syndrome was in 39.1%. MASLD was noted in 48.1%. Duke anxiety depression scale identified 26.9% with abnormality and 73.1% had normal scores. Mean Duke A D score significantly higher in individuals with MASLD (20.0 ± 20.9) compared to those without (15.9 ± 19.8, *P*<0.0001), Predictors of MASLD were male gender (OR: 2.09, 95% CI: 1.68-2.61), metabolic syndrome (OR: 2.69, 95% CI: 2.21-3.28), severe depression (OR: 1.69, 95% CI: 1.37-2.09), obesity (OR: 2.78, 95% CI: 2.29-3.38), and alcohol consumption (OR: 1.43, 95% CI: 1.05-1.96).

Conclusions: Depression in MASLD can increase the risk of adverse outcomes and early screening of depression is needed in MASLD subjects.

Keywords: Depression, Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Risk Factor, Population Cohort In S India

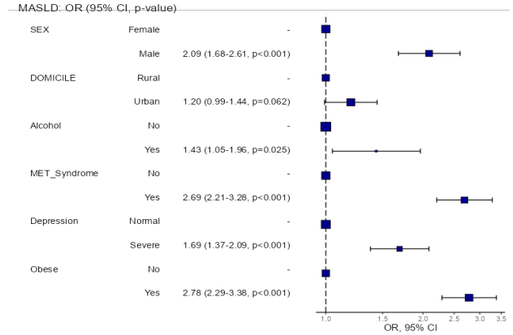

Figure 1. Odds Ratio Plot.

PE-32

Liver Histology and Non-invasive Tests (NITs) for Hepatic Fibrosis in a Large Cohort of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in Kerala, S India

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Aims: To evaluate liver histology and Non invasive tests (NITs) for hepatic fibrosis in a large cohort of metabolic dysfunction-associated steatotic liver disease (MASLD) in Kerala, S India

Methods: We have two population cohorts of MASLD in,2012-2016 (Trivandrum NAFLD Cohort) and 2017-2023 (Scarred liver in Trivandrum: SLIT cohort) in the urban and rural population of Trivandrum. We reviewed the data of 391 liver biopsies as per the CRN criteria and compared for its utility along with NITs (FIB 4 (fibrosis-4), NFS (NAFLD fibrosis score), AST to Platelet Ratio Index (APRI). AST and ALT were also determined.

Results: Mean age (SD) was 43.2 (10.1) and 55.5% were males. 56.3% were males and mean (SD) BMI was 27.4 (4.5). Waist circumference was abnormal in 76.5%. Morbidities were: diabetes (81.3%); hypertension (34.6%); abnormal triglyceride (52.4%); low HDL (53.4%). AST and ALT were abnormal in 67 and 65% of subjects. Mean liver stiffness was 7.6Kpa (SD 2.3). LSM was >10.2Kpa. Fib-4 was >2.67 in 49 subjects CRN stage was 1c and above in 35 subjects. 41 subjects had NAS score of 4 and above. APRI score was high in 41 subjects and 32 had stage 1c and above. NFS was intermediate in 113 and high in 6 and 82 subjects has NAS score of 4 and above.

Conclusions: FIB-4 score had comparable utility with CRN stage and NAS score and results highlight the potential of FIB-4 as a reliable screening tool for MASLD. APRI had had a similar performance compared to CRN. These two NITs can be utilised in clinical practice

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Liver Histology, Non Invasive Tests (NITS), Cohort Study

PE-33

A Machine Learning Model for Predicting Hepatocellular Carcinoma in Patients with MASLD

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Aims: The risk of hepatocellular carcinoma (HCC) is significantly elevated in individuals with metabolic-associated steatohepatitis liver disease (MASLD). This study aimed to develop and validate a machine learning model to predict the risk of HCC in patients with MASLD.

Methods: A total of 18,848 patiA total of 18,848 patients with MASLD were enrolled from five centers in South Korea between 2000 and 2022. The dataset was divided into a training set (n=13,193) and a validation set (n=5,655). The primary outcome was HCC development.

ents with MASLD were enrolled from five centers in South Korea between 2000 and 2022. The dataset was divided into a training set (n=13,193) and a validation set (n=5,655). The primary outcome was the development of HCC.

Results: During a median follow-up of 51.6 (interquartile range 28.8–81.6) months, 819 cases of HCC were confirmed, with an incidence rate of 1.01 per 100 person-years. The model with the best predictive performance in the training cohort was selected as the final model, designated as MASLD-HCC-Insight. This model, developed using a gradient boosting algorithm, incorporated eight variables which were independently associated with an increased risk of HCC development: cirrhosis, platelet count, age, alanine aminotransferase, serum albumin, low-density lipoprotein cholesterol, sex, and type 2 diabetes. Compared to the HCC risk score, MASH-HCC-Insight showed significantly superior predictive accuracy in the training cohort (c-index: 0.86 vs. 0.72. $P<0.05$; area under the receiver-operating characteristic curve: 0.93 vs. 0.78, $P<0.01$; area under the precision-recall curve 0.55 vs. 0.43, $P<0.05$). In sensitivity analysis, the use of angiotensin II receptor blockers (hazard ratio [HR]=0.710, 95% confidence interval [CI] 0.513–0.985), sodium-glucose cotransporter-2 inhibitors (HR=0.563, 95% CI 0.297–1.068), and statins (HR=0.621, 95% CI 0.442–0.872) were associated with a decreased risk of HCC development.

Conclusions: The machine learning model comprising eight key variables may serve as a valuable tool for risk stratification in patients with MASLD. Further external validation is necessary to confirm its clinical utility.

Keywords: Metabolic Dysfunction-Associated Steatotic Liver Disease, Hepatocellular Carcinoma, Machine Learning, Prediction

PE-34

Trajectory of Trivandrum Cohort of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) over Two Decades

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Aims: To evaluate the prevalence and risk factors for MASLD across thre population cohorts in Trivandrum District, South India over two decades

Methods: MAFLD shows a high prevalence over time. We are reporting three cohorts of MASLD Methods: Three cohorts: I: 2005-2006 (484 subjects); II: 2013-2016 (2222 subjects) and II : May 2022 to September 2023, 2846 participants. All were recruited through multistage cluster sampling. Using the recent criteria for MAFLD, we reanalysed the data.

Results: Cohort 1: 52.9% males and 47.1% females. Metabolic risk factors included diabetes (24.8%), hypertension (50.8%) and prevalence of NAFLD (39.9%) and MASLD (38.0%);increased waist circumference (64.9%), elevated triglycerides (23.1%), low HDL (23.1%).

Cohort II: MASLD prevalence was 48.2 % (males 45.7 and females 54.3%) and the NAFLD prevalence was 49.8% .MASLD Odds ratios after adjusting for age, sex, domicile, BMI category (with normal weight as baseline), diabetes and metabolic syndrome are in Table 1.

Cohort III: MASLD prevalence was 65.8% (95% CI 64-67.52 %%). Mean age was 51.71 years. Median Stiffness of liver >10.2 was seen in 20.5% in MASLD compared to those without MASLD (13.2%: $P<0.001$) MASLD 65.8% (95% CI 64-67.52 %%). Age (Ref- <50 years) Ad OR (95% CI) 1.23(1.1 - 1.46);Gender (Ref-Female)Ad OR (95% CI) 2.14(1.63 - 2.47);Domicile (Ref- Rural) Ad OR (95% CI) 1.2(0.99 - 1.45; Diabetes Adj OR (95% CI) 1.77(1.41 - 2.19)Metabolic syndrome : Ad OR (95% CI) 1.57(1.23 - 1.98)

Conclusions: MASLD is prevalent in 66% of general population and the main risk factors are obesity, diabetes and metabolic syndrome. Population based life style interventions are needed

Keywords: Metabolic Dysfunction Associated Steatotic Liver Disease, Trajectory, Cohort, South India, Kerala

Table 1. Cohort_II image

Cohort II

Variable	Unadjusted OR (95%CI)	p	Adjusted OR (95%CI)	p
Age (Ref- <50 years)	1.4(1.18 - 1.67)	<0.001	1.21(1 - 1.47)	0.051
Gender (Ref- Female)	1.54(1.3 - 1.83)	<0.001	2.04(1.66 - 2.49)	<0.001
Domicile (Ref- Rural)	1.58(1.33 - 1.87)	<0.001	1.2(0.99 - 1.45)	0.059
BMI- Normal		<0.001		<0.001
Under weight- Normal	0.13(0.05 - 0.37)	<0.001	0.17(0.06 - 0.48)	0.001
Over weight	2.22(1.7 - 2.91)	<0.001	2.1(1.59 - 2.78)	<0.001
Obese	3.98(3.18 - 4.98)	<0.001	3.74(2.92 - 4.79)	<0.001
Diabetes	2.6(2.18 - 3.11)	<0.001	1.75(1.42 - 2.18)	<0.001
Metabolic syndrome	2.55(2.15 - 3.04)	<0.001	1.56(1.24 - 1.95)	<0.001

PE-35

Impact of Menopause on Liver Fibrosis Progression in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Aims: The hormonal changes during menopause may exacerbate the progression of metabolic dysfunction-associated steatotic liver disease (MASLD), particularly liver fibrosis. This study aimed to evaluate the relationship between menopausal status and the progression of MASLD, focusing on clinical and histological differences and the impact of estrogen exposure.

Methods: A total of 907 patients with MASLD were analyzed, with 706 patients having complete data on age and sex. Participants were stratified into four groups: males ≤50 years (n=211), premenopausal females (n=74), males >50 years (n=142), and postmenopausal females (n=279). Liver histology, fibrosis stage, and clinical parameters were assessed at baseline and during follow-up. Fibrosis progression was defined as either liver stiffness measurement (LSM) ≥9.6 kPa in patients with baseline fibrosis stages 0–2 or a ≥20% increase in LSM in those with baseline stages 3–4 over a follow-up period (median: 45 months).

Results: Baseline characteristics revealed notable differences, with postmenopausal females exhibiting higher BMI, hypertension prevalence, and fibrosis markers (e.g., FIB-4 score and Agile 3+). Estrogen exposure measures, including reproductive lifespan and endogenous estrogen exposure, were inversely associated with fibrosis severity ($P<0.05$). Liver histology demonstrated a higher prevalence of advanced steatosis and fibrosis in postmenopausal females. Postmenopausal females had significantly higher rates of fibrosis progression compared to other groups ($P<0.05$).

Conclusions: Menopause is an independent risk factor for liver fibrosis progression in MASLD. The findings underline the need for targeted management strategies to address the increased risk of advanced liver disease in postmenopausal women.

Keywords: Menopause, MASLD, Liver Fibrosis

PE-36

Intermittent Calorie Restriction Modulates Gut Microbiota in Patients with MASLD without Diabetes

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Aims: Our previous randomized controlled trial (RCT) demonstrated that a 12-week intermittent calorie restriction (ICR) diet significantly reduced liver fat content (LFC) compared to the standard of care (SOC) diet. In this study, we aim to explore the changes in gut microbiome composition following a 12-

week dietary intervention in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) to elucidate the underlying mechanisms contributing to these effects.

Methods: Patients with MRI-proton density fat fraction (PDFF) ≥8% were randomly assigned to either the ICR group (5:2 diet) or the SOC group (receiving 80% of the recommended caloric intake). The primary outcome was the relative change in gut microbiota composition following the dietary intervention.

Results: From baseline to week 12, ICR increased microbiome diversity and was associated with a reduction in Megamonas (linear discriminant analysis [LEfSe]=4.14; *P*<0.001) and Enterobacter (LEfSe=2.71; *P*=0.01), while promoting an increase in Alistipes (LEfSe=3.87; *P*<0.001), Clostridium (LEfSe=3.51; *P*=0.03), Romboutsia (LEfSe=3.67; *P*=0.04), and Lachnospira (LEfSe=3.16; *P*=0.02), compared to SOC. In patients with obesity, ICR was associated with a reduction in Enterobacter (LEfSe=2.55; *P*=0.03), whereas SOC was associated with an increase in Enterobacter (LEfSe=3.08; *P*=0.001). In patients without obesity, ICR was associated with reductions in Megamonas (LEfSe=4.37; *P*<0.001), Ruminococcus (LEfSe=3.61; *P*=0.03), Lachnospira (LEfSe=3.44; *P*=0.03), and Clostridium (LEfSe=3.39; *P*=0.004), compared to SOC. A response to the dietary intervention (relative LFC reduction ≥30%) was associated with reductions in Megamonas (LEfSe=4.11; *P*<0.001) and Enterobacter (LEfSe=2.87; *P*=0.005), along with increases in Bacteroides (LEfSe=4.44; *P*=0.01) and Alistipes (LEfSe=3.83; *P*=0.02), compared to non-responders. Conversely, non-response to the diet was associated with a reduction in Lachnospira (LEfSe=3.26; *P*=0.007), compared to responders.

Conclusions: ICR significantly altered gut microbiome composition, increasing microbial diversity and beneficial bacteria while reducing potentially harmful taxa. Gut microbiome modulation may be a key mechanism underlying the metabolic benefits of ICR in patients with MASLD.

Keywords: Intermittent Calorie Restriction, Metabolic Dysfunction-Associated Steatotic Liver Disease, Gut Microbiota, Megamonas

18. Others, Medical

PE-1

Prevalence and Risk Factors Associated with Human Fascioliasis Infection at Cam Khe 103 Clinic

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Cam Khe 103 Clinic, Vietnam

Aims: Liver fluke infections pose a significant public health threat, often asymptomatic but capable of causing severe biliary and liver diseases. Identifying prevalence and risk factors is vital for effective prevention and control.

To determine the prevalence and risk factors of human fascioliasis at Cam Khe 103 Clinic.

Methods: A prospective study was conducted from July 2020 to November 2024 on individuals visiting Clinic 103 in Cam Khe District. Liver fluke infections were diagnosed using real-time PCR to detect *Clonorchis sinensis* and *Opisthorchis viverrini*. Risk factors, including demographics, diet, and environmental exposures, were analyzed.

Results: The infection rates of *C. sinensis* and *O. viverrini* were 20.09% and 21.31%, respectively, with an overall rate of 17.32%. Most cases (88.7%) were mild, with a median egg count of 396.2 ± 131.6 EPG.

Males had a significantly higher infection rate (27.15%) than females (15.03%, *P*<0.01).

The highest infection rate was observed in individuals over 50 years old (31.6%), while the lowest was in the 19–30 age group (12.6%).

Those using fresh manure in farming or aquaculture were 1.83 times more likely to be infected (*P*<0.01).

Consuming raw fish salad increased infection risk by 8.25 times (*P*<0.01). Frequent consumption (at least once a week) was associated with significantly higher infection rates than occasional consumption (*P*<0.01).

Conclusions: Eating raw fish salad and using fresh manure in farming and aquaculture are major risk factors for liver fluke infection. Public health measures should promote safe food practices and improved sanitation to reduce infection rates.

Keywords: Prevalence, Factors Risk, Fascioliasis Infection, Liver Fluke

PE-2

Senolytics in Liver Disease: Unlocking the Secret to Reversing Aging and Restoring Liver Vitality

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Aims: Aging-related liver dysfunction is characterized by the accumulation of senescent hepatocytes, which contribute to chronic inflammation, fibrosis, and impaired regenerative capacity. Senolytic therapies, which selectively eliminate senescent cells, have emerged as a potential strategy to reverse these pathological changes. This systematic review aims to evaluate the role of senescent hepatocytes in liver disease progression and assess the preclinical and clinical efficacy of senolytic interventions in mitigating fibrosis, promoting liver regeneration, and restoring hepatic function.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted following PRISMA guidelines to identify preclinical and clinical studies on senolytics in liver disease. Inclusion criteria comprised studies investigating the effects of senolytic agents such as dasatinib, quercetin, fisetin, navitoclax, and FOXO4-DRI in experimental models and human trials of chronic liver disease. Data extraction focused on key outcomes, including fibrosis regression, hepatocyte proliferation, inflammatory markers, and functional liver recovery. Risk of bias was assessed using Cochrane's ROBINS-I tool for clinical studies and SYRCLE's risk-of-bias tool for animal studies.

Results: A total of 46 studies were included, comprising 32 preclinical studies and 14 clinical investigations. Preclinical data demonstrated that senolytic therapies effectively reduced fibrosis (≥40% reduction in collagen deposition), decreased senescence-associated secretory phenotype (SASP) expression, and restored hepatocyte proliferative capacity. Mechanistic studies revealed that senolytic treatment downregulated p16^INK4a^ and p21^CIP1^ pathways, leading to improved regenerative signaling. Early-phase clinical trials showed a significant improvement in liver enzyme profiles and reduced fibrotic burden in patients with cirrhosis. However, variations in dosing, treatment duration, and patient selection remain challenges for clinical translation.

Conclusions: Senolytic therapies hold significant promise in reversing age-related liver dysfunction by selectively targeting senescent hepatocytes. While preclinical findings are compelling, robust clinical trials with optimized senolytic regimens are necessary to establish safety, efficacy, and long-term benefits. Future research should prioritize liver-specific senolytic drug development and combination strategies to enhance therapeutic efficacy in cirrhosis and chronic liver disease.

Keywords: Senolytics, Liver Regeneration, Senescence-Associated Secretory Phenotype (SASP), Precision Medicine In Liver Disease

PE-3

Elevated Levels of IL-1β, IL-2 and IL-6 Correlate with Disease Severity in Non-Alcoholic Acute Pancreatitis

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Aims: In recent years, there has been an increase in cases of non-alcoholic acute pancreatitis (NAAP) globally, including in the Republic of Uzbekistan. Key risk factors include poor dietary habits and a sedentary lifestyle, which contribute to metabolic disorders such as obesity and type 2 diabetes mellitus. These conditions significantly impact the pathogenesis of the disease. This study aims to evaluate serum levels of interleukins IL-1β, IL-2, and IL-6 in patients with NAAP and determine their association with disease severity

Methods: A total of 66 patients aged 22–45 years were included in the study, divided into two groups: 41 patients with an abortive course of NAAP and 25 patients with a progressive course. The control group consisted of 27 healthy individuals of comparable age. Serum concentrations of IL-1β, IL-2, and IL-6 were assessed using the sandwich ELISA method

Results: Patients with an abortive course of NAAP exhibited significantly elevated IL-1β and IL-6 levels compared to the control group (61.99±1.87 pg/mL vs. 17.10±0.91 pg/mL for IL-1β; 41.51±1.29 pg/mL vs. 8.11±0.42 pg/mL for IL-6). In the progressive NAAP group, these cytokine levels were even higher (94.56±3.57 pg/mL for IL-1β and 64.84±2.35 pg/mL for IL-6). IL-2 levels were reduced in both patient groups compared to controls, with the most significant decrease observed in the progressive course of NAAP (5.64±0.33 pg/mL vs. 12.27 ±0.44 pg/mL).

Conclusions: Elevated IL-1β and IL-6 levels correlate with the severity of non-alcoholic acute pancreatitis, reflecting the intensity of the inflammatory response. The observed decline in IL-2 levels may indicate immune dysregulation in patients with a progressive disease course. Measuring these interleukin levels may provide valuable prognostic insights and contribute to the optimization of therapeutic strategies for NAAP.

Keywords: Non-Alcoholic Acute Pancreatitis, Interleukin, Inflammation, Therapeutic Strategies

PE-4

Clinico-Immunological Features of Chronic Hepatitis in Children

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Aims: Chronic liver diseases in children remain a significant healthcare challenge. The etiopathogenesis involves viral and non-viral infections, along with immune-mediated mechanisms that contribute to the progression of liver fibrosis and cirrhosis. This study aims to evaluate the role of viral and infectious agents and immunopathological reactions in the development of chronic liver diseases in pediatric patients

Methods: A total of 69 children (32 girls, 37 boys) aged 9 to 17 years with chronic active hepatitis of various etiologies were observed at the Department of Gastroenterology, Republican Children's Clinical Hospital, between 2002 and 2005. Of these, 41 children (59.4%) had already developed cirrhosis. Thirty children were diagnosed with autoimmune hepatitis, and 21 (30.4%) exhibited progression to cirrhosis.

Comprehensive immunological assessments included immunoglobulin profiling, circulating immune complexes, flow cytometry for lymphocyte subpopulations, and apoptosis markers. Serological testing for hepatitis B, hepatitis C, cytomegalovirus, and toxoplasmosis was conducted using ELISA. Autoimmune components were assessed by detecting anti-DNA and antinuclear antibodies

Results: Among the study population, 29 children (42%) tested positive for hepatitis B or C, while 30 (43.4%) were seronegative. Immunological testing revealed: Elevated humoral response: Hyperimmunoglobulinemia (IgM and IgG) exceeding age-specific upper limits by 2–3 times.

High levels of CIC: Exceeding normal values by 2.5–6 times.

Cellular immune response: Increased CD4+ lymphocytes, activated NK cells, and persistently elevated CD4/CD8 immunoregulatory index.

Clinical signs of cirrhosis with severe cytolytic activity were present in 41.3% of children with hepatitis B or C and in 70% of seronegative cases. Among seronegative adolescents, high levels of antibodies to CMV and toxoplasmosis were detected. The severity of clinical symptoms and cirrhosis progression correlated with CMV infection (37.5%) or CMV + toxoplasmosis coinfection (31%), with the latter group exhibiting more pronounced liver pathology.

Conclusions: Our findings highlight the combined nature of immune dysregulation in chronic liver diseases in children, with a strong influence of infectious factors. CMV and toxoplasmosis may play an underestimated role in the progression of pediatric liver pathology, especially in seronegative patients.

Keywords: Chronic Hepatitis, Pediatric Liver Disease, Autoimmunity, Cirrhosis

PE-5

Silent Invaders: Exploring Microplastic Accumulation and Toxicity in the Human Liver

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Aims: Microplastics (MPs), plastic particles smaller than 5 mm, are pervasive environmental pollutants found in consumer products and ecosystems, posing growing health risks. Humans can absorb MPs via ingestion, inhalation, and skin contact, leading to their accumulation in organs, particularly the liver—the body's detoxification hub. Emerging evidence links MPs to liver damage, fibrosis, and metabolic disorders, yet the precise toxicological mechanisms remain unclear. This systematic review explores current insights into MP accumulation, liver toxicity, and associated health impacts.

Methods: A thorough literature search of PubMed, Scopus, and Web of Science (January 2010–January 2025) was conducted using keywords like "microplastics," "liver toxicity," "hepatic fibrosis," "cGAS/STING pathway," and "oxidative stress." Eligible studies included both in vitro and in vivo research on microplastics' effects on liver function, structure, and molecular pathways. Extracted data covered study design, MP characteristics (size, type, concentration), biological models, liver-specific biomarkers, and identified toxicological mechanisms.

Results: The review analyzed 25 studies, including 15 in vivo, 7 in vitro, and 3 human observational studies. MPs, particularly smaller particles (0.1 μm), accumulated in hepatocytes, showing high bioavailability. Key findings revealed that MPs induce nuclear and mitochondrial DNA damage, releasing cytoplasmic dsDNA and activating the cGAS/STING pathway. This triggers NF-κB translocation, promoting pro-inflammatory cytokines and contributing to hepatic fibrosis. MPs also induced oxidative stress, lipid metabolism disruption, and gut-liver axis dysregulation. Human studies found MPs in cirrhotic, but not healthy, liver tissues.

Conclusions: Microplastics (MPs) threaten liver health by inducing DNA damage, activating the cGAS/STING pathway, and driving chronic inflammation that leads to fibrosis. Their bioaccumulation, particularly in those with pre-existing liver conditions, highlights the urgent need for research into long-term health impacts. Targeting pathways like cGAS/STING may offer therapeutic strategies against MP-induced liver damage. Future studies should prioritize human epidemiological assessments, explore chronic low-dose exposure effects, and develop interventions to mitigate MP-related hepatic toxicity.

Keywords: Microplastics, Liver Toxicity, Hepatic Fibrosis, CGAS/Sting Pathway

PE-6

Validation of Metallothionein Immunohistochemistry for Diagnosis of Wilson Disease in Korean Patients

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Aims: Wilson disease (WD) is an autosomal recessive disorder caused by germline *ATP7B* mutations, leading to copper accumulation in the liver and central nervous system. Its diagnosis relies on multiple features such as Kayser-Fleischer rings, neurological abnormalities, low serum ceruloplasmin level, increased urine copper excretion, hepatic dry copper weight, and *ATP7B* mutation testing, all of which have significant limitations. We evaluated the diagnostic accuracy of recently developed metallothionein immunohistochemistry (IHC) for WD in Korean patients.

Methods: Twenty WD cases were included, consisting of 11 needle biopsies and 9 explants of liver. Eighty-two control cases were also examined, including drug-induced liver injury, metabolic dysfunction-associated steatotic liver disease, alcoholic liver disease, autoimmune hepatitis, chronic hepatitis B, and fulminant hepatitis of unknown cause. Metallothionein IHC was performed on formalin-fixed, paraffin-embedded tissue blocks. Positivity was defined as moderate to strong, homogeneous cytoplasmic staining in ≥10% of hepatocytes, while staining in intracytoplasmic granules was considered negative. For comparison, rubeanic acid staining was performed to detect hepatic copper deposition.

Results: Among the 20 WD cases, 14 had cirrhotic or pre-cirrhotic livers, while 6 had fatty livers with minimal or mild fibrosis. The median age was 16.5 years (range: 6 – 61 years), with a male-to-female ratio of 1.5:1. Conventional rubeanic acid staining showed only 25% sensitivity (5/20) and 78% specificity (64/82) for WD. In contrast, metallothionein IHC demonstrated significantly higher 90% sensitivity (18/20) and 100% specificity (82/82) for WD. Metallothionein IHC was compatible with routine IHC platforms, with an expected cost comparable to other IHC tests. The turnaround time for metallothionein IHC was one day, compared to two days for rubeanic acid staining.

Conclusions: Metallothionein IHC demonstrated remarkably high sensitivity and specificity for WD diagnosis, as well as being fast, cost-effective, and easily implementable. Its adoption could significantly improve the accuracy and efficiency of WD diagnosis.

Keywords: Wilson Disease, Diagnosis, Immunohistochemistry, Metallothionein

PE-7

Wilson Disease: Clinical Presentation and Management at Gastroenterology and Hepatology Center

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Aims: Wilson's disease is a rare autosomal recessive inherited disorder of copper metabolism that is characterized by excessive deposition of copper in many organs, especially in the liver and brain. This study aimed to describe clinical and para-clinical characteristics of Wilson patients and follow up mortality due to complications related to liver failure or treatment process.

Methods: This cross-sectional descriptive research involved 35 diagnosed Wilson patients that received inpatient treatment and/or outpatient follow – up at Bach Mai Hospital's Gastroenterology and Hepatology Center from October 2018 to December 2024

Results: The mean age of studied patients was 25,0 ± 6,9 years old, and the average age at the time of diagnosis was 20,4 ± 8,7 years old (ranged from 8 to 44 years old), of which 52,9% of patients were diagnosed before 20 years old. The female/male ratio was 1,19. The incidence of neuropsychiatric symptoms, acute liver failure, cirrhosis, Kayser-Fleischer ring was 28.6%, 22.9%, 74.3%, 40%, respectively. The rate of ATP7B gene mutation among 14 patients underwent genetic testing was 92,9%. Level of serum ceruloplasmin, serum free copper and the 24-hours urinary copper excretion of newly diagnosed patients were 6,3 ± 2,7 mg/dL (2 – 11), 418,2 ± 228,6 µg/L (196,5 – 934,25) and 2170,1 ± 2901,9 µg/24h (216 – 11165), respectively. There was no significant difference in these tests index between groups with or without neuropsychiatric symptoms. The prognostic index in Wilson's disease (modified King score) in the ongoing maintenance treatment group was 3,94 ± 3,64, which was significantly lower than in the untreated or discontinued (6,56 ± 3,67), *P*=0,045. Among newly diagnosed Wilson patients, 2 patients died of acute liver failure without liver transplantation, and 1 patient died after liver transplantation due to graft rejection.

Conclusions: Wilson disease is common in young people (52.9% of patients diagnosed before age 20). While cirrhosis and acute

liver failure are the most frequent symptoms, neuro-psychiatric symptoms and the Kayser-Fleischer rings are less common. In the newly diagnosed patients, level of serum ceruloplasmin, free copper concentration and the 24-hours urinary copper excretion typically changed and there was no significant difference between groups with or without neuropsychiatric symptoms. In the treated group, the modified King score was significantly lower.

Keywords: Wilson Disease, Ceruloplasmin, Serum Free Copper, Urinary Copper Excretion

PE-8

Effectiveness of the acNASH Index in Diagnosing Dyselectrolytemia in Subjects with Liver Disease – A Retrospective Study

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Aims: The global prevalence of nonalcoholic steatohepatitis (NASH) is on the rise, yet liver biopsy remains the gold standard for its diagnosis. The acNASH index, a simple formula derived from serum AST (aspartate aminotransferase) and SCr (serum creatinine) levels, has shown promise in identifying patients with biopsy-proven NASH. This index outperforms existing non-invasive prediction models and reduces the need for unnecessary liver biopsies. In this study, we aimed to evaluate the efficacy of the acNASH index in diagnosing dyselectrolytemia in patients with liver disease.

Methods: This retrospective study was conducted in the Department of Biochemistry at ACS Medical College and Hospital. Data from 183 patients were collected, including demographic and clinical parameters such as age, gender, urea, creatinine, total protein, albumin, AST, ALT, ALP, direct, indirect, and total bilirubin levels, as well as electrolyte levels (sodium, potassium, and chloride). The acNASH index was calculated by multiplying AST and creatinine values. Patients were categorized into four quartiles based on their acNASH values. Statistical analysis was performed using SPSS 28, with data expressed as mean ± standard deviation (SD) and median. Differences between groups were analyzed using one-way ANOVA for parametric data and the Kruskal-Wallis test for non-parametric data.

Results: The study revealed significant alterations in key parameters, including urea, creatinine, AST, ALT, and sodium levels, across the groups. Notably, serum sodium levels were significantly decreased in patients with acNASH values above 10.8. result is shown in the table below.

Conclusions: The findings suggest that an acNASH value above 10.8 can serve as a useful indicator for detecting dyselectrolytemia in subjects with liver disease. This highlights the potential of the acNASH index as a non-invasive tool for identifying electrolyte imbalances in this patient population. Further studies are warranted to validate these findings and explore their clinical applicability.

Keywords: ACNASH, Dyselectrolytemia, Retrospective Study, Liver Disease

VARIABLES	GROUP 1 (n = 41)	GROUP 2 (n = 40)	GROUP 3 (n = 56)	GROUP 4 (n =46)	P VALUE
SEX (M/F)	14/27	16/24	33/23	30/16	NS
Sodium (mEq/L)	138 ± 5 (138*)	139 ± 4 (139*)	136 ± 4 (136*)	135 ± 4 (135*)	<.001
Potassium (mEg/L)	4.8±5.6 (4*)	5.9±8.3 (4*)	4±0.5 (4*)	5.8±8.3 (4*)	NS
UREA(mg/dl)	19 ± 6 (18*)	21 ± 5.5 (19.5*)	23 ± 9 (20*)	35± 38 (24*)	.001
CREATININE (mg/dl)	0.5 ± 0.2 (0.5*)	0.7 ± 0.1 (0.7*)	0.8 ± 0.1 (0.8*)	1.2 ± 0.8 (0.9*)	<.001
T. BILIRUBIN (mg/dl)	1 ± 0.5 (0.6*)	0.7 ± 0.2 (0.7*)	0.7± 0.7 (0.7*)	1±1.1 (0.7*)	NS
D. BILIRUBIN (mg/dl)	0.3± 0.1 (0.3*)	0.3±0.1 (0.4*)	0.3±0.3 (0.2*)	0.3±0.5 (0.2*)	NS
I . BILIRUBIN (mg/dl)	0.5±1 (0.3*)	0.4±0.2 (0.3*)	0.4± 0.2 (0.4*)	0.6±0.6 (0.5*)	<.001
AST (U/L)	16 ± 8 (14*)	16 ± 2 (17*)	23 ± 8 (20.5*)	70±150 (39.5*)	.000
ALT (U/L)	23.2±14.3 (21*)	25.8±18 (23*)	26±13 (23.5*)	53±87.5 (34*)	<.001
ALP (U/L)	100±41 (98*)	83±27 (95*)	86±26 (88*)	89±46 (82*)	NS
ALBUMIN (gr/dl)	4±4 (3.5*)	3.7 ± 1 (3.6*)	4.3±4.2 (3.8*)	4 ± 0.6 (3.7*)	NS
GLOBULIN (gr/dl)	3 ± 0.3 (3.2*)	3 ± 0.3 (3.2*)	3 ± 0.5 (3.2*)	3 ± 0.6 (3.1*)	NS
T. PROTEIN (gr/dl)	7.8±8.6 (6.7*)	6.5±0.7 (6.7 *)	7.9±8.3 (6.9*)	8±10.7 (6.5*)	NS

*median

PE-9

Epidemiological Analysis of Hepatitis E Virus Infections in South Korea Using Serum Samples from the Korea National Health and Nutrition Examination Survey

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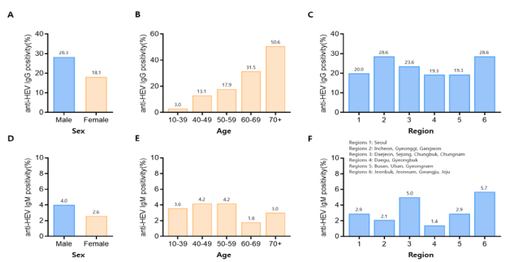
Aims: Epidemiological data on hepatitis E prevalence in South Korea are limited. This study aimed to comprehensively evaluate its nationwide status across sex, age, and regional variations.

Methods: A total of 840 blood samples were selected based on sex, age, and regional distribution from participants of the 2020 Korea National Health and Nutrition Examination Survey (KNHANES). All sera were qualitatively stored at the National Biobank of Korea.

Results: Among the analyzed samples, 195 (23.2%) tested positive for hepatitis E virus (HEV) IgG antibodies. The seropositivity rate was higher in men (28.3%) than in women (18.1%) and showed a marked increase with age, rising from 3.0% in those aged 10–39 to 50.6% in those aged 70 and older. HEV IgG-positive individuals exhibited elevated liver fibrosis markers. The HEV IgM positivity rate was 3.3% (28/840), with the highest prevalence among those aged 40–59. Among them, 13 (46.4%) were also positive for HEV IgG antibodies. HEV IgM-positive individuals showed higher liver fibrosis markers and a greater frequency of alanine aminotransferase elevation. Additional genetic analysis was performed on 28 HEV IgM-positive samples, and real-time reverse transcription polymerase chain reaction results for hepatitis E virus were all negative.

Conclusions: Analysis of KNHANES blood samples showed a notably high seroprevalence of HEV IgG and IgM, indicating a significant burden of past and recent HEV infections. These findings highlight the importance of hepatitis E as a public health concern in South Korea.

Keywords: Viral Hepatitis, Hepatitis E, Epidemiology



PE-10

A Retrospective Analysis of the Predictive Value of Serum Albumin-to-Creatinine Ratio in Assessing Hepatorenal Function

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Aims: The serum albumin-to-creatinine ratio (ACR) has been established as a predictor of mortality risk in severe heart failure. In this study, we aimed to evaluate the predictive potential of the serum albumin-to-creatinine ratio in assessing hepatorenal dysfunction.

Methods: This retrospective study was conducted in the Department of Biochemistry at ACS Medical College and Hospital. Data from 308 patients were collected, including demographic and clinical parameters such as age, gender, urea, creatinine, total protein, albumin, AST, ALT, ALP, and direct, indirect, and total bilirubin levels. The albumin-to-creatinine ratio was calculated and categorized into four quartiles. Patients were grouped based on these quartiles for analysis. Statistical analysis was performed using SPSS 28, with data expressed as mean ± standard deviation (SD) and median. Differences between groups were assessed using one-way ANOVA for parametric data and the Kruskal-Wallis test for non-parametric data.

Results: The study revealed significant alterations in key parameters across the groups, including urea, creatinine, total bilirubin, AST, ALT, ALP, total protein, and albumin levels. These findings suggest a strong association between the albumin-to-creatinine ratio and hepatorenal function. results shown in table below.

Conclusions: This study is the first to demonstrate that a serum albumin-to-creatinine ratio is less than 4.2 is associated with more severe liver disease. However, further research is necessary to validate these findings and explore their clinical implications.

Keywords: Serum Albumin-to-Creatinine Ratio, Hepatorenal Function, Retrospective Analysis, Liver Disease

VARIABLES	GROUP 1 (n=69)	GROUP 2 (n=77)	GROUP 3 (n=81)	GROUP 4 (n=80)	P VALUE
AGE	49±15 (49*)	42±14 (41*)	43±13 (43*)	42±15 (41*)	<0.06
SEX M/F	31/38	38/39	41/32	28/52	
UREA (mg/dl)	32±31 (28*)	22±6 (21*)	20±9 (18*)	19±6 (18*)	<.001
CREATININE (mg/dl)	2±8 (1*)	0.8±0.1 (0.8*)	0.6±0.1 (0.6*)	0.4±0.2 (0.4*)	.000
T.BILIRUBIN (mg/dl)	0.9±0.9 (0.7*)	0.6±0.2 (0.7)	0.7±0.7 (0.6*)	0.5±0.3 (0.3*)	<.001
D.BILIRUBIN(mg/dl)	0.5±0.8 (0.3*)	0.3±0.1 (0.3*)	0.3±0.1 (0.3*)	0.3±0.2 (0.3*)	NS
I.BILIRUBIN (mg/dl)	0.4±0.3 (0.4*)	0.3±0.1 (0.3*)	0.4±0.3 (0.3*)	0.5±0.8 (0.3*)	NS
AST (U/L)	23*	18*	18*	25*	<.001
ALT (U/L)	26*	23*	23*	42*	<.001
ALP (U/L)	97±42 (98*)	90±25 (97*)	93±32 (100*)	107±32 (110*)	.002
T.PROTEIN (g/dl)	7.5±8 (6.5*)	7.4±7 (6.7)	8±9.6 (6.7*)	8.3±9.5 (6.5*)	.015
ALBUMIN (g/dl)	3±0.6 (3.3*)	3.6±0.3 (3.6*)	3.7±0.4 (3.7*)	5.7±7.7 (3.7*)	<.001
GLOBULIN (g/dl)	3.1±0.6 (3*)	3.4±3.4 (3.2*)	3.1±0.3 (3.2*)	3.2±0.3 (3.2*)	NS
ALBUMIN/CREATININE	3.2±0.9 (3.4*)	4.6±0.3 (4.6*)	5.7±0.3 (5.6*)	17±25 (9.5*)	

*median

PE-11

Epidemiological Analysis of Hepatitis E Virus Infections in South Korea Using Infectious Disease Reporting Data from the Korea Disease Control and Prevention Agency

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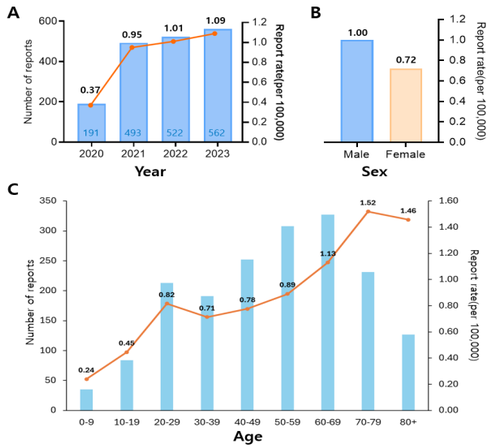
Aims: Since July 2020, South Korea has mandated the reporting of all diagnosed hepatitis E cases to the Korea Disease Control and Prevention Agency (KDCA). This study aimed to analyze infectious disease reporting data to investigate the trends and characteristics of reported hepatitis E cases.

Methods: From July 2020 to December 2023, hepatitis E case reports from the KDCA were analyzed to assess reporting trends by sex, age, and region, along with their clinical and epidemiological characteristics.

Results: After excluding duplicate reports, a total of 1,768 hepatitis E cases were reported. Analysis of KDCA infectious disease reporting data revealed a rising trend in reported HEV cases, increasing from 493 cases in 2021 (0.95 per 100,000 population) to 562 cases in 2023 (1.07 per 100,000). The average reporting rate during the study period was 0.86 per 100,000 population. While regional variations in reporting rates were observed, no clear seasonality was identified. HEV cases were more frequently reported in men than in women, with a statistically significant difference ($p < 0.001$). The number of reported HEV cases increased with age, from 35 cases in the 0–9 age group to 327 cases in the 60–69 age group, showing a statistically significant difference across age groups ($p < 0.001$). Symptomatic cases accounted for 62.8% of all reports, showing a higher proportion among younger age groups, with no significant differences by gender.



Conclusions: Hepatitis E reported cases in South Korea, based on KDCA infectious disease reporting data, have increased since the implementation of a comprehensive surveillance system in 2020, with higher rates in men and older age groups.

Keywords: VIRAL Hepatitis, Hepatitis E, Epidemiology

PE-12

Hepatic Whispers: Decoding GGT, ALP, and Genetic Clues in Ischemic Stroke Risk

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Aims: Stroke remains a leading cause of morbidity and mortality globally, with ischemic stroke accounting for the majority of cases. Recent studies have identified potential correlations between liver enzyme levels and stroke risk, particularly ischemic stroke. Liver enzymes such as gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) have been explored as biomarkers for stroke prediction. This meta-analysis aims to synthesize existing evidence to evaluate the relationship between liver enzymes and stroke risk, emphasizing potential diagnostic and prognostic implications.

Methods: A systematic review and meta-analysis were conducted following PRISMA guidelines. Databases including PubMed, Scopus, and Web of Science were searched for studies up to March 2024 that investigated the association between liver enzymes and stroke risk. Inclusion criteria encompassed prospective cohort studies, Mendelian randomization (MR) analyses, and observational studies assessing serum levels of GGT, ALT, AST, and ALP in relation to stroke incidence. The Newcastle Ottawa Scale was used to assess study quality, and risk ratios (RR), hazard ratios (HR), and odds ratios (OR) were extracted. Data were analyzed using RevMan and R software, and the certainty of evidence was graded using the GRADE framework.

Results: Meta-analysis of 17 prospective studies and MR analyses yielded the following key findings:

Gamma-Glutamyl Transferase (GGT): Elevated GGT levels were consistently associated with increased stroke risk. The relative risk (RR) for ischemic stroke was 1.43 (95% CI: 1.30 to 1.57, $P<0.00001$). In the ARIC study cohort, the highest GGT quartile had a hazard ratio (HR) of 2.01 (95% CI: 1.68 to 2.41) for ischemic stroke, indicating a strong dose-response relationship.

Alkaline Phosphatase (ALP): Higher ALP levels significantly increased stroke risk, with an RR of 1.60 (95% CI: 1.22 to 2.10, $P=0.0006$). Multivariable MR analyses confirmed ALP as a significant risk factor for both overall stroke and ischemic stroke.

Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST): No significant association was found between ALT levels and ischemic stroke risk (RR: 0.92, 95% CI: 0.68 to 1.24, $P=0.58$). AST showed inconsistent results, with some studies indicating an association with intracerebral hemorrhage (ICH) but not ischemic stroke (RR: 1.43, 95% CI: 0.83 to 2.49, $P=0.20$).

Sex Differences and Genetic Factors: Subgroup analyses revealed sex-specific differences in liver enzyme-related stroke risk, supported by gene set enrichment and tissue enrichment analyses.

Conclusions: This meta-analysis highlights GGT and ALP as potential biomarkers for predicting ischemic stroke risk, suggesting their utility in early identification of high-risk individuals. Elevated GGT levels, even within normal ranges, were robustly associated with increased ischemic stroke risk, while ALP also showed a significant correlation. ALT and AST did not demonstrate consistent associations with ischemic stroke, though AST may be linked to ICH risk. Personalized, sex-specific interventions targeting liver enzyme modulation could offer novel strategies for stroke prevention. Future research should focus on large-scale validation studies to confirm these findings and explore underlying mechanisms.

Keywords: Gamma-Glutamyl Transferase (GGT), Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate AminotransferasE (AST)

PE-13

Effect of High-Sensitivity C-Reactive Protein on Gallstones in Janata Pharmacy for Early Diagnosis Rather than Accidentally

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Aims: High-sensitivity C-reactive protein (hs-CRP), a classical indicator of inflammation, holds significant clinical value in various diseases, which indicates inflammation in the body, which can be a sign of infection, injury, or chronic disease. The relationship between hs-CRP and gallstones, however, remains poorly studied at present. Gallstones are hardened deposits of bile that can form in your gallbladder. Bile is a digestive fluid produced in the liver and stored in the gallbladder.

Methods: Data from January 2022 to December 2024 were analyzed in the Janata pharmacy with proper and formal consent. focusing on participants aged 40 years and older who had provided gallstone information. We had categorized low risk, mild elevation, moderate, and high elevation. After getting demographic data, we had to measure highly sensitive CRP in MISPA i3 (quantitative estimation) after getting the video x-ray report. We had applied various statistical tools to determine the relationship between hs-CRP and the presence of gallstones.

Results: The study included 2400 participants; out of them, 62% were female and the remaining were male. About 13% were refused to give information owing to various reasons. with an average (hs-CRP) of 6.0 ± 0.84, where the normal range was below 0.3 mg/dl. We had categorized it as low risk (<0.3 mg/dl), mild elevation (0.3-1 mg/dl), moderate elevation (1 to 10 mg/dl), and high elevation (>10 mg/dl). We found that moderate elevation was a significant relationship ($p < 0.0001$) with gallstones. We also found that alcoholics and smokers had a higher chance of having gallstones, as well as the habit of hurrying, worrying, and eating curry, and low fluid intake also had a significant role in having gallstones.

Conclusions: Higher log (hs-CRP) levels are linked to a greater prevalence of gallstones. We still need to carry out further large prospective research to explore the causal relationship of this association. We have to discover further best or sensitive biomarkers to diagnose gallstones rather than accidentally diagnosed ones like video x-rays for other purposes. We have to eliminate the hurry, worry, and curry habit. As well as drinking more water and testing HsCRP with other normal tests, it will help with the early diagnosis of GSD.

Keywords: Gallstones, Cross-Sectional Study, High-Sensitivity C-Reactive Protein, Inflammatory

PE-14

Hepatoprotective Effect of ALD-1 (4′,7-Dihydroxy-3′-methoxyflavone) Isolated from Albizzia lebbeck Benth. in Experimental Liver Injury

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Aims: The study aimed to evaluate the hepatoprotective potential of ALD-1 (4′,7-Dihydroxy-3′-methoxyflavone) isolated from *Albizzia lebbeck* Benth. against experimentally induced liver injury. The effect of ALD-1 on biochemical, oxidative stress, and histopathological markers was assessed to determine its therapeutic efficacy in hepatotoxicity.

Methods: Liver injury was induced in experimental animals using a hepatotoxic agent (such as carbon tetrachloride [CCl_4] or paracetamol). ALD-1 was administered at different doses, and its effects were compared with a standard hepatoprotective drug (e.g., silymarin). Serum biomarkers of liver function, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total and direct bilirubin, total protein, and albumin, were analyzed. Additionally, oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), glutathione (GSH), and catalase (CAT) levels were assessed. Histopathological examination of liver tissue was performed to evaluate morphological changes and cellular damage.

Results: ALD-1 treatment significantly reduced serum ALT, AST, ALP, and bilirubin levels, indicating restoration of normal liver function. The total protein and albumin levels were preserved, reflecting improved hepatocellular integrity. Furthermore, ALD-1 exhibited strong antioxidant activity by decreasing MDA levels and enhancing SOD, GSH, and CAT activities, suggesting a protective role against oxidative damage. Histopathological analysis revealed a reduction in hepatocellular degeneration, necrosis, and inflammation in ALD-1-treated groups compared to the hepatotoxin group, supporting its protective effect.

Conclusions: The findings indicate that ALD-1 exerts significant hepatoprotective effects by improving liver enzyme profiles, reducing oxidative stress, and preserving liver architecture. These results suggest that ALD-1, isolated from *Albizzia lebbeck* Benth., could be a promising natural hepatoprotective agent for managing liver disorders. Further studies are warranted to elucidate its precise molecular mechanisms and potential clinical applications.

Keywords: 4′,7-Dihydroxy-3′-Methoxyflavone, Albizzia Lebbeck Benth, CCL_4-Induced Hepatotoxicity, Hepatoprotection

Table: Effect of ALD-1 on Hepatic Gluconeogenic Enzymes in CCl4-induced Hepatotoxic Rats

Groups	Glucose-6-Phosphate Dehydrogenase (units/min/mg protein)	Glucose-6-Phosphatase (units/min/mg protein)	Fructose-1,6-Biphosphatase (units/min/mg protein)	Hepatic Hexokinase (units/min/mg protein)
Group 1: Normal Control	0.1840 ± 0.0024	0.0306 ± 0.0005	0.0212 ± 0.0005	0.1880 ± 0.0037
Group 2: Normal + ALD-1 (60 mg/kg p.o.)	0.1800 ± 0.0032	0.0304 ± 0.0008	0.0222 ± 0.0007	0.1860 ± 0.0051
Group 3: Hepatotoxic Control (CCl4 60 mg/kg i.p.)	0.0554 ± 0.0012 a	0.0712 ± 0.0004 a	0.08574 ± 0.0024 a	0.0430 ± 0.0213 a
Group 4: Hepatotoxic + ALD-1 (20 mg/kg p.o.) (45 days)	0.0506 ± 0.0005	0.0712 ± 0.0009	0.0750 ± 0.0011	0.0432 ± 0.0212
Group 5: Hepatotoxic + ALD-1 (40 mg/kg p.o.) (45 days)	0.0840 ± 0.0016	0.0552 ± 0.0012	0.0566 ± 0.0010	0.1260 ± 0.0040
Group 6: Hepatotoxic + ALD-1 (60 mg/kg p.o.) (45 days)	0.1048 ± 0.0051***	0.0400 ± 0.0009***	0.0344 ± 0.0012***	0.1460 ± 0.0024**
Group 7: Hepatotoxic + Silymarin (10 mg/kg p.o.) (45 days)	0.1600 ± 0.0032**	0.0316 ± 0.0004**	0.0232 ± 0.0006***	0.1800 ± 0.0045***

The data are expressed as **mean ± SEM** (n = 5 per group).
Comparisons were made with:
"a" indicates significant differences compared to the normal control group.
"*" p < 0.05 (significant), ** p < 0.01 (very significant), *** p < 0.001 (extremely significant).

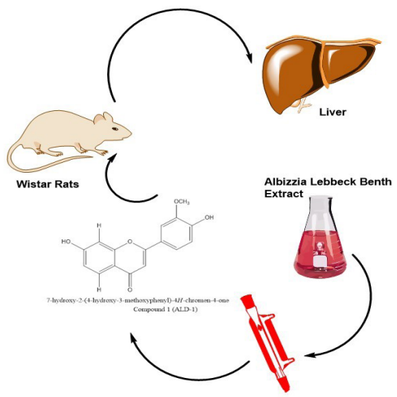

Figure: Hepatoprotective effects of ALD-1 on CCL4 induced liver injury in rats.

PE-15

Precision Insights into Gender-Specific Liver Fibrosis: Evaluating FIB-4, AAPRI, and mFIB-4 as Predictive Markers of Disease Progression

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Aims: Liver fibrosis, characterized by excessive extracellular matrix protein accumulation, is a central feature of all chronic liver diseases (CLD). It results from recurrent liver injury and a sustained wound-healing response, leading to architectural disruption, cirrhosis, and complications such as portal hypertension, liver failure, and hepatocellular carcinoma (HCC). Biological and socio-cultural factors, including sex, gender, age, reproductive status, and CLD etiology significantly influence fibrogenesis through genetic, hormonal, metabolic, and lifestyle-related mechanisms. This study explores the sex- and gender-specific determinants of liver fibrosis and its systemic complications, aiming to enhance personalized treatment strategies.

Methods: This study was carried out in ACS Medical College and Hospital. Retrospective data from June 2023 to January 2025 was collected from the Clinical Biochemistry lab. Lipid Parameters like total cholesterol, triglycerides, HDL, LDL and VLDL were collected. Hematology parameters like Heamoglobin, Platelets, RBC, WBC, Neurophil, Lymphocyte, Eosinophil, Monocyte, basophil, PCV, MCV, MCH, and MCHC were collected. Serum bilirubin, AST, ALT, ALP, Urea, Creatinine were also collected. Liver fibrosis indices like FIB-4, m FIB-4, APRI, AARPRI were calculated. All the datas were analysed using SPSS 28 software. Student-t test and Mann-Whitney U Test was used analyse the statistical differences between the two gender groups. All the data were expressed as mean ± sd., median and interquartile range.

Results: FIB-4, m-FIB4 and AARPRI values were significantly low in females compared with males. In this study significant difference in bun creatinine ratio, Heamoglobin, Platelets, PCV, MCH, MCHC, Total bilirubin, albumin bilirubin ratio, basophil was observed between 2 gender groups, But there were no significant difference in Lipid parameters.

Conclusions: Higher platelet count is associated with less fibrosis; hence Females are protected from profibrogenic pathomechanisms leading to liver fibrosis. Genetic, hormonal and immunogenic factors contribute to lower risk of fibrosis in females compared to males. Biological factors of females contribute to lesser risk for liver fibrosis.

Keywords: Interquartile Range, Profibrogenic Pathomechanisms, Aspartate Aminotransferase to Platelet Ratio Index (AARPRI)

INDEPENDENT SAMPLE T- TEST		
PARAMETERS	GROUP 1 (MEAN ±SD)	GROUP 2 (MEAN ±SD)
BUN CREATININE	15.14 ± 9.00	12.63 ± 6.11
HEAMOGLOBIN	11.21 ± 1.80	12.53 ± 2.85
PLATELET	2.92 ± 0.824	2.64 ± 1.11
PCV	34.63 ± 5.91	37.51 ± 8.09
MCH	27.10 ± 5.85	29.86 ± 9.03
MCHC	31.98 ± 1.97	32.99 ± 2.01

MANN-WHITNEY U TEST			
PARAMETERS		GROUP 1 (MEAN SD)	GROUP 2 (MEAN ±SD)
TOTAL BILIRUBIN	median	0.51	0.72
	Interquartile Range	0.36	0.59
AARPRI	median	0.599	0.688
	Interquartile Range	0.48	0.66
BASOPHIL	median	0.5	0.6
	interquartile range	0.3	0.4
ALBI	median	-0.7625	-0.661
	interquartile range	0.213	0.326
FIB-4	median	0.884	1.8519
	interquartile range	0.54	3.2
mFIB-4	median	1.983	2.214
	interquartile range	1.69	2.49

PE-16

Impact of Diabetes on the activity of the Chronic Viral Hepatitis in Mongolia: A Cross-Sectional Study

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Aims: Mongolia has one of the highest prevalence rates of chronic viral hepatitis worldwide, with HBV at 11.1%, HCV at 8.5%, and HDV at 60.1%. While HCV is known to increase the risk of diabetes, the roles of HBV and HDV in diabetes remain unclear. This study aims to assess whether diabetes impacts the prognosis of viral hepatitis and vice versa.

Methods: We analyzed data from 564 participants in the DETECT-HCC study, collected between September 23, 2023, and February 5, 2025. Participants included 285 chronic hepatitis cases and 279 healthy controls, categorized into diabetic (n = 55), pre-diabetic (n = 126), and non-diabetic (n = 383) groups based on diabetes status. Diabetes was confirmed if at least one of the following criteria was met: history of diabetes, history of diabetes medication use, fasting glucose ≥7 mmol/L, or HbA1C ≥6.5%. Pre-diabetes was defined by fasting glucose between 5.6–6.9 mmol/L or HbA1C between 5.7–6.4%. ANOVA was used to assess statistical significance.

Results: Among body measurement indices, height-to-weight ratio and BMI showed significant differences between diabetes status groups in both the hepatitis and control groups (p-value = 0.0000). Among liver function tests, total bilirubin, direct bilirubin, and ALT showed significant differences in diabetes status groups in the chronic hepatitis group (p-values = 0.0026, 0.0013, and 0.0143, respectively), with mean values significantly higher in the diabetic group. Additionally, GGT, HDL, and UA showed significant differences in the chronic hepatitis group (p-values = 0.0006, 0.0031, 0.0000, respectively). No significant differences were observed in the control group.

Conclusions: This study demonstrates significant associations between diabetes status and liver function in chronic hepatitis patients. However, the diabetic sample size was relatively small, and further research with a larger sample size is needed to validate these findings. Managing diabetes could improve the prognosis of chronic hepatitis, particularly in diabetic patients.

Keywords: Mongolia, Chronic Viral Hepatitis, Diabetes, Liver Function Tests

PE-17

Revolutionizing Wilson's Disease Management: Gene Therapy and RNA-Based Interventions for Copper Homeostasis

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Aims: Wilson's disease (WD) is a rare autosomal recessive disorder caused by mutations in ATP7B, leading to defective hepatic copper transport and toxic accumulation. Current treatments, such as chelation therapy and zinc supplementation, do not correct the underlying genetic defect. This review explores gene therapy and RNA-based interventions as next-generation therapeutic strategies to restore physiological copper homeostasis.

Methods: A comprehensive review of emerging gene editing, RNA-based therapies, and targeted drug delivery systems was conducted. Studies on AAV-mediated ATP7B gene replacement, CRISPR-based gene correction, and RNA interference (RNAi) therapies were analyzed for their efficacy in preclinical and early clinical models.

Results: Gene Therapy for ATP7B Restoration:

Adeno-associated virus (AAV)-mediated ATP7B delivery restores hepatic copper transport in WD animal models.

CRISPR/Cas9-based correction of ATP7B mutations demonstrates long-term correction of copper metabolism.

RNA-Based Therapeutics: RNA interference (siRNA, ASOs) targeting copper overload pathways shows promise in reducing hepatic copper accumulation.

mRNA therapy encoding functional ATP7B circumvents gene delivery limitations by transiently restoring ATP7B function.

Targeted Drug Delivery Systems: Lipid nanoparticle (LNP) technology enhances RNA stability and targeted hepatic uptake.

Exosome-based ATP7B mRNA delivery shows potential for non-viral gene therapy approaches.

Challenges & Future Directions: Immune response to AAV vectors, off-target CRISPR effects, and long-term gene expression stability remain key barriers to clinical translation.

Conclusions: Gene therapy and RNA-based interventions offer a paradigm shift in Wilson's disease treatment, addressing the root genetic cause rather than managing symptoms. Future research should focus on optimizing vector safety, refining RNA-based approaches, and initiating clinical trials for long-term correction of copper metabolism.

Keywords: Wilson's Disease, Gene Therapy

PE-18

Clinical and Epidemiological Features of Acute Viral Hepatitis in South Korea: A Nationwide Prospective Multicenter Study

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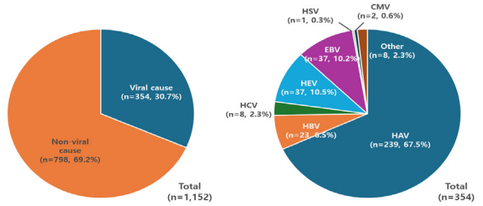
Aims: This study aims to examine acute hepatitis, particularly acute viral hepatitis (AVH), focusing on its epidemiology and clinical characteristics in South Korea.

Methods: From 2020 to March 2024, we recruited participants from 17 centers, specifically targeting patients who met the criteria for acute hepatitis. We conducted analyses on the etiology, clinical characteristics, and progression of acute hepatitis.

Results: After excluding patients with non-hepatic causes, we enrolled a total of 1,152 patients. Of these, 354 (30.7%) were diagnosed with AVH based on specific serologic markers. The predominant etiology was hepatitis A virus (HAV, 67.5%), followed by hepatitis E virus (HEV, 10.5%), Epstein-Barr virus (EBV, 10.2%), hepatitis B virus (6.5%), hepatitis C virus (2.3%), cytomegalovirus (0.6%), herpes simplex virus (0.3%), and other pathogens (2.3%). When comparing viral and non-viral causes, AVH patients exhibited a male predominance and a younger average age. They also had higher levels of liver enzymes indicative of liver injury, while markers of liver function remained preserved. Among viral etiologies, HEV patients were the oldest on average, while EBV patients were the youngest. Clinical symptoms were common across all groups but less frequent in HEV cases. AST and ALT elevations were most pronounced in HAV patients, whereas PT and albumin levels remained similar among HAV, HEV, and EBV groups. Prognostic outcomes were also comparable across these viral etiologies.

Conclusions: AVH accounts for approximately 30% of acute hepatitis cases in South Korea, with HAV, HEV, and EBV being the most prevalent etiologies. These findings provide insights into AVH and support its management.

Keywords: Hepatitis, Viral, Human, Hepatitis A, Hepatitis E, Epidemiology



PE-19

Dietary Diversity and Its Impact on Liver Disease Risk: A Population-Based Study in Indonesia

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Aims: Liver disease is a significant public health issue, contributing to high morbidity and mortality worldwide. Lifestyle factors, such as diet, also play a crucial role in liver health. The Dietary Diversity Score (DDS) has been proposed as a tool to assess diet quality by measuring the variety of food groups consumed. This study aims to explore the relationship between DDS and liver disease in the Indonesian population.

Methods: This cross-sectional study used data from the Indonesian Family Life Survey 5 (IFLS-5). Participants meeting inclusion criteria were included. DDS was calculated based on the number of food groups consumed over a specific period and categorized into three groups: low, medium, and high. Logistic regression analysis was performed to assess the relationship between DDS and liver disease.

Results: The mean age of participants was 38.71 ± 16.2 years, with 55.5% male participants. Logistic regression analysis revealed a significant inverse association between DDS and liver disease, with higher DDS linked to a lower likelihood of liver disease (P<0.001). Other significant covariates included obesity, gender, comorbidities, stress, marital status, health insurance, and employment status.

Conclusions: Our findings suggest that higher DDS is associated with a lower risk of liver disease in the Indonesian population. This study emphasizes the importance of promoting dietary diversity as a preventive measure for liver disease. Further longitudinal research is needed to explore this relationship in greater detail and understand the underlying mechanisms.

Keywords: Dietary Diversity, Indonesia, Liver Disease, Population-Based Study

PE-20

Diagnostic Performance of FIB-4, APR, and APRI in Liver Fibrosis: A study of 586 patients

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Aims: To evaluate the diagnostic accuracy and clinical utility of the FIB-4, APR, and APRI indices in assessing liver fibrosis.

Methods: In this retrospective study, a total of 586 patients (289 males, 297 females) were included. AST, ALT, albumin, and platelet counts were analyzed using a Beckman Coulter analyzer and a 5-part hematology machine. The diagnostic performance of the FIB-4, APR, and APRI indices for liver fibrosis was evaluated using specific cutoff values. The indices were categorized into three groups based on their cutoff values: low, intermediate, and high, as outlined in Table 1. The diagnostic performance was assessed using ANOVA to compare group means and Receiver Operating Characteristic (ROC) curve analysis with SPSS. This study aims to assess the sensitivity, specificity, and overall diagnostic accuracy of the FIB-4, APR, and APRI indices in detecting liver fibrosis.

Results: The diagnostic performance of FIB-4, APR, and APRI was evaluated using ANOVA, which showed a statistically significant difference between the indices (P<0.001). ROC curve analysis (Graph 1) demonstrated that FIB-4 had the highest significance, with a sensitivity of 98.6% and specificity of 98.4%, though its AUC (0.805) indicated moderate discrimination ability.

Among the three indices, FIB-4 emerged as a better marker for fibrosis detection, while APR and APRI showed relatively lower diagnostic performance. Values were expressed as mean ± standard deviation, ensuring accurate data representation. The significant p-value (<0.001) reinforces the superior diagnostic utility of FIB-4, making it a reliable non-invasive tool for liver fibrosis assessment.

Conclusions: FIB-4 is a reliable non-invasive marker for assessing liver fibrosis, especially in advanced cases.

APR and APRI remain useful but are less effective in early-stage fibrosis detection. These indices provide cost-effective alternatives for large-scale fibrosis screening.

Keywords: FIB4, Non Invasive Method to Asses Liver Fibrosis

GRAPH 1.

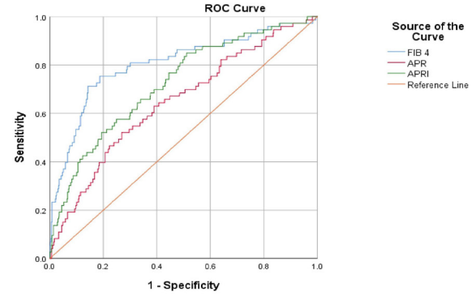

TABLE 1.

	LOW	INTERMEDIATE	HIGH
FIB4	<1.3	1.3 - 2.67	>2.67
APR	>0.020	0.012 - 0.02	<0.012
APRI	<0.5	0.5 - 2	>2

TABLE 2.

	LOW	INTERMEDIATE	HIGH	SIGNIFICANCE
FIB-4	0.7 ± 0.28	1.77 ± 0.37	6.92 ± 7.83	<0.001
Age	45.4 ± 16.14	58.93 ± 14.8	56.57 ± 18.68	<0.005
Male	218	48	23	
Female	191	71	35	
APR	0.05 ± 0.12	0.02 ± 0.01	0.01 ± 0.01	<0.001
Age	52.52 ± 17.41	47.66 ± 16.52	49.96 ± 17.88	<0.005
Male	49	149	91	
Female	64	154	79	
APRI	0.21 ± 0.09	0.97 ± 0.39	7.26 ± 5.88	<0.001
Age	50.1 ± 16.8	48.3 ± 18.1	35.96 ± 17.15	<0.005
Male	252	28	9	
Female	243	40	15	

PE-21

"Hey SIRI, Tell Me about My Liver!"– A Reliable Inflammatory Marker Meets FIB-4

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Aims: Systemic Inflammatory Response Index (SIRI) is an emerging marker of inflammation and has been associated with various disease states, including hepatic fibrosis. This study aims to evaluate the association between SIRI and fibrosis markers, particularly FIB-4, in individuals with varying degrees of hepatic function. Given that inflammation plays a crucial role in hepatic fibrosis progression, SIRI may serve as a useful indicator for assessing fibrosis severity, especially in individuals with normal hepatic function.

Methods: This study was carried out at ACS Medical College and Hospital. Retrospective data from June 2023 to January 2025 was collected from the Clinical Biochemistry lab. Lipid parameters such as total cholesterol, triglycerides, HDL, LDL, and VLDL were collected. Hematology parameters including hemoglobin, platelets, RBC, WBC, neutrophils, lymphocytes, eosinophils, monocytes, basophils, PCV, MCV, MCH, and MCHC were also collected. Additionally, serum bilirubin, AST, ALT, ALP, urea, and creatinine levels were recorded. Liver fibrosis indices such as FIB-4, mFIB-4, APRI, and AARPRI were calculated. All the data were analyzed using SPSS 28 software. A Student's t-test was used to analyze statistical differences. Pearson correlation analysis was performed to assess the association with fibrosis indices.

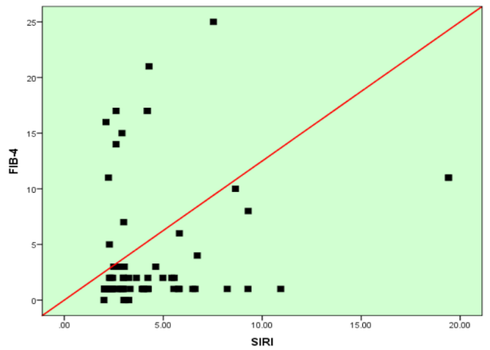
Results: In this study, a significant difference was observed in total cholesterol, total bilirubin, direct bilirubin, AST, ALP, ALBI, urea, creatinine, WBC, neutrophils, lymphocytes, lymphocyte-to-WBC ratio, neutrophil percentage, SII, basophils, absolute lymphocyte count, APRI, and mFIB-4. The analysis demonstrated a significant correlation between SIRI and FIB-4 based on a cutoff of 2.0 (P<0.05), particularly in individuals with normal hepatic function. Higher SIRI values were associated with increased FIB-4 scores, indicating that systemic inflammation may contribute to fibrosis progression.

Conclusions: SIRI, a non-invasive marker of inflammation, correlates with liver fibrosis. Hence, SIRI can be measured alone or along with the FIB-4 score to evaluate liver fibrosis non-invasively. The findings suggest that SIRI could be integrated into fibrosis assessment models to enhance early detection and monitoring of hepatic fibrosis progression.

Keywords: AARPRI (AST/ALT Ratio to Platelet Ratio Index), Systemic Inflammatory Response Index (SIRI), Hepatic Fibrosis

PARAMETER	GROUP 1 (Mean ± SD)	GROUP 2 (Mean ± SD)	p VALUE
Age	50.07 ± 8.50	52.28 ± 9.25	0.057
Gender (F/M)	132/111	32/2	0.107
Total Cholesterol	182.34 ± 52.876	162.38 ± 57.539	0.009
Total Bilirubin	0.78 ± 0.935	1.56 ± 3.346	0.001
Direct Bilirubin	0.11 ± 0.538	0.72 ± 2.404	0.0
AST	28.05 ± 28.853	52.89 ± 103.402	0.001
ALP	88.71 ± 36.240	119.04 ± 67.578	0.0
ALBI	-0.86 ± 0.858	-0.62 ± 0.543	0.025
Urea	28.09 ± 22.335	40.63 ± 36.904	0.0
Creatinine	1.19 ± 0.815	1.84 ± 2.088	0.0
WBC	8.40 ± 2.126	12.71 ± 6.531	0.0
Neutrophils	62.30 ± 10.841	79.71 ± 7.199	0.0
Lymphocytes	28.06 ± 8.119	12.37 ± 4.727	0.0
LYM/WBC*100	361.5 ± 179.95	118.21 64.85	0.0
Absolute Lymphocyte Count	33.93 ± 92.47	12.36 ± 12.36	0.048
Neutrophil percent	786.13 ± 235	713.94 ± 226.18	0.021
SII	7.13 ± 4.32	20.34 ± 11.15	0.0
Basophil	0.46 ± 0.53	0.178 ± 0.38	0.0
mFIB-4	2.65 ± 2.41	3.42 ± 3.02	0.026
APRI	0.17 ± 0.64	0.45 ± 1.45	0.02

p value less than 0.05 level is considered significant



PE-22

Unraveling Metabolic Interplay: Insights from TG/HDL Ratio and RBC-TLLRI Correlations across Thyroid, Liver, Lipid, and Renal Indices

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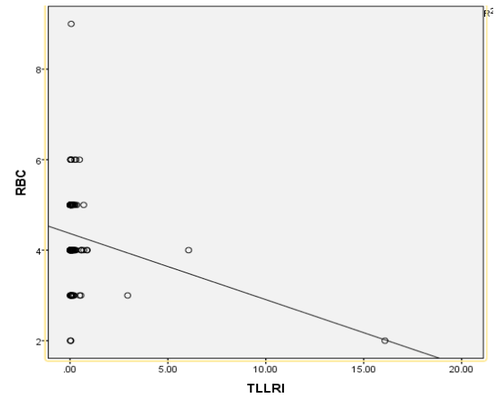
Aims: This retrospective study evaluates the interrelationships between thyroid, liver, lipid, and renal indices in 200 individuals stratified into four quartiles. It focuses on the Thyroid-Liver-Lipid-Renal Index (TLLRI) as a metabolic biomarker and the correlation between red blood cell (RBC) count and the triglyceride-to-HDL (TG/HDL) ratio. Additionally, it explores whether renal dysfunction impairs haemopoietin production, leading to reduced RBC count.

Methods: Statistical analysis was conducted on key metabolic parameters across quartiles, calculating mean ± standard deviation (SD) for each group from the data collected from ACS Medical College and Hospital. Pearson correlation analysis was performed to assess the association between RBC and TLLRI, as well as other metabolic indices. Comparative analysis of quartile-specific variations in thyroid, liver, lipid, and renal parameters was performed to identify significant trends and potential interdependencies.

Results: The TG/HDL ratio demonstrated a progressive increase across quartiles (2.81 ± 1.86 in Q1 to 5.89 ± 5.97 in Q4), indicating a strong association with metabolic dysregulation. TLLRI exhibited a marked elevation from Q1 (0.0115 ± 0.0062) to Q4 (0.7583 ± 2.3944), reflecting worsening metabolic status. A negative correlation was observed between RBC count and TLLRI (r = -0.62, P<0.01), supporting the hypothesis that declining renal function—evidenced by rising creatinine (from 0.68 ± 0.24 in Q1 to 1.51 ± 1.70 in Q4) and urea levels (21.28 ± 14.04 in Q1 to 32.52 ± 23.28 in Q4)—could impair erythropoietin production, thereby reducing RBC count. Additionally, elevated VLDL and MASLDSEV values in higher quartiles suggest an interplay between lipid metabolism and metabolic dysfunction.



PARAMETER	Group 1(0.00-0.02)	Group 2(0.02-0.04)	Group 3(0.04-0.11)	Group 4(0.11-16.09)
RBC	4.20 ± 0.639	4.45 ± 0.914	4.40 ± 0.926	4.30 ± 0.863*
PCV	35.13 ± 6.74	36.59 ± 8.05	35.92 ± 5.92	36.22 ± 6.29*
TSH	2.15 ± 6.55	1.89 ± 1.20	3.31 ± 1.72	6.04 ± 6.83*
VLDL	23.71 ± 14.94	25.63 ± 19.73	28.39 ± 17.49	37.95 ± 28.49*
CREAT	0.68 ± 0.24	0.77 ± 0.18	0.79 ± 0.21	1.51 ± 1.70*
UREA	21.28 ± 14.04	21.96 ± 8.42	20.96 ± 9.25	32.52 ± 23.28*
TGHDL	2.81 ± 1.86	3.27 ± 2.79	4.50 ± 4.16	5.89 ± 5.97*
TSHFT4	0.28 ± 0.81	0.31 ± 0.39	0.47 ± 0.93	2.68 ± 8.65*
MASLDSEV	30.62 ± 72.61	46.30 ± 70.92	139.72 ± 270.63	415.46 ± 680.86*
TLRI(Thyroid-Liver-Renal Index)	0.0024 ± 0.0029	0.0077 ± 0.0062	0.0244 ± 0.0328	0.2286 ± 0.6853*
RLCI(Renal Lipid Cardiovascular index)	0.0175 ± 0.0310	0.0219 ± 0.0096	0.0290 ± 0.0201	0.3131 ± 0.9441*
CKDDI(Chronic Kidney Disease-Dyslipidemia Index)	0.0201 ± 0.0327	0.0268 ± 0.0274	0.0417 ± 0.0403	0.4918 ± 1.3307*
HRI(Hepato-Renal Index)	0.0366 ± 0.0669	0.0486 ± 0.0409	0.0828 ± 0.0866	0.8596 ± 2.7295*
TLLRI(Thyroid liver-lipid renal index)	0.0115 ± 0.0062	0.0333 ± 0.0079	0.0713 ± 0.0206	0.7583 ± 2.3944*
LDCI(Liver Dysfunction-Cardiometabolic Index)	16.24 ± 22.80	25.43 ± 55.04	45.84 ± 70.11	70.97 ± 134.05*
KCMI(Kidney-Cardiometabolic Risk Index)	0.0175 ± 0.0310	0.0219 ± 0.0096	0.0290 ± 0.0201	0.3131 ± 0.9441*
CMDI(Cardiometabolic Dysfuntion Index)	620.46 ± 878.10	713.86 ± 802.06	1225.61 ± 1580.69	4416.17 ± 9756.46*
HRDS(Hepato Renal Dysfunction Score)	0.0983 ± 0.2201	0.1376 ± 0.1606	0.2611 ± 0.2884	2.4730 ± 7.5529*

* INDICATES P<0.05

Conclusions: These findings underscore the intricate relationships between thyroid, liver, lipid, and renal indices, with significant implications for metabolic health. The progressive increase in TG/HDL ratio across quartiles reinforces its potential utility as a metabolic risk marker. Furthermore, the negative association between RBC count and TLLRI suggests that renal dysfunction may contribute to impaired erythropoiesis, emphasizing the need for comprehensive metabolic assessment in clinical practice. Future research should further explore these associations to elucidate underlying mechanisms and potential therapeutic interventions for metabolic disorders.

Keywords: Metabolic Dysregulation, TLLRI- Thyroid Liver Lipid Index, Renal Dysfunction, Erythropoiesis

PE-23

Gut-Liver-Brain Axis in Hepatic Encephalopathy: Microbiome-Derived Neurotransmitters as Novel Therapeutic Targets

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Aims: Hepatic encephalopathy (HE) is a debilitating neuropsychiatric complication of liver disease, traditionally linked to hyperammonemia. However, growing evidence suggests a crucial role of the gut-liver-brain axis (GLBA) in HE pathogenesis. This review explores microbiome-derived neurotransmitters as key modulators of HE and highlights emerging microbiota-targeted therapies.

Methods: A detailed review of recent clinical, translational, and microbiome research was conducted, focusing on gut microbial composition, neurotransmitter metabolism, and gut-targeted therapeutic interventions in HE patients.

Results: HE is driven not only by ammonia toxicity but also by gut microbial dysbiosis, which disrupts neuroactive metabolite production. Studies reveal:

Microbiome shifts in HE patients: Increased ammoniagenic bacteria (Klebsiella, Enterococcus) and depletion of beneficial strains (Faecalibacterium, Bifidobacterium).

Neurotransmitter dysregulation: Reduced GABA, serotonin, dopamine, and short-chain fatty acids (SCFAs) impair BBB function and neuroinflammation.

Key metabolites influencing astrocytes and neuroinflammation: Tryptophan-derived indoles drive neurotoxicity, while SCFAs modulate microglial activity.

Therapeutic breakthroughs: Fecal microbiota transplantation (FMT) restores eubiosis and improves cognition.

Engineered probiotics (Bacteroides fragilis, Lactobacillus strains) enhance gut-derived neuroprotection.

Microbiome-modulating drugs (rifaximin, lactulose, postbiotics, bacteriophage therapy) show promise in HE recurrence prevention.

Conclusions: This review highlights a paradigm shift from ammonia-centric to microbiome-based HE management. Precision microbiome therapeutics—including AI-driven gut profiling, synbiotic formulations, and gut-brain-targeted interventions—offer non-invasive, highly effective strategies for long-term HE control.

Keywords: Gut Liver Brain Axis, Neurotransmitters

PE-24

Hepatic Glymphatic System: A Hidden Pathway for Detoxification and Liver-Brain Crosstalk

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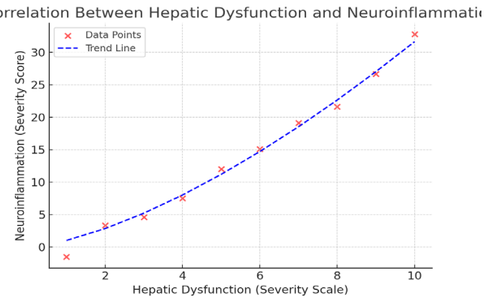
Aims: This systematic review investigates the hepatic glymphatic system, a recently identified clearance mechanism that facilitates detoxification and metabolic waste removal from the liver. Additionally, it explores the complex liver-brain crosstalk, particularly the role of astrocyte-mediated neuroinflammatory responses in hepatic encephalopathy. By integrating multidisciplinary insights, this study aims to elucidate the pathophysiological significance of hepatic glymphatic dysfunction in cirrhosis and its impact on neurodegenerative processes.

Methods: A systematic literature search was conducted across PubMed, Scopus, and Web of Science databases, adhering to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies published in the last decade (2013–2025) were included, focusing on hepatic glymphatic transport, liver-brain metabolic signaling, and astrocyte-driven neuroinflammation. Inclusion criteria encompassed clinical trials, in vivo and in vitro studies, and mechanistic reviews with relevant biomarkers and neurophysiological outcomes. Data extraction and quality assessment followed Cochrane risk-of-bias tools to ensure methodological rigor. A meta-analysis was considered where applicable to strengthen quantitative insights.

Results: The hepatic glymphatic system is emerging as a vital yet underrecognized clearance and metabolic exchange pathway. Dysfunction in this system, particularly in cirrhotic patients, impairs ammonia and neurotoxin clearance, leading to astrocyte activation, neuroinflammation, and increased blood-brain barrier permeability. Key findings highlight a bidirectional astrocyte-liver axis, where hepatic dysfunction exacerbates central nervous system oxidative stress, accelerating cognitive decline. Additionally, neuroinflammatory cascades triggered by impaired glymphatic transport correlate with systemic metabolic dysregulation, contributing to hepatic encephalopathy and neurodegenerative diseases.

Conclusions: The hepatic glymphatic system represents a pivotal detoxification mechanism linking hepatic and neurological health. Dysfunction within this pathway exacerbates neuroinflammation, oxidative stress, and blood-brain barrier disruption, highlighting a crucial intersection between hepatic encephalopathy and neurodegeneration. Understanding these mechanisms provides a foundation for novel therapeutic interventions targeting both hepatic and neuroprotective pathways. Future research should prioritize translational studies to define clinical implications and therapeutic modulation strategies for hepatic glymphatic function.

Keywords: Hepatic Glymphatic System, Liver-Brain Crosstalk, Neuroinflammation, Hepatic Encephalopathy



PE-25

Impact of Klebsiella Pneumoniae Strain and Serotype on Mortality and Clinical Outcomes in Liver Abscess Patients

Young Chang[1], Hyoju Kim[1], Jae Young Jang[1], Tom Ryu[1], Soung Won Jeong[1], Jeong-Ju Yoo[2], Sae Hwan Lee[3], Sang Gyune Kim[2], Young Seok Kim[2], Hong Soo Kim[3]

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Aims: Klebsiella pneumoniae (KPN) is a major pathogen associated with liver abscesses, but its impact on mortality and severe complications remains unclear. This study evaluates whether specific KPN strains or serotypes influence mortality and clinical outcomes, including vasopressor use, ventilator support, septic lung, and endophthalmitis.

Methods: A retrospective cohort study was conducted on patients with KPN-induced liver abscess. Whole-genome sequencing identified the most closely matching KPN strains. Statistical analyses included Firth logistic regression to address perfect separation, random forest models for feature importance, and survival analysis.

Results: Neither KPN strains nor serotypes were independent predictors of mortality. No specific KPN strain showed a consistent association with severe outcomes. Instead, host factors played a critical role. Patients with A1c levels >7.5% had a 3.2-fold increased mortality risk (P<0.01), while those with chronic liver disease had a 2.8-fold increased risk (P=0.02). Chronic liver disease showed no significant effect, and each additional year of age increased mortality risk by 1.04 times (P=0.03). Shorter hospital stays (<10 days) were associated with higher mortality, suggesting rapid clinical deterioration in fatal cases. While septic lung showed some association with certain KPN strains, host factors such as A1c and CLD appeared to have a greater influence, though these associations were not statistically significant. Endophthalmitis was not significantly linked to KPN strain or serotype but appeared more associated with host factors such as diabetes and CLD, though statistical significance was not achieved.

Conclusions: KPN strains and serotypes do not independently predict mortality in liver abscess patients. Instead, host factors such as age, diabetes, and CLD are stronger predictors of clinical outcomes.These findings highlight the importance of patient comorbidities over bacterial strain variation in mortality risk assessment.

Keywords: Liver Abscess, Klebsiella Pneumoniae, Diabetes Meletus

PE-26

Research about Biliary Stent's Cover Produced by Alternative Materials Compared to Conventional Materials

Hyung Tae Kim

R&D Team, S&G Biotech Inc, Republic of Korea

Aims: Polymer material can be used as a material of cover related to biliary stent. Some of them can be made by melting with heat, so extrusion and high-frequency processing are possible. In stent implantation into human body, superior cover material's performance is essential. Especially performance related to function is point which has to be proved. Cover of biliary stent must be biocompatible, strong, conformable. This idea was starting point in this research.

Methods: First intention was producing cover of biliary stent using our polymer based materials. Method that we use was electrospraying and electrospinning method. Bioavailability tests were conducted and it was confirmed that cover of biliary stent with our polymer based material has biocompatible improved properties. Research institute checked possibility about alternative biomaterial for conventional biliary stent's cover.

Results: There was no issue related to cover of biliary stent produced by our polymer material. Toxicity is closely related to bioavailability factor. Tests which are closely related to bioavailability were held. And there was no problem. Genetoxicity test proceeds according to ISO 10993-3. Acute toxicity test result passes the test criteria based on ISO 10993-11. After 72 hours observation, there was no toxicity change was observed.

Conclusions: Even though there was no problem during the tests related to bioavailability tests. But it has to be reviewed more. Further studies are needed and necessary. By checking lots of factors, bioavailabilty for biliary stent's cover can be improved in applicable medical device.

Keywords: Biliary, Stent, Alternative Material

PE-27

Coexistence of Shock Liver, Tumor Lysis Syndrome, and Rasburicase Toxicity in Waldenström Macroglobulinemia: A Complex Case Study

Monika Jain, Amulya Bellamkonda, Ladan Enayati, Amanuel Megiste, Chhabilal Bastola

Internal Medicine, Interfaith Medical Center One Brooklyn Health, United States of America

Aims: Waldenström macroglobulinemia is a rare B-cell lymphoma characterized by monoclonal IgM production, which leads to hyperviscosity syndrome, cytopenias, and organomegaly. Complications such as shock liver and tumor lysis syndrome are infrequent but severe. Shock liver arises from hypoperfusion or systemic illness, while TLS results from rapid tumor cell lysis. Rasburicase, used to treat TLS-induced hyperuricemia, can cause toxicity, including methemoglobinemia. This case highlights the rare coexistence of these complications in WM

Methods: CASE REPORT

Results: A 79-year-old male with a history of Waldenström macroglobulinemia, COPD, and deep vein thrombosis, presented with altered mental status likely from shock liver vs sepsis secondary from a right foot infection. BP 90/50, Hr of 80, Spo2 of 92% on RA Wbc 13 k with Neutrophil 96%, LA 10, Troponin 279, EKG Sinus rhythm with PAC Qtc 485, Lipase 18, BNP 3151 PT 36.2, INR 3.18, aPTT 35.6, CK 164, VBG Ph 7.15, 62.1, Po2 47.7, Plasma K 6, H/H 8.4/22.8, MCV 114, MCH41.9RDW 19.5, Pt 11,000/uL PS: Clumped Plt, Bun/Crt 52/2.7, ALT and AST levels >2500, hyperphosphatemia and a uric acid level of 10. He was treated with rasburicase but He developed rasburicase toxicity with methemoglobin levels of 11.7%. The patient was treated with immunosuppressive therapy and ascorbic acid. While the patient showed some response to the treatment, their clinical status remains critical, and the prognosis appears poor.

Conclusions: The management of this complex case requires a tailored approach to addressing each complication. Clinicians must be vigilant to mitigate risks and improve patient outcomes.

Keywords: Shock Liver, Waldenström Macroglobulinemia, Methemoglobinemia

19. Others, Surgical

PE-1

Surgical Outcomes and Quality of Life between Laparoscopic and Open Approach for Giant Hepatic Hemangioma

Le Anh Van, Le Van Thanh, Vu Van Quang, Le Trung Hieu, Nguyen Thi Xuan Linh, Quach Thi Ha

108 Military Central Hospital, Vietnam

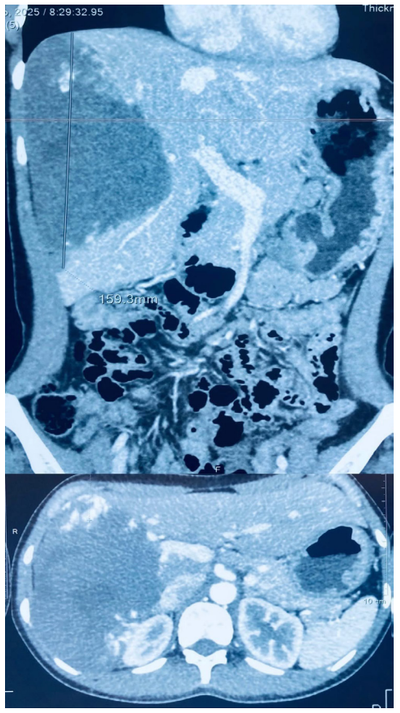
Aims: The main objective of the study was to compare the surgical outcomes and quality of life (QOL) of patients with giant hepatic hemangioma (defined by a diameter larger than 10 cm) either by laparoscopic or open surgery using a propensity score analysis.

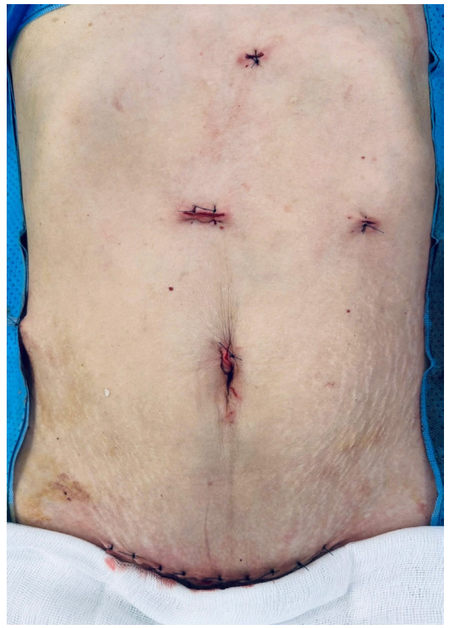
Methods: A retrospective study reviewed patients with giant hepatic hemangioma undergoing laparoscopic liver surgery (LLS) and open liver surgery (OLS) between January 2016 and December 2024. Quality of life according to Short Form-36 Healthy Survey (SF-36) questionnaire, were compared between groups. We performed 1:1 propensity score matching (PSM) between the LLS and OLS groups.

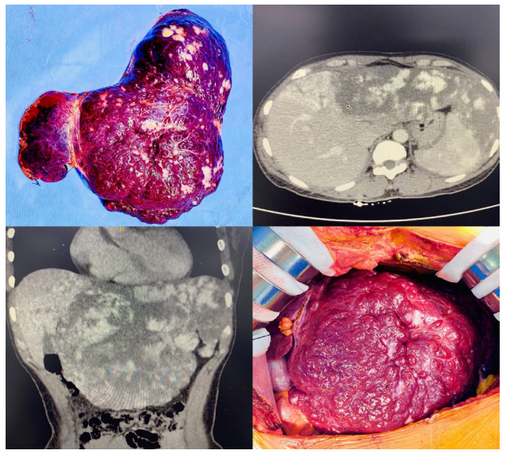
Results: Patients who involved in the analysis were matched (1:1) by age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, previous upper abdominal surgery, comorbidities, operation method, type of resection, tumor localization, size, and number. After PSM, 30 well-matched patients in each group were obtained. LLS was associated with significantly less blood loss, shorter postoperative hospital stay and fewer complications. The QOL scores weren't significantly different between the 2 groups, though the LLS group tended to be superior to the OLS group in terms of bodily pain (BP) and mental health (MH) at 3 months after surgery.

Conclusions: In comparison with the conventional open approach, laparoscopic liver surgery for hepatic hemangioma appears to have improved short-term surgical outcomes and comparable QOL in selected patients.

Keywords: Laparoscopic and Open Hepatectomy, Giant Hepatic Hemangioma







PE-2

Quality of Life of Laparoscopic versus Open Left Hemihepatectomy for Left-Sided Hepatolithiasis

Le Anh Van, Le Van Thanh, Vu Van Quang, Le Trung Hieu, Nguyen Thi Xuan Linh, Quach Thi Ha

108 Military Central Hospital, Vietnam

Aims: The purpose of this study was to evaluate and compare the quality of life of open versus laparoscopic left hemihepatectomy (OLH *vs.* LLH) for left-sided hepatolithiasis.

Methods: Between January 2018 and December 2024, 62 patients with left-sided hepatolithiasis who underwent LLH (n = 28) or OLH (n = 34) were evaluated. Quality of life, according to Short Form-36 Healthy Survey (SF-36) questionnaire, were compared between groups.

Results: The LLS group tended to be superior to the OLS group in terms of bodily pain (BP) and mental health (MH) at 3 months after surgery.

Conclusions: In comparison with the conventional open approach, laparoscopic liver surgery for left-sided hepatolithiasis appears to have improved QOL in selected patients.

Keywords: Quality of Life, Left-Sided Hepatolithiasis, Laparoscopic Versus Open Left Hemihepatectomy

PE-3

Implementing Virtual Reality (VR) In Surgical Education for Pancreatic Procedures

Nandha Kumar

ACS Medical College and Hospital, India

Aims: Training for complex pancreatic surgeries requires innovative methods to improve surgical skills and reduce errors. Virtual reality (VR) offers immersive, risk-free training environments.

Methods: A VR-based curriculum was tested on 30 surgical trainees performing virtual pancreaticoduodenectomies. Performance metrics included task completion time, accuracy, and error rates.

Results: VR-trained trainees showed a 20% improvement in task completion time and a 25% reduction in errors compared to the control group. Post-training assessments revealed enhanced confidence and technical skills in VR-trained participants.

Conclusions: VR technology is a transformative tool in surgical education, providing a safe, controlled environment to master complex procedures like pancreatic surgery. Its adoption could standardize training and reduce complications in real surgeries.

Keywords: VR, Surgical Education, Pancreatic Procedures

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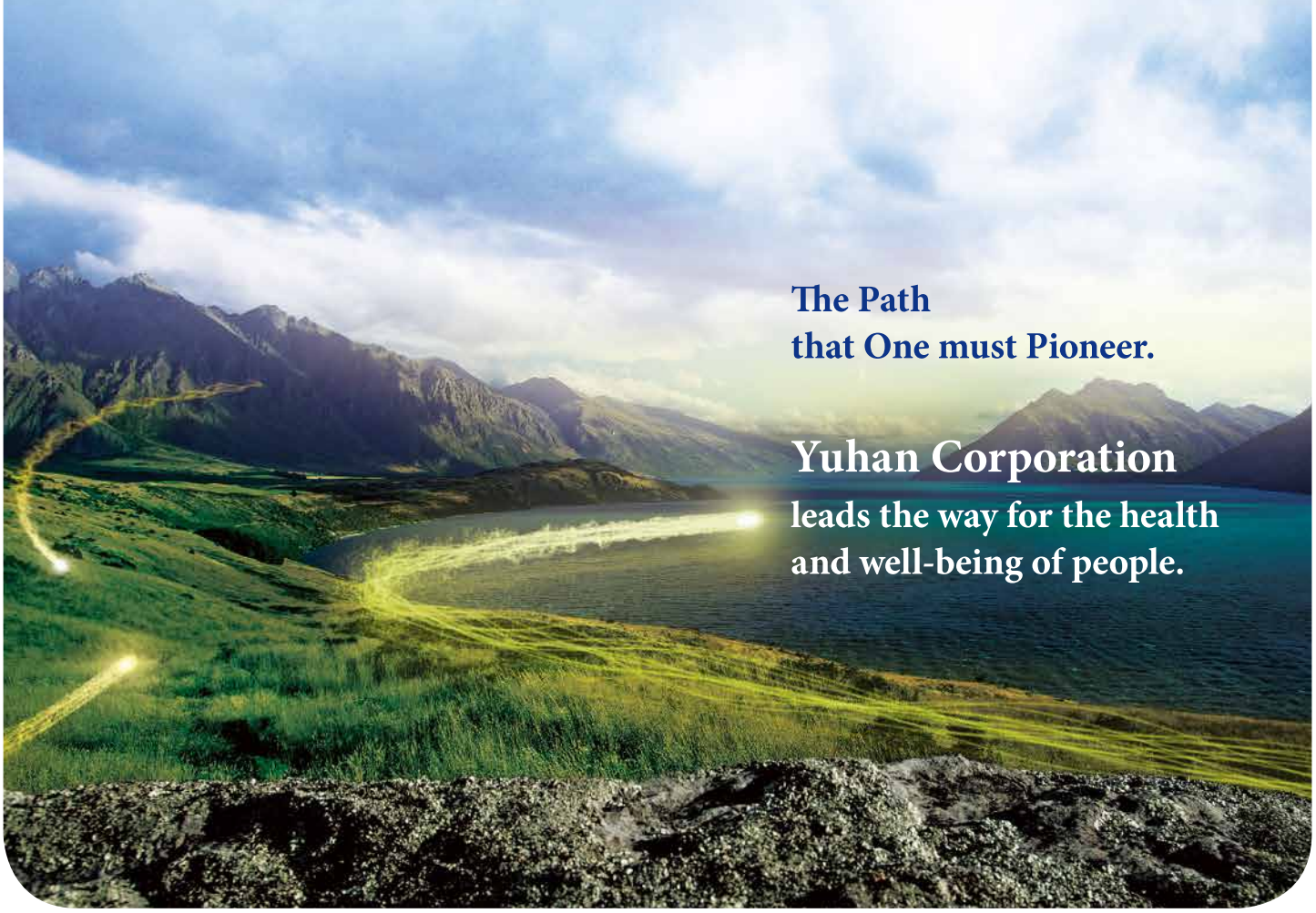

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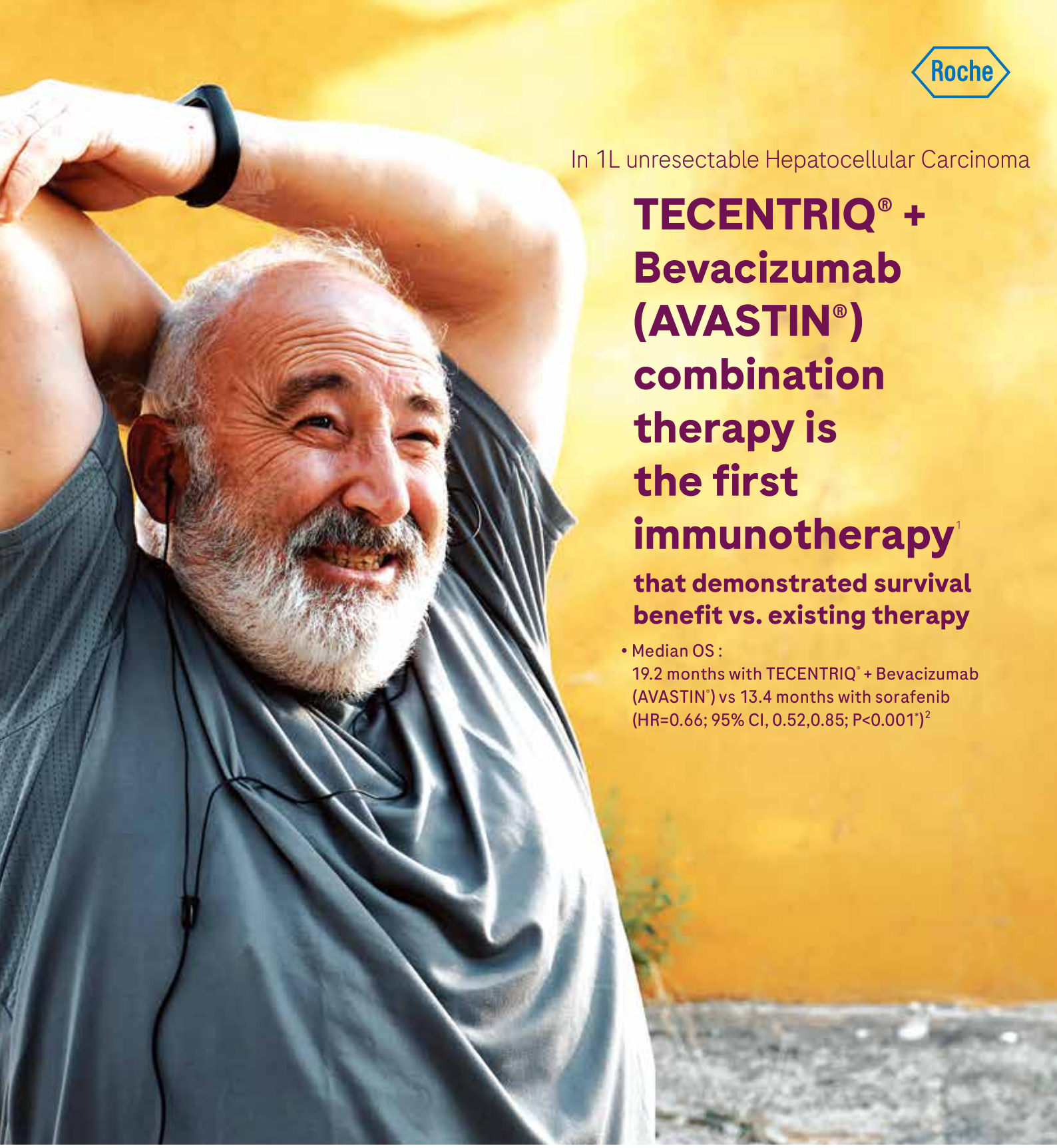

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1. Elecsys PIVKA-II (체외 수허 20-8호) *"**민감도** 86.9%, **특이도** 83.7%"*
2. Roche studies No. RD002542 and RD002543

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References 1. 2018 대한간학회 만성 B형 간염 진료 가이드라인 2. Oh H, et al. Aliment Pharmacol Ther 2020;52:371-81. 3. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection 4. Terrault NA, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018 Apr;67(4):1560-1599.

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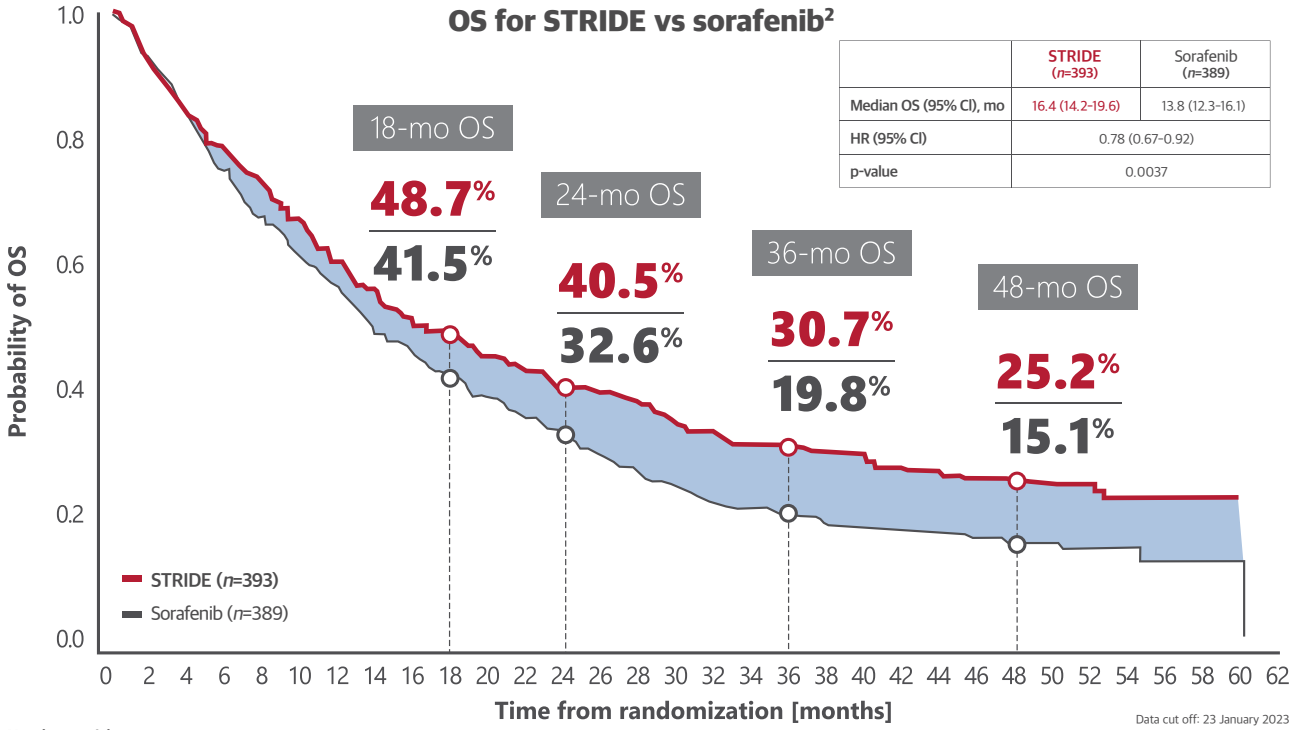
HR (95% CI)	0.78 (0.67-0.92)	
p-value	0.0037	



Data cut off: 23 January 2023

Number at risk

STRIDE	393	365	333	308	285	262	235	217	197	190	176	168	158	154	144	131	118	110	103	97	94	88	75	62	54	40	31	19	13	5	0	0
Sorafenib	389	356	319	283	255	231	211	183	170	155	142	131	121	108	93	83	73	69	64	56	53	50	45	36	28	21	14	9	3	1	1	0

※ STRIDE Regimen:Tremelimumab (300mg, one dose) plus Durvalumab (1500mg every 4 weeks)

HIMALAYA study design[1] :
In this global, open-label, phase 3 trial, the majority of the patients we enrolled with unresectable hepatocellular carcinoma and no previous systemic treatment were randomly assigned to receive one of three regimens: tremelimumab (300mg, one dose) plus durvalumab (1500mg every 4 weeks; STRIDE), durvalumab (1500mg every 4 weeks), or sorafenib (400mg twice daily). In total, 1171 patients were randomly assigned to STRIDE (n=393), durvalumab (n=389), or sorafenib (n=389). The primary objective was overall survival for STRIDE versus sorafenib. Noninferiority for overall survival for durvalumab versus sorafenib was a secondary objective.

1L = first-line; HCC = hepatocellular carcinoma; OS = overall survival; STRIDE = Single Tremelimumab Regular Interval Durvalumab; vs. = versus.

References
1. Abou-Alfa GK, et al. Tremelimumab Plus durvalumab in unresectable hepatocellular carcinoma. NEJM Evid. 2022 Aug;1(8):EVIDoa2100070. **2.** Sangro. et al, Four-year overall survival update from the phase III HIMALAYA study of tremelimumab plus durvalumab in unresectable hepatocellular carcinoma. Ann Oncol. 2024 May;35(5):448-457. **3.** 이뮤도주 제품설명서 (https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetailCache?cacheSeq=202301925&upDateTs2025-02-25%2019:15:59.0b) (Accessed on March 27, 2025) **4.** 임핀지주 제품설명서 (https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetailCache?cacheSeq=201804918&upDateTs2025-02-26%2016:23:21.0b) (Accessed on March 27, 2025)

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- ✓ Improvement of Sarcopenia[3]
- ✓ Improvement of Nutrition status for patients with Liver cirrhosis[4]

References **1.** Nutr Clin Pract. 2013 Oct;28(5):580-8 **2.** Muto Y et al. Clinical Gastorenterology and Hepatology 2005;3:705-713 **3.** Hanai T, Shiraki M, Shimizu M, Moriwaki H et al. Nutrition. 2015;31:193-9, Koya et al.,Hepatol Res 2017;47;E22-34 **4.** J Gastroenterol (2016) 51:629-650

Product name: LIVACT granules **Composition:** L-isoleucine 925mg, L-leucine 1904mg, L-Valine 1144mg **Indication:** decompensated Liver cirrhosis patients with hypoalbuminemia even though diet intake is sufficient **Dosage:** three times a day after meals **Unit:** 4.15g X 42

오리지널 BCAA
LIVACT®
Granules

Vemlia

tenofovir alafenamide 25mg tabletes

Our heartfelt wish for curing HBV, we present Vemlia.

- Comparable antiviral efficacy vs. TDF[1]
- Improved safety profile in renal and bone parameters[2]
- Increased affordability with lower price, 2,474/tablet[3]*
- Improved patients' compliance with daily pill bottle[4]

1. Agarwal K, et al. J Hepatol. 2018, 68, 672–681
2. Lampertico P, et al. Lancet Gastroenterol Hepatol. 2020 May;5(5):441-453.
※ The data above are clinical data conducted with Tenofovir alafenamide hemi-fumarate.
3. https://www.health.kr/searchDrug/result_drug.asp?drug_cd=2022122100010 약학정보원, 베믈리아 의약품 상세정보, accessed on April 2023
4. Vervloet M, et al. J Am Med Inform Assoc 2012;19(5):696-704.
*896 won lower price than Original drug (June 2023)

동아ST

VMA-23F011

GC Cell

Korea Food and Drug Administration Approval in 2007

Advanced Biopharmaceutical Re-Approval in 2021

HCC anticancer cellular Immunotherapeutics[1]

Immuncell-LC

Anticancer cellular Immunotherapeutics

Recognize & Kill Cancer Cells

Reduction in Recurrence Risk

37%

Reduction in Mortality Risk

79%

Reference.
1. Lee JH, et al. *Gastroenterology*. 2015;148(7):1383-1391.e6.

GCC-OM-MT-24060073

Ethical drugs

· Product

Immuncell-LC (Autologous Blood-Derived Lymphocytes)

· Physical

A cloudy fluid of pale-yellow color contained in an opaque polyethylene or polyvinyl chloride bag

· Efficacy/Effect

Adjuvant therapy in patients with tumor removal after hepatocellular carcinoma resection (surgery, radiofrequency ablation, percutaneous ethanol injection)

· Active Pharmaceutical Ingredient (200ml)

Number	Ingredient	Dosage	Unit	Specification
1	Autologous Blood-Derived Lymphocytes	$1.0x10^9$~$2.0x10^{10}$	cells	Special Specification

Expedients: Multiple Electrolytes Injection, Type 1, Human serum albumin

· Dose/Dosage

Gently shake the bag 3-4 times before administration to ensure that the cells are fully suspended in the solvent. Administer the product intravenously with 22G or smaller needle within 1 hour. A single dose is 200 ml containing 1.0×10^9-2.0×10^{10} cells, and the numbers and intervals of administration are as follows. 4 times, once a week 4 times, once every two weeks 4 times, once every four weeks 4 times, once every eight weeks 16 times in total

· Package Unit

1 pack/box (200mL/pack)

· Reimbursement Information

not reimbursed (676600031)

· Storage Method

Store in a sealed container, at 2-25 ℃
Shelf Life: 36 hours from the manufacturing date (36 hours from the time of manufacture)

GC Cell

107, Lee Hyun-ro 30, Giheung-gu, Yongin-si, Gyeonggi-do, Republic of Korea

Website
www.gccell.com

Customer support center
080-597-3540

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Oral Suspension Megace® F

(megestrol acetate, USP)

Reformulation of MG OS by utilizing NanoCrystal® Technology.
50 times smaller particles increased surface area

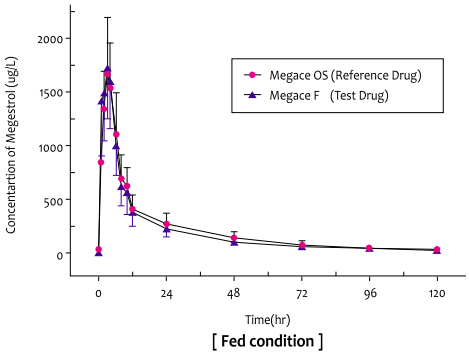
rapid dissolution & increased absorption.
Improved bioavailability

I. Originality

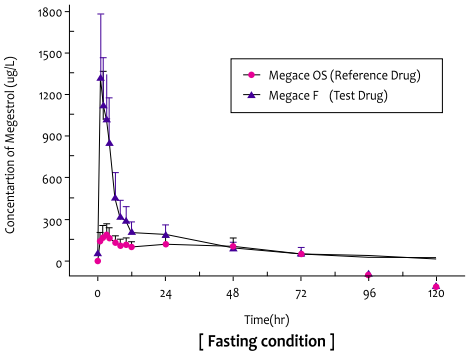
- licensed the Megace® name from Bristol-Myers Squibb Company
- High Quality

II. Improved Bioavailability!

*** Food effect differences between a nanocrystal dispersion of megestrol acetate 625 mg/5 mL and a micronized formulation of megestrol acetate oral suspension(MGOS) 800 mg/20 mL. ***



[Fed condition]



[Fasting condition]

In-house data(Boryung pharm)

III. Improved Efficacy!

- Weight gain occurred more rapidly at each time point
- Patients in the nanocrystal dispersion arm gained an average of 10% of the baseline weight over 12 weeks (Vs 6% weight gain in MG OS arm)

International Journal of Nanomedicine 2009:4 185–192

IV. Improved Convenience!

	Megace F-OS	Megace-OS
Recommended dose [1,17]	1 teaspoon 625 mg/5mL	4 teaspoon 800 mg/20mL
Viscosity[5]	10 cP*	163 cP*

*cP=centipose, a measure of viscosity, with higher numbers indicating greater viscosity.

- 1/4 the total volume per dose
- 94% less viscous ⟶ easier to take

GODEX® cap.

Confidence for MASLD treatment

Evidenced by numerous clinical results

- ✓ Restoration of Hepatic Mitochondrial Dysfunction by Carnitine Complex[1]
- ✓ Rapid Normalization of ALT Level[2]
- ✓ Improving effect for MASLD as Evidenced by CT scans[2]

Product Information

Description | Reddish brown colored hard gelatin capsule containing yellowish brown colored powder | **Composition** | Each capsule contains Carnitine Orotate 150mg (73.8mg as orotic acid, 76.2mg as carnitine), Liver Extract Antitoxic fraction 12.5mg, Adenine HCl 2.5mg, Pyridoxine HCl 25mg, Riboflavin 0.5mg, Cyanocobalamin 0.125mg, Biphenyl dimethyl dicarboxylate 25mg | **Indication** | 1) General therapeutics for the following hepatic disease – Acute, Subacute and Chronic Hepatitis, Hepatic cirrhosis, Fatty liver, Drug or chemical induced hepatitis 2) Acute, chronic hepatitis involving high transaminase value | **Dosage & Administration** | Usually, each time 2 capsules, 2~3 times a day as adult dosage. Dosage unit can be changeable depending on symptom or age of patient. | **Special caution** | 1) Severe state of chronic hepatitis 2) Severe state of hapatic cirrhosis | **General caution** | 1) Rarely skin rash can be represented, in this case general antihistamin therapy will be required. 2) In severe case, sometimes intermittent jaundice can be occur in this case, discontinue administration for awhile and other adjuvant therapy for jaundice shall be required. 3) Rarely nausea, gastric discomfortness can be represented. 4) Rarely itching or reddness can be occur, in this case, discontinue administration and follow physician's instruction. | **Insurance Code** | 693900080 | **Packing Unit** | 100, 300 caps. (bottle)/ 100 caps. (PTP) | **Storage** | Tight closed container, room temperature (1~30℃) in dry place. Expiry – 60 months from Manufacturing date.

Diagnostic Codes

B15–19 Viral hepatitis **K70.0** Alcoholic fatty liver **K71.0** Toxic liver disease **K73.0** Chronic persistent hepatitis, NEC **K74.0** Hepatic fibrosis **K75.8** Other specified inflammatory liver disease, Nonalcoholic steatohepatitis **K77.0** Liver disorders in disease classified elsewhere

Reference 1. Lim CY et al., Effects of carnitine on peripheral blood mitochondrial DNA copy number and liver function in non-alcoholic fatty liver disease, *Korean J Gastroenterol 2010;55:384-389.*
2. Bae JC et al., Improvement of nonalcoholic fatty liver disease with carnitine-orotate complex in type 2 diabetes (CORONA), *Diabetes Care 2015;38:1245-1252.*

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glecaprevir/pibrentasvir

Quickly† deliver cure‡ with 8-week MAVIRET so your patients§ can move forward free from HCV.

*Free from HCV with cure. †For GT 1–6 treatment-naïve, non-cirrhotic and compensated-cirrhotic patients, 8-week MAVIRET versus 12-week MAVIRET.
‡Cure=sustained virologic response (SVR12), defined as HCV RNA less than the lower limit of quantification at 12 weeks after the end of treatment.
§GT 1–6 treatment-naïve, non-cirrhotic and compensated-cirrhotic patients. MAVIRET is not indicated in decompensated cirrhosis.

MAVIRET is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C).[1]
MAVIRET is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adult and adolescent patients over 12 years of age.[1]

References 1. MAVIRET® Product information(Revised from 16th Feb 2023).

[Product name] Maviret® Tab. **[Ingredients and quantity]** Glecaprevir 100.0mg, pibrentasvir 40.0mg
[Importer/Distributor] AbbVie Korea, 6th floor, Samtan Building, 421, Yeongdong-daero, Gangnam-gu, Seoul, Korea, Tel: 02) 3429-9300, www.abbvie.co.kr
※ For the latest and full product information, please refer to the QR code or product information.
※ To report adverse events and apply for damage relief: Korea Institute of Drug Safety & Risk Management (1644-6223 or 14-3330, www.drugsafe.or.kr)
KR-MAVI-240023 / Mar 2024

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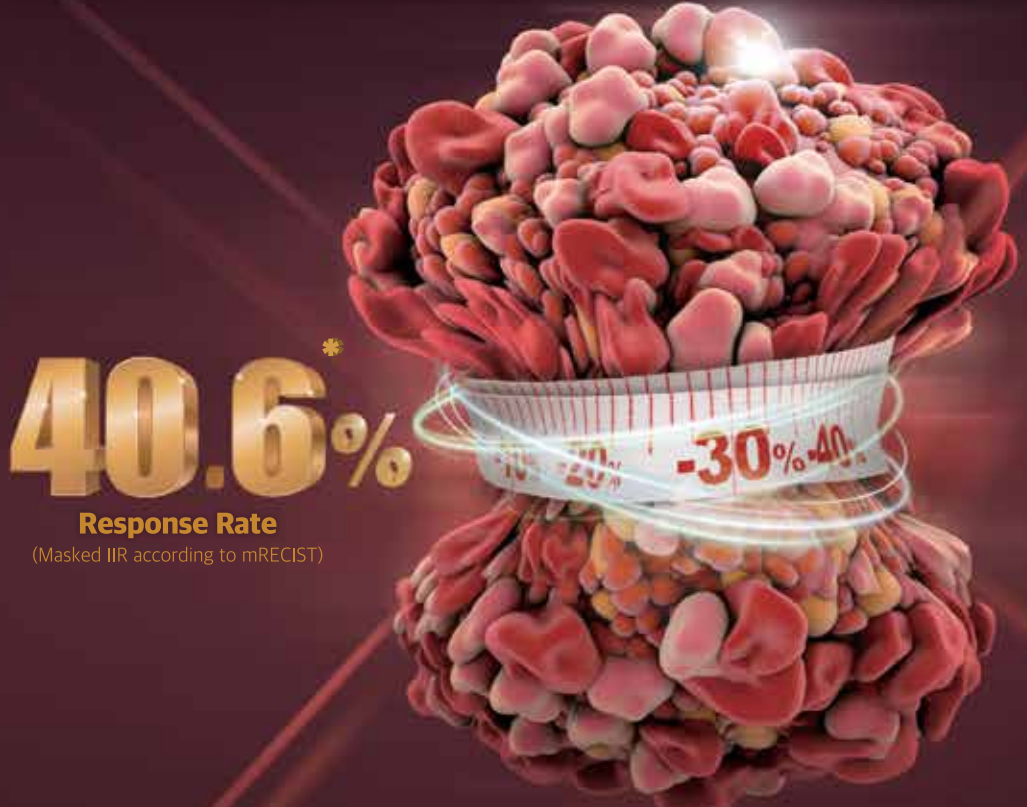
LENVIMA® (lenvatinib) capsules
RESPONSE THAT MATTERS

Remarkable Response

The ORR was more than three times higher with lenvatinib versus control group.[1]

Based on the masked IIR according to mRECIST,

about 41% of patients* showed ≥ 30% decrease in tumor size.[1,2]



* ORR is one of the secondary endpoints and this is the result of the post-hoc exploratory tumour assessments using mRECIST by masked central independent imaging review. For more information, please refer to the full text of the article. (Kudo M, et al. 2018)

[Study design] This was an open-label, phase 3, multicentre, non-inferiority trial that recruited patients with unresectable hepatocellular carcinoma, who had not received treatment for advanced disease, at 154 sites in 20 countries throughout the Asia-Pacific, European, and North American regions. Patients were randomly assigned (1:1) via an interactive voice-web response system-with region; macroscopic portal vein invasion, extrahepatic spread, or both; Eastern Cooperative Oncology Group performance status; and bodyweight as stratification factors-to receive oral lenvatinib (12 mg/day for bodyweight ≥60 kg or 8 mg/day for bodyweight <60 kg) or sorafenib 400 mg twice-daily in 28-day cycles. The primary endpoint was overall survival, measured from the date of randomisation until the date of death from any cause. The efficacy analysis followed the intention-to-treat principle, and only patients who received treatment were included in the safety analysis. Lenvatinib(median OS 13.6 months, 95% CI 12.1-14.9) was non-inferior to sorafenib(median OS 12.3 motnhs, 95% CI 10.4-13.9) in overall survival in untreated advanced hepatocellular carcinoma(HR 0.92, 95% CI 0.79-1.06).[1]

	Lenvatinib (n=478)	Sorafetinib (n=476)	Effect size (95% CI)	*P* value
Investigator review according to mRECIST				
Objective response (%, 95% CI)	115 (24.1%, 20.2-27.9)	44 (9.2%, 6.6-11.8)	OR 3.13 (2.15-4.56)	<0.0001
Masked Independent Imaging review according to mRECIST				
Objective response (%, 95% CI)	194 (40.6%, 36.2-45.0)	59 (12.4%, 9.4-15.4)	OR 5.01 (3.59-7.01)	<0.0001
Masked Independent Imaging review according to RECIST 1.1				
Objective response (%, 95% CI)	90 (18.8%, 15.3-22.3)	31 (6.5%, 4.3-8.7)	OR 3.34 (2.17-5.14)	<0.0001

mRECIST, modified Response Evaluation Criteria in Solid Tumors; IIR, Independent imaging review; ORR, Objective Response Rate; CI, Confidence Interval; uHCC, unresectable hepatocellular carcinoma; OR, Odds ratio; OS, Overall Survival

[References] 1. Kudo M et al. Lancet. 2018 Mar 24;391(10126):1163-1173 2. Lencioni R, Llovet JM. Semin Liver Dis. 2010 Feb;30(1):52-60

Lenvim 4mg, 10mg Capsules (Lenvatinib mesilate) [Composition] 4mg capsule: Active ingredient: lenvatinib mesilate (in house specification) -4.90mg (4.0mg equivalent to lenvatinib free base) 10mg capsule: Active ingredicent: lenvatinib mesilate (in house specification) -12.25mg (10.0mg equivalent to lenvatinib free base) **[Therapeutic indication]** 1. Lenvima is indicated for the treatment of patients with progressive, locally recurrent or metastatic, differentiated thyroid carcinoma (DTC), refractory to radioactive iodine (RAI). 2. LENVIMA is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma. 3. LENVIMA, in combination with pembrolizumab, is indicated for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation. **[Dosage and administration]** 1) Posology **DTC** In Adults the recommended daily dose of Lenvima is 24 mg taken once daily. The daily dose is to be modified as needed according to the dose/toxicity management plan (See 2) Dose Adjustment section below). **HCC** The recommended dosage of LENVIMA is based on actual body weight: • For patients greater than or equal to 60 kg: 12 mg • For patients less than 60 kg: 8 mg Take LENVIMA orally once daily until disease progression or until unacceptable toxicity. There is no clinical evidence to support the use of 10 mg dose in HCC. **Endometrial Carcinoma** The recommended dosage of LENVIMA is 20 mg orally once daily, in combination with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks, until unacceptable toxicity or disease progression. Refer to the pembrolizumab prescribing information for recommended pembrolizumab dosing information. **[Precautions for Use]** 1. Contraindications 1) Hypersensitivity to the active substance or to any of the excipients 2) Breast-feeding 2. Careful Administration 1) Patients with hypertension 2) Patients with thromboembolism or a history of the condition 3) Patients with brain metastasis 4) Patients in whom the wound from a surgical procedure has not yet healed 5) Patients with tumor invasion to the cervical artery/vein, etc. **[Importer]** Eisai Korea Inc. 10F Revessant, 6, Bongeunsa-ro 86-gil, Gannam-gu, Seoul, 135-878, Korea (tel 02-3451-5500) - Date of written manual: Jul 1st, 2021 - For details, please refer to the full prescribing information.

Eisai Korea Inc.

EISAI KOREA 10F Revessant, 6, Bongeunsa-ro 86-gil, Gangnam-gu, Seoul, 06163, Korea TEL: 02-3451-5500

KR-LVM-2106-01

Give every
little star
the power
to shine

Bylvay®
odevixibat

The first approved treatment worldwide for patients with PFIC[1,2]

Bylvay®
odevixibat

Bylvay® reduces **sBA** and preserves **native liver.**[3]

Bylvay® reduces **cholestatic pruritus** and improves **sleep disturbances.**[3]

Bylvay® is **well tolerated** with simple **once daily dosing.**[4]

PFIC, progressive familial intrahepatic cholestasis; **sBA**, serum bile acid

BYL-PFIC-KR-000081[04/27]

References **1.** Bylvay (odevixibat) FDA Approval. July 2021. **2.** U.S. Food & Drug Administration (FDA): News Release: FDA approves therapy for severe itching in patients with rare liver disease. https://content.govdelivery.com/accounts/USFDA/bulletins/2e93908 (20 July 2021). accessed on 2025.04.23. **3.** Thompson RJ, Arnell H, Artan R, et al. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. Lancet Gastroenterol Hepatol. 2022;7(9):830-842. **4.** Bylvay® Product Information (Revision Date: August 23, 2024)

IPSEN

Prescribing Information
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200mcg 400mcg 600mcg 1200mcg

GODEX® cap.

Carnitine Complex의
NAFLD 치료 효과

Beyond ALT/AST normalization effect

- ✔ Carnitine 성분의 **미토콘드리아 회복** 효과
- ✔ 영상학적으로 입증된 **지방간 개선**효과
- ✔ **인슐린 저항성 개선**효과

고덱스®캡슐

성상 | 황갈색의 분말이 들어있는 상 · 하 적갈색 불투명의 경질캡슐제 | **성분 · 함량** | 1캡슐 중 Carnitine orotate 150mg Liver extract antitoxic fraction 12.5mg Pyridoxine HCl 25mg Riboflavin 0.5mg Cyanocobalamin 0.125mg Biphenyl Dimethyl Dicarboxylate 25mg Adenine HCl 2.5mg | **효능 · 효과** | 트란스아미나제(SGPT)가 상승된 간질환 | **용법 · 용량** | 통상 성인 1회 2캡슐, 1일 2~3회 복용, 연령, 증상에 따라 적의 증감. | **사용상의 주의사항** | 1. 다음 환자는 투여 하지 말 것. 1) 이 약 및 이 약에 포함된 성분에 과민반응이 있는 환자 2) 레보도파를 투여 받고 있는 환자 2. 다음 환자는 신중히 투여할 것. 1) 만성 활동성 간염 환자 2) 간경화 환자 3. 이상반응 1) 간혹 입안마름, 메스꺼움, 발진, 가려움증, 발적 등이 생길 수 있으며, 이러한 이상반응은 투약을 중지하거나 항과민약을 병용투여하면 소실된다. 2) 일과성 황달이 나타날 수 있으나 투약을 중지하거나 황달치료제를 병용투여하면 소실된다. 3) 드물게 구역, 복부팽만, 변비, 메스꺼움, 상복부 불쾌감이 나타날 수 있다. | **보험코드** | 693900080 | **포장단위** | 100캡슐, 300캡슐(병) / 100캡슐(PTP) | **저장방법** | 기밀용기, 실온보관(1~30℃)

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B15-19 바이러스성 간염(Viral hepatitis) K70.0 알코올성 지방간(Alcoholic fatty liver) K71.0 독성 간질환(Toxic liver disease) K73.0 달리 분류되지 않은 만성 지속성 간염(Chronic persistent hepatitis, NEC) K74.0 간섬유증(Hepatic fibrosis) K75.8 기타 명시된 염증성 간질환, 비알코올성 지방간염(Other specified inflammatory liver disease, Nonalcoholic steatohepatitis) K77.0 달리 분류된 질환에서의 간장애(Liver disorders in disease classified elsewhere)

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BG2024-01

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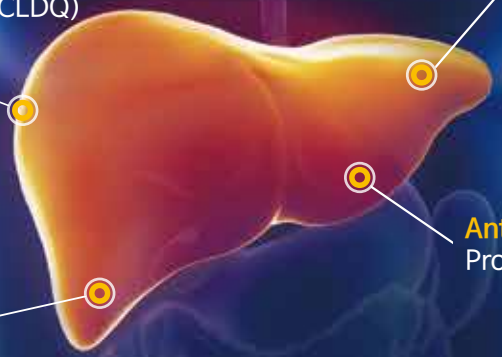
Safe Medicine Proven to Improve Quality of Life for Patients
Patients' Improved Quality of Life Verified Through Chronic Liver Disease Questionnaire (CLDQ)



Antioxidative Effect Reduces Fat in the Liver
Proven to Reduce MDA Level

Proven Efficacy
Quickly Reduces and Helps You Maintain Optimal Level of Alanine Transaminase (ALT)
Contains Garlic Oil Which is Known to Have Strong Antioxidative and Anti-Inflammatory Effects

PENNEL®

[Ingredients] Chronics hepatitis with continuously elevated ALT level
[Directions] Take 1 or 2 capsules each time, 3 times a day, after meals

Diagnostic Code
B15-19 Viral hepatitis K70.0 Alcoholic fatty liver K71.0 Toxic liver disease K73.0 Chronic persistent hepatitis, NEC
K74.0 Hepatic fibrosis K75.8 Other specified inflammatory liver disease,
Nonalcoholic steatohepatitis K77.0 Liver disorders in disease classified elsewhere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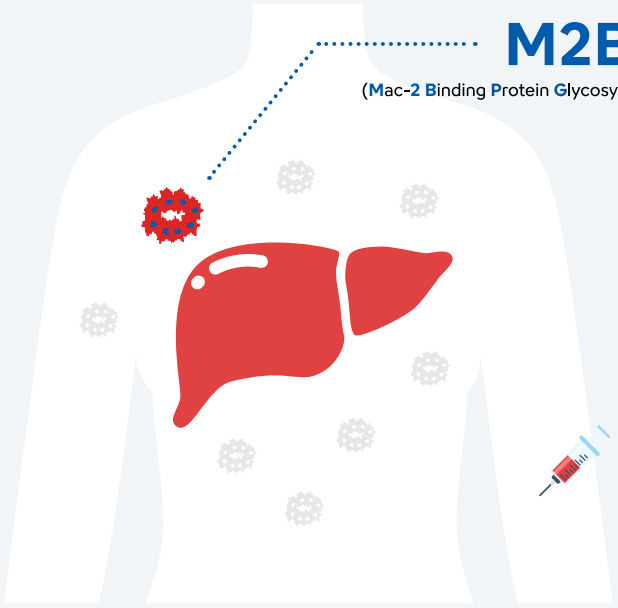
Prograf® Tacrolimus
MAT-KR-PRO-2023-00095

Liver Fibrosis Single Biomarker

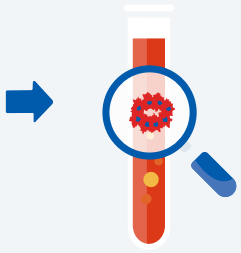


M2BPGi

(Mac-2 Binding Protein Glycosylation isomer)

M2BPGi forms in blood when hepatic fibrosis occurs

Collect blood for M2BPGi test



Measure with full **automated system**

Sysmex "HISCL-800"

The only single biomarker that is approved reimbursement (Code: D1980)

Pick up only 10㎕ of serum

Test time **17min**

Included in the KASL clinical practical guidelines for managing NAFLD and CHB

Subject & Utility of M2BPGi Test

Diabetes: There is a high possibility of advanced hepatic fibrosis with an abnormal M2BPGi level (>1.0).[1]

NAFLD patients: Serum M2BPGi could serve as a reliable biomarker for diagnosing advanced fibrosis and cirrhosis.[2]

Liver fibrosis risk population: Serum M2BPGi has proven to be a dependable, non-invasive surrogate marker for predicting advanced fibrosis.[3]

CHB patients receiving long-term antiviral treatment: The serum M2BPGi level functions as an independent predictor of HCC and complements the stratification of HCC risks.[4]

CHB with oral antiviral therapy: A baseline M2BPGi level above 1.73 consistently demonstrated predictive value for higher HCC risk.[4]

TACE treatment for HCC: The combination of M2BPGi and up-to-seven criteria could serve as a surrogate marker for predicting CP grade deterioration.[5]

CHB: The M2BPGi level can predict HCC development independently.

References

1. Park H, *et al. Ann Transl Med.* 2020;8(23):1583 **2.** Jang SY, *et al. Ann Lab Med.* 2021;41(3):302-309. **3.** Kim M, *et al. J Clin Med.* 2020;9(4):1119. **4.** Tseng TC, *et al. Liver Cancer.* 2020;9(2):207-220. **5.** Eso Y, *et al. Cancers (Basel).* 2019;11(3):405. **6.** Kim SU. *et al. Liver Int.* 2016; 1-9.

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BUKWANG PHARM

Protect from Various Liver Disease with Legalon® Cap

As the original brand of silymarin, Legalon® always be with doctors for the treatment of various liver disease.

Originality & Worldwide

- The original silymarin for treatment of liver disease by numerous Clinical trials since 1960's.[1-2]

Treatment of Liver disease

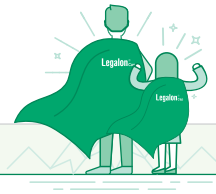
- Proven efficacy in improvement of liver function [5-11]
  * NAFLD, NASH, ALD, cirrhosis

Various MoA & All stages

- Multi-therapeutic targets in all-stage of liver disease by various MoA.[3-4]
  * Improvement of insulin resistance
  * Anti-oxidative stress, Anti-inflammation, Anti-fibrosis

Safety & Good tolerance

- Good tolerance and safety with lower side effects [5-9]



[Reference] 1. Bijak M. Molecules 2017 Nov 10;22(11). / 2. LEGALON Cap. 140 – Insert Paper(KOREA) / 3. Federico A, et al. Molecules 2017 Jan 24;22(2). / 4. Hellerbrand C, et al. Clinical Phytoscience 2017 Jan;2:7. / 5. Zhong S, et al. Medicine (Baltimore) 2017 Dec;96(49):e9061. / 6. Hajaghamohammadi AA, et al. Hepatitis Monthly 2008;8(3):191-5. / 7. Hashemi SJ, et al. Hepatitis Monthly 2009;9(4):265-70. / 8. Wah Kheong C, et al. Clin Gastroenterol Hepatol 2017 Dec;15(12):1940-9.e8. / 9. Saller R, et al. Drugs 2001;61(14):2035-63. / 10. Velussi M, et al. J Hepatol 1997 Apr;26(4):871-9. / 11. Mastron JK, et al. Anticancer Drugs 2015 Jun;26(5):475-86.

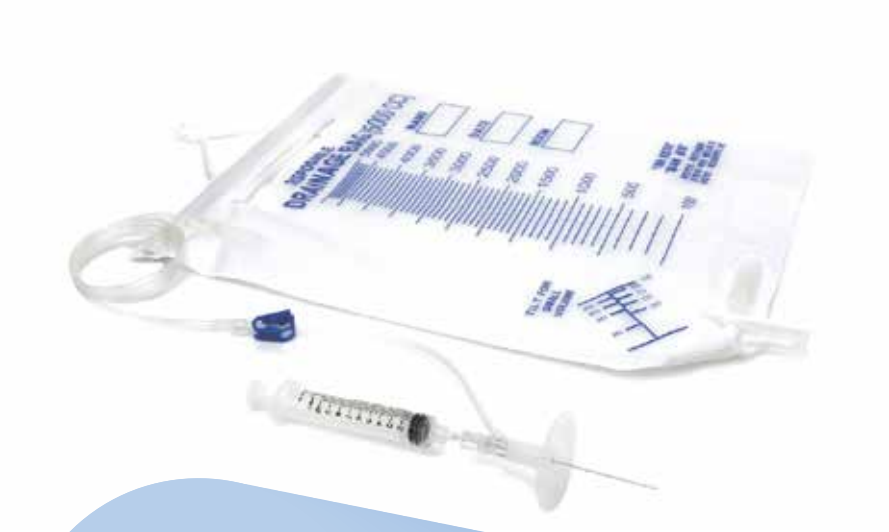
[제품정보] 레가론 캡슐 70mg / 140mg **[성분,함량]** 밀크시슬건조엑스산 169.7mg / 339.4mg(실리마린으로서 70mg / 140mg) **[효능,효과]** 다음 질환의 보조 치료 : 독성 간질환 , 만성 간염, 간경변 **[용법,용량]** 성인 : 실리마린으로서 초기용량 1회 140mg(또는 실리빈으로서 1회60mg), 1일 3회, 유지용량 1회 70mg(또는 실리빈으로서 1회 30mg), 1일 3회(또는 1회 140mg(또는 실리빈으로서 60mg), 1일 2회)복용한다. **[금기]** 1) 심한 담도 폐쇄 환자 2) 이 약의 과민증 환자 3) 12세 이하의 소아 **[신중투여]** 다음과 같은 사람은 이 약을 복용하기 전에 의사, 치과의사, 약사와 상의 할 것 : 임부, 수유부 [이상반응] 다음과 같은 경우 이 약의 사용을 즉각 중지하고 의사, 치과의사, 약사와 상의할 것. 상담시 가능한 한 이 첨부문서를 소지할 것. 1) 드물게 위통 또는 설사 2) 알레르기 반응 **[일반적주의]** 1) 정해진 용법 · 용량을 지킬 것. 2) 황달의 경우에는 의사 또는 약사와 상의할 것. 3) 1개월 정도 복용하여도 증상의 개선이 없을 경우나 장기복용시에는 의사 또는 약사와 상의할 것.

Manufacturer / Distributor
BUKWANG PHARM. CO., LTD.
Seoul, Korea / www.bukwang.co.kr

Technical Partnership
MADAUS GmbH
Federal Republic of Germany

Use for Paracentesis & Thoracentesis

KARAHOC



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Enhanced Liver Fibrosis (ELF) Test

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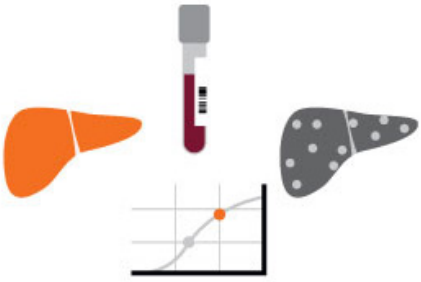
혈청 간섬유화 검사 (Enhanced Liver Fibrosis Test, ELF)

간단한 혈액 검사로 간섬유화 평가, 예후예측 및 치료효과 평가 가능

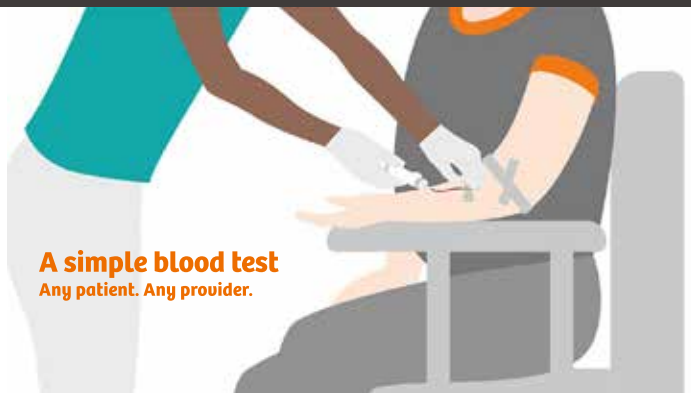
- **지멘스 헬시니어스의 혈청 간섬유화 검사 (ELF)**: 간섬유화에 대한 직접적인 마커를 측정하는 비침습적 혈액 검사입니다.
- ELF 검사는 자동화된 면역 장비로 **대용량 검사**가 가능하며, 통상적인 혈액 검체로 측정하므로 숙련된 검사자가 필요치 않은 검사법입니다.
- 2형 당뇨병 및 비만 환자를 포함한 모든 환자를 대상으로 실시할 수 있으며, 비알코올성 지방간 (Nonalcoholic fatty liver disease, NAFLD) 환자를 식별하고 간경변으로 진행될 위험이 있는 환자를 계층화하여 환자 관리 개선이 가능합니다.[1, 2, 3]



ELF 점수: 간섬유화 직접적인 혈청 마커 조합

- Hyaluronic acid (HA)
- Procollagen III N-terminal peptide (PIIINP)
- Tissue inhibitors of metalloproteinase 1 (TIMP-1)

ELF Score = ● (C_{HA}) + ▲ (C_{PIIINP}) + ■ (C_{TIMP-1})



HA, PIIINP, TIMP-1의 혈청 농도

↓

면역측정법 원리 이용한
정량적 측정

↓

알고리즘을 통해 산출된 점수로
결과 해석 (ELF Score)

1. Patel P, et al. Hepatol Commun. 2018;2:893-905. 2. Karlas T, et al. PLoS ONE. 2015;10(11):e0141649. 3. Sanyal AJ, et al. Hepatology. 2019;70(6):1913-1927

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