The Liver Week 2019

June 20-22, 2019 | BEXCO, Busan, South Korea

The 25th Annual Meeting of the Korean Association for the Study of the Liver
The Korean Association of HBP Surgery Symposium
The 22nd General Symposium of the Korean Liver Cancer Association
The Korean Liver Transplantation Society Symposium
Dear colleagues,

On behalf of all the organizing committee members, we sincerely welcome you to The Liver Week 2019.

Since the first meeting was held in 2014, The Liver Week has become a multidisciplinary international conference hosted by the Korean Association for the Study of the Liver (KASL), in partnership with three co-hosting societies: the Korean Association of HBP Surgery (KAHPS), the Korean Liver Cancer Association (KLCA), and the Korean Liver Transplantation Society (KLTS).

The theme of The Liver Week 2019, ‘Expanding Frontiers in Liver Diseases’, pursues the objectives of encouraging all participants to study the recent research trends and views related to liver disorders from the perspectives of eminent experts, and of facilitating the exchange of up-to-date information on liver disease with the ultimate goal of improving liver disease management. The organizing committee has prepared an attractive and valuable scientific program focused on the latest trends, issues, and advances made in various areas of liver diseases.

In particular, we have prepared various joint symposia for exchanging knowledge among 4 liver-related societies. The experts debate session will cover an issue regarding cessation of anti-HBV therapy. The Korea Center for Disease Control and Prevention (KCDC) will participate in the policy forum, and the National Health Insurance Big Data Research forum will also be held in partnership with the National Health Insurance Service (NHIS). Lectures and a hands-on course for abdominal ultrasound specialist certification and relevant major education are prepared as well. The Asian Forum is a new session covering current status and emerging liver disease issues in Asia.

We firmly believe that The Liver Week 2019 will be a valuable experience for all attendees and we look forward to your active participation.

Thank you.
# PROGRAM AT A GLANCE

## DAY 1 Thursday, June 20, 2019

<table>
<thead>
<tr>
<th>ROOM A (1F)</th>
<th>ROOM D (2F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>102-105 / 107-110</td>
<td>205</td>
</tr>
</tbody>
</table>

### ROOM A (1F)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00</td>
<td>Postgraduate Course: Diagnosis and Management of Liver Disease: Past, Present, and Future</td>
</tr>
<tr>
<td>09:00</td>
<td>PS1. Viral Hepatitis (09:00-10:30)</td>
</tr>
<tr>
<td>10:00</td>
<td>Coffee Break (10:30-10:50)</td>
</tr>
<tr>
<td>11:00</td>
<td>PS2. Cirrhosis and Its Complications (11:00-12:30)</td>
</tr>
<tr>
<td>12:00</td>
<td>Lunch Symposium 1 (Above) (12:00-13:30)</td>
</tr>
<tr>
<td>13:00</td>
<td>Break (13:30-13:50)</td>
</tr>
<tr>
<td>14:00</td>
<td>PS3. Alcohol-Related and Non-Alcoholic Fatty Liver Disease (14:00-15:30)</td>
</tr>
<tr>
<td>15:00</td>
<td>Coffee Break (15:30-15:50)</td>
</tr>
<tr>
<td>16:00</td>
<td>PSA. Liver Tumors (16:00-17:30)</td>
</tr>
</tbody>
</table>

### ROOM D (2F)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00</td>
<td>Basic Forum 1 (10:00-12:00)</td>
</tr>
<tr>
<td>12:00</td>
<td>Lunch Symposium 2 (12:30-13:30)</td>
</tr>
<tr>
<td>15:00</td>
<td>Basic Forum 2 (15:00-15:30)</td>
</tr>
<tr>
<td>15:30</td>
<td>Research Consortium Forum (15:30-17:00)</td>
</tr>
</tbody>
</table>
## POSTGRADUATE COURSE  “Diagnosis and Management of Liver Disease: Past, Present, and Future”

**Course Director’s Message**  Moon Young Kim, Yonsei University Wonju

The Postgraduate Course is prepared to be a practical help for the participants in the treatment of various liver diseases by organizing the parts that are often encountered in the clinical field but have not been dealt with systematically so far. In addition, we have focused on introducing new concepts and preparing ourselves for changes in the future of liver diseases in areas that have recently been newly defined and are growing in scope.

---

### ROOM A [1F] 102-105 / 107-110

**K Session in Korean**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:50-10:30</td>
<td>PG 1. Viral Hepatitis (*)</td>
<td>Seong Gu Hwang (CHA Unik), Hong Soo Kim (Soochunhyang Unik)</td>
</tr>
<tr>
<td>08:50-09:15</td>
<td>Anti-Hepatitis B Virus Therapy in Special Population</td>
<td>Jeong-Moon Lee (Seoul National Unik)</td>
</tr>
<tr>
<td>09:15-09:40</td>
<td>Anti-Hepatitis C Virus Therapy in Real-World Practice</td>
<td>Geum-Youn Gwak (Sungkyunkwan Unik)</td>
</tr>
<tr>
<td>09:40-10:05</td>
<td>Hepatitis E Virus: Epidemiology, Diagnosis, and Management</td>
<td>Nae-Yun Heo (Inje Unik)</td>
</tr>
<tr>
<td>10:05-10:30</td>
<td>Future Hepatitis B Virus Therapy</td>
<td>Jung Hyun Kwon (The Catholic Univ of Korea)</td>
</tr>
<tr>
<td>10:30-10:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>10:50-12:30</td>
<td>PG 2. Cirrhosis and Its Complications (*)</td>
<td>Byung Ik Kim (Sungkyunkwan Unik), Chang Hyeong Lee (Daegu Catholic Unik)</td>
</tr>
<tr>
<td>10:50-11:15</td>
<td>Covert and Overt Hepatic Encephalopathy</td>
<td>Sang Gyu Soo (Soochunhyang Unik)</td>
</tr>
<tr>
<td>11:15-11:40</td>
<td>Frailty and Sarcopenia in Cirrhosis</td>
<td>Seung Up Kim (Yonsei Unik)</td>
</tr>
<tr>
<td>11:40-12:05</td>
<td>Interventional Treatment of Varices: TIPS, BRT0, and PART0</td>
<td>Dongho Hyan (Sungkyunkwan Unik)</td>
</tr>
<tr>
<td>12:05-12:30</td>
<td>Sepsis in Cirrhosis: New Definition and Application</td>
<td>Dae Hye Choi (Konkuk National Unik)</td>
</tr>
<tr>
<td>12:30-13:30</td>
<td>Luncheon Symposium 1 (Abbvie)</td>
<td></td>
</tr>
<tr>
<td>13:30-13:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>13:50-15:30</td>
<td>PG 3. Alcohol-Related and Non-Alcoholic Fatty Liver Disease (*)</td>
<td>Yung Sang Lee (Univ of Ulsan), Youn-Jae Lee (Inje Unik)</td>
</tr>
<tr>
<td>13:50-14:15</td>
<td>Alcoholic Hepatitis from 1971 to 2019</td>
<td>Seong Won Jeong (Soochunhyang Unik)</td>
</tr>
<tr>
<td>14:15-14:40</td>
<td>Update on Imaging and Serum Biomarkers of Non-Alcoholic Fatty Liver Disease</td>
<td>Won Kim (Seoul National Unik)</td>
</tr>
<tr>
<td>14:40-15:05</td>
<td>Real Treatment Target of Non-Alcoholic Fatty Liver Disease: Steatosis vs. Fibrosis</td>
<td>Dae Won Jun (Hanyang Unik)</td>
</tr>
<tr>
<td>15:05-15:30</td>
<td>Metabolic Syndrome in Non-Alcoholic Fatty Liver Disease from Hepatologist’s Perspective</td>
<td>Yang Hyon Baek (Dong A Unik)</td>
</tr>
<tr>
<td>15:30-15:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>15:50-17:30</td>
<td>PG 4. Liver Tumors (*)</td>
<td>Chang Min Kim (National Cancer Center), Kyung Suk Kim (Yonsei Unik)</td>
</tr>
<tr>
<td>15:50-16:15</td>
<td>Radiologic Assessment of Hepatic Nodules</td>
<td>Jim-Young Choi (Yonsei Unik)</td>
</tr>
<tr>
<td>16:15-16:40</td>
<td>Surveillance of Hepatocellular Carcinoma: Risk Stratification</td>
<td>Sung Bum Cho (Chonnam National Unik)</td>
</tr>
<tr>
<td>16:40-17:05</td>
<td>Clinical Decision of Surgical Management: Benign Lesions</td>
<td>Sae Byoung Choi (Korea Unik)</td>
</tr>
<tr>
<td>17:05-17:30</td>
<td>Clinical Decision of Surgical Management: Hepatocellular Carcinoma and Cholangiocarcinoma</td>
<td>Gi-Won Song (Univ of Ulsan)</td>
</tr>
</tbody>
</table>
## DAY 1 Thursday, June 20, 2019

### ROOM D [2F] 205

#### SCIENTIFIC PROGRAM

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:50-12:30</td>
<td>Basic Forum 1. Hepatitis Virus <em>(K)</em></td>
<td>Soon Bong Hwang [Chonbuk National Univ.], Jin-Wook Kim [Seoul National Univ.]</td>
</tr>
<tr>
<td>10:50-11:15</td>
<td>Molecular Basis for Cure of Hepatitis B Virus Infection</td>
<td>Kyun-Hwan Kim [Konkuk Univ.]</td>
</tr>
<tr>
<td>11:15-11:40</td>
<td>Drug Development for Hepatitis B Virus Treatment</td>
<td>Sung-Gyoo Park [GIST]</td>
</tr>
<tr>
<td>11:40-12:05</td>
<td>Identification and Validation of Druggable Targets in the Hepatitis C Virus Life Cycle</td>
<td>Soon Bong Hwang [Chonbuk National Univ.]</td>
</tr>
<tr>
<td>12:05-12:30</td>
<td>Hepatitis C Virus Vaccine Development</td>
<td>Eui-Cheol Shin [KAIST]</td>
</tr>
<tr>
<td>12:30-13:00</td>
<td>Luncheon Symposium 2 [(Il-dong)]</td>
<td></td>
</tr>
<tr>
<td>13:30-13:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>13:50-15:30</td>
<td>Basic Forum 2. Hepatocellular Carcinoma and Steatohepatitis <em>(K)</em></td>
<td>S. Hoon Park [Hallym Univ.], Yong-Han Paik [Gyeongsangbuk-Do Univ.]</td>
</tr>
<tr>
<td>13:50-14:15</td>
<td>Understanding of Immune Checkpoint Inhibitors in Hepatocellular Carcinoma</td>
<td>Su-Hyung Park [KAIST]</td>
</tr>
<tr>
<td>14:15-14:40</td>
<td>Hepatocarcinogenesis and Animal Model</td>
<td>Wonsang Ro [Nonsan Univ.]</td>
</tr>
<tr>
<td>14:40-15:05</td>
<td>Hepatic mGlur5 Signaling in Endocannabinoid-Mediated Alcoholic Steatosis</td>
<td>Won-il Jeong [KAIST]</td>
</tr>
<tr>
<td>15:05-15:30</td>
<td>Pathogenesis of Non-Alcoholic Steatohepatitis</td>
<td>Sang Geon Kim [Seoul National Univ.]</td>
</tr>
<tr>
<td>15:30-15:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>15:50-17:30</td>
<td>Research Consortium Forum <em>(K)</em></td>
<td>Sung Kyu Choi [Chonnam National Univ.], Young Oh Kweon [Kyungpook National Univ.]</td>
</tr>
<tr>
<td>15:50-16:00</td>
<td>Gangwon Branch</td>
<td>Minjong Lee [Gangwon National Univ.]</td>
</tr>
<tr>
<td>16:00-16:10</td>
<td>Gyeonggi-Incheon Branch</td>
<td>Jeong-Ju Ioo [Gosan University]</td>
</tr>
<tr>
<td>16:10-16:20</td>
<td>Gwangju- Jeonnam Branch</td>
<td>Chung Ilwan Jun [Chonnam National Univ.]</td>
</tr>
<tr>
<td>16:20-16:30</td>
<td>Daegu-Kyungpook Branch</td>
<td>Jung Gil Park [Yeungnam Univ.]</td>
</tr>
<tr>
<td>16:30-16:40</td>
<td>Daejeon-Chungcheong Branch</td>
<td>Suk Rae Kim [Dankook Univ.]</td>
</tr>
<tr>
<td>16:40-16:50</td>
<td>Busan-Ulsan-Kyungnam Branch</td>
<td>Nae-Yun Heo [Inje Univ.]</td>
</tr>
<tr>
<td>16:50-17:00</td>
<td>Jeonbuk Branch</td>
<td>Chang Hun Lee [Chonbuk National Univ.]</td>
</tr>
<tr>
<td>17:00-17:10</td>
<td>Jeju Branch</td>
<td>Young Nam Kim [Cheju Halla General Hospital]</td>
</tr>
<tr>
<td>17:10-17:30</td>
<td>Discussion</td>
<td></td>
</tr>
</tbody>
</table>
# PROGRAM AT A GLANCE

## DAY 2 Friday, June 21, 2019

<table>
<thead>
<tr>
<th>Time</th>
<th>(ROOM A)</th>
<th>(ROOM BC)</th>
<th>(ROOM D)</th>
<th>(ROOM E)</th>
<th>(ROOM A)</th>
<th>(ROOM B)</th>
<th>(ROOM C)</th>
<th>(ROOM D)</th>
<th>(ROOM E)</th>
<th>(ROOM F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>07:00</td>
<td>103-105/108-110</td>
<td>101-102</td>
<td>106</td>
<td>107</td>
<td>201-202</td>
<td>203</td>
<td>204</td>
<td>205</td>
<td>206</td>
<td>207</td>
</tr>
<tr>
<td>08:00</td>
<td></td>
<td>Early Morning Workshop (08:30-08:45)</td>
<td>Early Morning Workshop (08:30-08:45)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>09:00</td>
<td>Symposium 1: NASH/LD/ALD (08:30-09:45)</td>
<td></td>
<td></td>
<td>KLTCS Symposium 1 (10:30-10:50)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:00</td>
<td>Opening Ceremony</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11:00</td>
<td>Plenary Session 1 (10:30-11:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:00</td>
<td>Special Lectures with Debates (11:10-12:10)</td>
<td>Hepatology Associates Course (11:10-12:10)</td>
<td>Health Policy Forum (11:10-12:10)</td>
<td>KAHBPS-KLTCS Joint Symposium (11:10-12:10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:00</td>
<td>Luncheon Symposium 3 (Silicon) (11:10-12:10)</td>
<td>Luncheon Symposium 4 (MSB) (11:10-12:10)</td>
<td></td>
<td>KLTCS General Meeting &amp; Luncheon Symposium 5 (Anastasia) (11:10-12:10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:00</td>
<td>State-of-the-Art Lecture 1 (12:30-13:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:00</td>
<td>Symposium 2: HBV (12:30-13:00)</td>
<td></td>
<td>KCDC-KASL Joint Symposium (11:30-12:30)</td>
<td>Satellite Symposium for Regeneration Medicine (11:30-12:30)</td>
<td>KLTCS Special Lecture (11:30-12:30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17:00</td>
<td>Clinical Hepatology Update (13:30-14:30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Coffee Break (09:30-09:50)
- Lunch Break (12:10-12:30)
- Break (13:10-13:30)
- Free Paper 3 Liver Cancer, Basic (12:30-13:00)
- Free Paper 4 Cirrhosis & Liver Failure (12:30-13:00)
- Free Paper 5 HCV (12:30-13:00)
- Free Paper 6 Liver Cancer (13:30-14:00)
- Poster Round (11:30-12:30)
- Free Paper 7 Surgery-Biopsy (12:30-13:00)
- Free Paper 8 Surgery-Technical Issues (12:30-13:00)
- Free Paper 9 AULIANLFD (12:30-13:00)
- Press Forum (16:30-16:50)

The Korean Association for the Study of the Liver (KASL)
The Korean Liver Cancer Association (KLCA)
The Korean Liver Transplantation Society (KLTS)
The Liver Cancer Study Group of Japan (LCSJG)
The Korean Association of HBP Surgery (KASL-HBP)
Korea Centers for Disease Control & Prevention (KCDC)
# DAY 2  Friday, June 21, 2019

## SCIENTIFIC PROGRAM

### ROOM A [1F] 103-105 / 108-110

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30-09:30</td>
<td>Symposium 1. Non-Alcoholic Fatty Liver Disease and Alcohol-Related Liver Disease</td>
<td>Dong Joon Kim (Hallym Univ.), Yong Kyeon Cho (Sungkyunkwan Univ.)</td>
</tr>
<tr>
<td>08:30-08:50</td>
<td>Fecal Microbiota Transplant in Alcoholic Hepatitis</td>
<td>SM Shasthy (Institute of Liver and Biliary Sciences, India)</td>
</tr>
<tr>
<td>08:50-09:10</td>
<td>Systemic Manifestation in Non-Alcoholic Fatty Liver Disease</td>
<td>Donghee Kim (Stanford Univ., USA)</td>
</tr>
<tr>
<td>09:10-09:30</td>
<td>Update on the Management of Non-Alcoholic Fatty Liver Disease</td>
<td>Vincent Wong (The Chinese Univ. of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>09:30-09:50</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>09:50-10:10</td>
<td>Opening Ceremony</td>
<td></td>
</tr>
<tr>
<td>10:10-11:10</td>
<td>Plenary Session 1</td>
<td>Young Il Lee (Kyung Hee Univ.), Hee Jung Wang (Ajou Univ.), Jung-Hwan Yoon (Seoul National Univ.)</td>
</tr>
<tr>
<td>11:10-12:10</td>
<td>Special Lectures with Debates. Can We Discontinue Hepatitis B Virus Therapy? Pros. vs. Cons.</td>
<td>Jordan Feld (Univ. of Toronto, Canada), Henry LY Chan (The Chinese Univ. of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>11:10-11:25</td>
<td>Nucleoside Analogue [NUC] Treatment Can Be Discontinued</td>
<td>Chun-Jen Liu (National Taiwan Univ., Taiwan)</td>
</tr>
<tr>
<td>11:25-11:40</td>
<td>NUC Treatment Should Be Continued</td>
<td>Young-Suk Lim (Univ. of Ulsan)</td>
</tr>
<tr>
<td>11:40-12:10</td>
<td>Panel Discussion</td>
<td>Wei-Kay Seto (Univ. of Hong Kong, Hong Kong), Hyung Joon Yim (Korea Univ.)</td>
</tr>
<tr>
<td>12:10-13:10</td>
<td>Luncheon Symposium 3 [Gilead]</td>
<td></td>
</tr>
<tr>
<td>13:10-13:30</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>13:30-14:00</td>
<td>State-of-the-Art Lecture 1</td>
<td>Dong Jin Suh (KMP Healthcare Seoul Clinic)</td>
</tr>
<tr>
<td>13:30-14:00</td>
<td>Hepatitis B Virus: From Control to Cure</td>
<td>Jia-Horng Kao (National Taiwan Univ., Taiwan)</td>
</tr>
<tr>
<td>14:00-15:30</td>
<td>Symposium 2. Hepatitis B Virus</td>
<td>Kwan Sik Lee (Yonsei Univ.), Jung Eun Yoon (Korea Univ.)</td>
</tr>
<tr>
<td>14:00-14:20</td>
<td>Viral Factors for Hepatitis B Virus-Related Hepatocellular Carcinoma</td>
<td>Jeong Won Jang (The Catholic Univ. of Korea)</td>
</tr>
<tr>
<td>14:20-14:40</td>
<td>Novel Biomarkers in Management of Chronic Hepatitis B</td>
<td>Yoshihiro Tanaka (Nagoya City Univ., Japan)</td>
</tr>
<tr>
<td>14:40-15:00</td>
<td>Current Treatment Strategy: Towards Hepatitis B Virus Cure</td>
<td>Seng Gee Lim (National Univ. of Singapore, Singapore)</td>
</tr>
<tr>
<td>15:00-15:20</td>
<td>Future Treatment Strategy: Towards Hepatitis B Virus Cure</td>
<td>Henry LY Chan (The Chinese Univ. of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>15:20-15:30</td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>15:30-16:30</td>
<td>Poster Round</td>
<td></td>
</tr>
<tr>
<td>16:30-17:50</td>
<td>Clinical Hepatology Update. Clinical Trials of Management in Chronic Liver Diseases™</td>
<td>Kwang Cheol Koh (Sungkyunkwan Univ.), II Han Song (Dankook Univ.)</td>
</tr>
<tr>
<td>16:30-16:50</td>
<td>Chronic Hepatitis B: Where Are We Now for Functional Cure?</td>
<td>Hyun Woon Lee (Yonsei Univ.)</td>
</tr>
<tr>
<td>16:50-17:10</td>
<td>Non-Alcoholic Steatohepatitis: Key Targets and Endpoints</td>
<td>Byung Kuk Jang (Keimyung Univ.)</td>
</tr>
<tr>
<td>17:10-17:30</td>
<td>Cirrhosis: Effort against Fibrosis and Portal Hypertension</td>
<td>Kyung Ah Kim (Inje Univ.)</td>
</tr>
<tr>
<td>17:30-17:50</td>
<td>Hepatocellular Carcinoma Treatment Showdown: Mono vs. Combination Therapy</td>
<td>Ju Hyun Shim (Univ. of Ulsan)</td>
</tr>
</tbody>
</table>

### ROOM BC [1F] 101-102

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:10-12:10</td>
<td>Hepatology Associates Course™</td>
<td>Byung Seok Lee (Chungnam National Univ.), Byung-Chool Song (Jeju National Univ.)</td>
</tr>
<tr>
<td>11:10-11:25</td>
<td>Treatment of Chronic Hepatitis B and C Virus</td>
<td>Eileen L. Yoon (Inje Univ.)</td>
</tr>
<tr>
<td>11:25-11:40</td>
<td>Management of Acute Variceal Bleeding</td>
<td>Seung Uk Shin (Gachon Univ.)</td>
</tr>
<tr>
<td>11:55-12:10</td>
<td>Hepatocellular Carcinoma: Diagnosis and Tumor Staging</td>
<td>Woo Jin Chung (Keimyung Univ.)</td>
</tr>
</tbody>
</table>
SCIENTIFIC PROGRAM

ROOM BC [1F] 101-102

12:10-13:10 Luncheon Symposium 4 [MSD]

ROOM D [1F] 106

07:30-08:30 Early Morning Workshop 1. Meet the Professor: Cirrhosis
- Rino Gani (Univ. of Indonesia, Indonesia), Sang Gyu Kim (Soochunhyang Univ.)
- C. Rinaldi A. Lesmana (Univ. of Indonesia, Indonesia)
- Paolo Angel (Univ. of Padua, Italy)

08:00-09:00 Discussion

11:10-12:10 Health Policy Forum: Policy Demand for Clinical Practice of Chronic Liver Disease **
- Young Seok Kim (Soochunhyang Univ.), Minsook Choi (Sungkyunkwan Univ.)
- Jeong Ha Kim (Konkuk Univ.)

11:40-11:55 Liver Disease-Related Issue to Strengthen Health Insurance Coverage
- Eun Sun Jun (Seoul National Univ.)

11:55-12:10 Future Policy of Government for Administration of Chronic Liver Disease
- Young Ki Jeong (Ministry of Health and Welfare)

14:00-15:30 KCDC-KASL Joint Symposium **
- Youngmee Lee (Korea National Institute of Health), Soo-Kyung Jeong (Seoul National Univ.)
- Sung Won Lee (The Catholic Univ. of Korea)
- Hyeon Lee (Korea Centers for Disease Control and Prevention)
- Baeum Kyung Kim (Yonsei Univ.)
- Eun Sun Jun (Seoul National Univ.)

15:10-15:30 Discussion

ROOM E [1F] 107

07:30-08:30 Early Morning Workshop 2. Meet the Professor: Non-Alcoholic Fatty Liver Disease
- Odin Tsakalakhv (Mongolian National Medical Univ., Mongolia), Joo Hyun Sohn (Hanyang Univ.)

07:30-07:50 Recent Epidemiology of Non-Alcoholic Fatty Liver Disease
- Donghee Kim (Stanford Univ., USA)

07:50-08:10 Non-Alcoholic Fatty Liver Disease and Diabetes: Chicken or Egg?
- Eun-Jung Rhee (Sungkyunkwan Univ.)

08:10-09:00 Discussion

14:00-15:00 The Liver Week Satellite Symposium for Regeneration Medicine
- Shoji Terai (Niigata Univ., Japan), Soon Koo Baik (Yonsei Univ. Wonju)
- Young Woo Eom (Yonsei Univ. Wonju)
- Gur Jin Kim (CNA Univ.)
- Soo Hyun Kim (KIST)
- Jung Hoan Cha (The Catholic Univ. of Korea)
- Kyungjin Kim (Univ. of Ulsan)

15:00-15:30 Proteomics Approach for Translational Research, Focusing on Liver Disease
- Kyungjin Kim (Univ. of Ulsan)

### DAY 2, Friday, June 21, 2019

### SCIENTIFIC PROGRAM

#### 08:30-09:30

**KLTS Symposium 1. Conundrum: Transplanted Liver Pathology**

- Shin Hwang (Univ. of Ulsan)
- Haeryoung Kim (Seoul National Univ.)

#### 08:30-09:10

**Liver Allograft Pathology: Developments in Antibody-Mediated Rejection**

- Christopher Bellamy (The Univ. of Edinburgh, UK)

#### 09:10-09:30

**Is a Protocol Biopsy Needed in a Liver Recipient?**

- Suk Kyun Hong (Seoul National Univ.)

#### 11:10-12:10

**KAHBP-RLTS Joint Symposium. Diagnosis and Management of Combined Hepatocellular Carcinoma (HCC) and Cholangiocellular Carcinoma (CCC)**

- Hee Chul Yu (Chonbuk National Univ.)
- Young Kyoungh You (The Catholic Univ. of Korea)

#### 11:10-11:25

**Pathological Point of View of Combined HCC and CCA: What is the Origin and Diagnostic Criteria of Combined HCC and CCA?**

- Young Nyeon Park (Yonsei Univ.)

#### 11:25-11:40

**Imaging Features of Combined HCC and CCC: What is the Difference Compared with HCC or CCC?**

- Chang Hee Lee (Seoul National Univ.)

#### 11:40-11:55

**Surgical Treatment and Prognosis of Combined HCC and CCC**

- Ryosue Matsuyama (Yokohama City Univ., Japan)

#### 11:55-12:10

**Issues of Combined HCC and CCC in Liver Transplantation**

- Young Seok Han (Kyungpook National Univ.)

#### 12:10-13:10

**KLTS General Meeting / Luncheon Symposium 5 [Astellas]**

#### 13:10-13:30

**Break**

#### 13:30-14:00

**KLTS Special Lecture**

- Kyung Suk Suh (Seoul National Univ.)

#### 13:30-14:00

**Donation after Circulatory Death Liver Procurement in Real Practice**

- Koji Hashimoto (Cleveland Clinic, USA)

#### 14:10-15:30

**KLTS Symposium 2. Use of Donation after Circulatory Death to Overcome the Decrease of Brain Death Donor**

- Yang Won Nah (Univ. of Ulsan)
- Myeong Soo Kim (Yonsei Univ.)

#### 14:10-14:30

**Current Status and Problems of Organ Donation in Korea**

- Won Hyun Cho (Korea Organ Donation Agency)

#### 14:30-14:50

**Current Status of Liver Allocation System**

- Je Geun Lee (Yonsei Univ.)

#### 14:50-15:10

**Institutional Issue and Limit of Donation after Cardiac Death**

- Dong Sik Kim (Seoul National Univ.)

#### 15:10-15:30

**Panel Discussion**

- Jeong Rim Lee (Korea Organ Donation Agency)
- Myeongyong Seo (Korea Centers for Disease Control and Prevention)

#### 15:30-16:30

**Poster Round**

#### 16:30-17:50

**KASL-RLTS Joint Symposium: Hepatorenal Syndrome (HRS)**

- Jae Won Joh (Sungkyunkwan Univ.)
- Jong Young Choi (The Catholic Univ. of Korea)

#### 16:30-16:50

**HRS: Definition, Pathophysiology, and Management**

- Yeon Sook Seo (Seoul National Univ.)

#### 16:50-17:10

**When to Consider Simultaneous Liver Kidney Transplantation and How to Prevent Adverse Renal Outcome after Liver Transplantation**

- Jae Min Chun (Sungkyunkwan National Univ.)

#### 17:10-17:30

**MELD Purgatory in HRS and Allocation Policy: When to Start Renal Replacement Therapy?**

- Shin Hwang (Univ. of Ulsan)

#### 17:30-17:50

**When to Start Renal Replacement Therapy for Hepatorenal Syndrome**

- Hyun Ryoun Jang (Sungkyunkwan Univ.)

---

## ROOM B [2F] 203

#### 14:10-15:30

**KLTS Coordinator Session**

- Kyung-Ock Jeon (Severance Hospital)
- Sunyoung Son (Gangnam Severance Hospital)

#### 14:10-14:30

**Recovery Management for Old Age Recipient**

- Man Ki Ju (Yonsei Univ.)

#### 14:30-14:50

**Transplantation Counseling for an Elderly Liver Transplantation Patient**

- Hyung Soo Kim (Seoul St. Mary’s Hospital)

#### 14:50-15:10

**Acute Liver Failure**

- Dong Jin Joo (Yonsei Univ.)

#### 15:10-15:30

**Patient Management after Liver Transplantation**

- Seung Heui Hong (Samsung Medical Center)
## ROOM D [2F] 205

### SCIENTIFIC PROGRAM

**DAY 2** Friday, June 21, 2019

### ROOM D [2F] 205

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker/Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30-09:30</td>
<td>KLCA Symposium 1. A Developing Strategy to Improve Diagnosis of HCC</td>
<td>Jin Wook Chung (Seoul National Univ.), June Sung Lee (Inje Univ.)</td>
</tr>
<tr>
<td>08:30-09:30</td>
<td>Surveillance for HCC in Patients with Non-Alcoholic Fatty Liver Disease</td>
<td>Vincent Wong (U.O. of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>08:50-09:10</td>
<td>Are Emerging Biomarkers and Imaging Tools Better than Routine Abdominal Sonography for HCC Surveillance?</td>
<td>Do Young Kim (Korea Univ.)</td>
</tr>
<tr>
<td>09:10-09:30</td>
<td>Is LI-RADS Better for Diagnosis of HCC?</td>
<td>Jeong Min Lee (Seoul National Univ.)</td>
</tr>
<tr>
<td>11:10-12:10</td>
<td>KLCA General Meeting <em>MK</em></td>
<td></td>
</tr>
<tr>
<td>11:10-11:15</td>
<td>0202 Liver Cancer Day Special Lecture</td>
<td>Hyun Wonsung Lee (Yonsei Univ.)</td>
</tr>
<tr>
<td>11:25-12:10</td>
<td>KLCA General Meeting</td>
<td></td>
</tr>
<tr>
<td>12:10-13:10</td>
<td>Luncheon Symposium 6 (Bayer)</td>
<td></td>
</tr>
<tr>
<td>13:10-13:30</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>13:30-14:30</td>
<td>LCSGJ-KLCA Joint Symposium 1. One Step Forward for Understanding Basic Knowledge</td>
<td>Yutaka Kawakami (Keio Univ., Japan), Young Nyun Park (Yonsei Univ.)</td>
</tr>
<tr>
<td>13:50-14:10</td>
<td>Immunotherapy: Adoptive Cell Therapy for Solid Cancers</td>
<td>Yutaka Kawakami (Keio Univ., Japan)</td>
</tr>
<tr>
<td>14:10-14:30</td>
<td>Oncolytic Virus Based Therapy for HCC</td>
<td>Jeong Heo (Pusan National Univ.)</td>
</tr>
<tr>
<td>14:30-15:30</td>
<td>LCSGJ-KLCA Joint Symposium 2. Similarities and Differences in Treatment of HCC</td>
<td>Shoji Kubo (Osaka City Univ., Japan), Seung Kew Yoon (The Catholic Univ. of Korea)</td>
</tr>
<tr>
<td>14:30-14:45</td>
<td>Recent Trends of Treatment for Intermediate Stage HCC: Japanese Experience</td>
<td>Masatoshi Kudo (Kindai Univ., Japan)</td>
</tr>
<tr>
<td>14:45-15:00</td>
<td>Recent Trends of Treatment for Intermediate Stage HCC: Korean Experience</td>
<td>Ji Hoon Kim (Korea Univ.)</td>
</tr>
<tr>
<td>15:00-15:15</td>
<td>Recent Trends of Treatment for Advanced Stage HCC: Japanese Experience</td>
<td>Kazumi Ueshima (Kindai Univ., Japan)</td>
</tr>
<tr>
<td>15:15-15:30</td>
<td>Recent Trends of Treatment for Advanced Stage HCC: Korean Experience</td>
<td>Won Young Tak (Hanyangju National Univ.)</td>
</tr>
<tr>
<td>15:30-16:30</td>
<td>Poster Round</td>
<td></td>
</tr>
<tr>
<td>16:30-17:30</td>
<td>KLCA Symposium 2. New and Emerging Systemic Therapies in Advanced HCC</td>
<td>Kwang-Hyub Han (Yonsei Univ.), Seung Woon Paik (Sungkyunkwan Univ.)</td>
</tr>
<tr>
<td>16:30-16:50</td>
<td>First Line Treatments for HCC</td>
<td>Arndt Vogel (Hannover Medical School, Germany)</td>
</tr>
<tr>
<td>16:50-17:10</td>
<td>Second Line Treatments for HCC</td>
<td>Stephen L. Chan (The Chinese Univ. of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>17:10-17:30</td>
<td>A Future of Systemic Agents: Emerging Therapies and Strategies</td>
<td>Baek-Yeol Ryu (Univ. of Ulsan)</td>
</tr>
<tr>
<td>17:30-17:50</td>
<td>Combination of Interventional and Systemic Therapies for HCC: Current Status and Future Direction</td>
<td>Joong-Won Park (National Cancer Center)</td>
</tr>
</tbody>
</table>

### ROOM F [2F] 207

*KSJA: Korea Science Journalists Association*

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker/Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:30-16:30</td>
<td>KSJA-The Liver Week 2019 Press Forum. Liver Disease Control in Korea <em>KSJA</em></td>
<td>Kang Mo Kim (Univ. of Ulsan)</td>
</tr>
<tr>
<td>15:30-15:40</td>
<td>Current Status and Suggestion for Eradication of Chronic Hepatitis C in Korea</td>
<td>Do Young Kim (Yonsei Univ.)</td>
</tr>
<tr>
<td>15:40-15:50</td>
<td>Epidemic of Acute Hepatitis A in Korea: Vaccination Policy</td>
<td>Ji Hoon Kim (Korea Univ.)</td>
</tr>
<tr>
<td>15:50-16:00</td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>16:00-16:10</td>
<td>The Liver Week 2019 Highlight Presentation</td>
<td>Bo Hyoung Kim (National Cancer Center)</td>
</tr>
<tr>
<td>16:10-16:20</td>
<td>Unresolved Reimbursement Issues in Liver Disease</td>
<td>Hyung Soon Kim (Chung Ang Univ.)</td>
</tr>
<tr>
<td>16:20-16:30</td>
<td>Discussion</td>
<td></td>
</tr>
</tbody>
</table>
# Program at a Glance

## Day 3 Saturday, June 22, 2019

<table>
<thead>
<tr>
<th>Time</th>
<th>Room A</th>
<th>Room BC</th>
<th>Room D</th>
<th>Room E</th>
<th>Room A</th>
<th>Room BC</th>
<th>Room D</th>
<th>Room E</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00-</td>
<td>Free Paper 10 LT (08:00-09:00)</td>
<td>Free Paper 11 HBV (08:00-09:00)</td>
<td>Free Paper 12 Liver Cancer Clinical (08:00-09:00)</td>
<td>Free Paper 17 (08:00-09:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>09:00-</td>
<td>Symposium 3: HCV (09:00-10:00)</td>
<td>KAHPBS Symposium 1 (09:00-10:00)</td>
<td>Ultrasound Trainer Session 1 (09:00-10:00)</td>
<td>KAHPBS-KLCA Joint Symposium 1 (09:00-10:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:00-</td>
<td>KASL Clinical Practice Guidelines (10:30-10:50)</td>
<td>National Health Insurance Big Data Research (10:00-11:00)</td>
<td>Ultrasound Trainer Session 2 (10:30-11:30)</td>
<td>Free Paper 14 Liver Cancer Clinical (11:00-12:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11:00-</td>
<td>State-of-the-Art Lecture 2 (11:00-11:30)</td>
<td>KAHPBS Symposium 2 (11:00-11:30)</td>
<td>KAHPBS Symposium 2 (11:00-11:30)</td>
<td>KAHPBS-KLCA Joint Symposium 2 (11:00-11:30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:00-</td>
<td>Plenary Session 2 (11:30-12:00)</td>
<td>Lunch Symposium 7 (12:00-12:30)</td>
<td>Lunch Symposium 9 (12:00-12:30)</td>
<td>Lunch Symposium 10 (12:00-12:30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:00-</td>
<td>Lunch Symposium 8 (12:00-12:30)</td>
<td>Lunch Symposium 9 (12:30-13:00)</td>
<td>Lunch Symposium 9 (12:30-13:00)</td>
<td>Free Paper 14 Liver Cancer Clinical (12:30-13:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:00-</td>
<td>Poster Round (13:30-14:30)</td>
<td>KAHPBS Special Lecture (13:30-14:00)</td>
<td>KAHPBS Symposium 3 (14:30-15:30)</td>
<td>Free Paper 16 Basic &amp; Others (13:30-14:30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:00-</td>
<td>KAHPBS Symposium 4 (14:30-15:00)</td>
<td>KAHPBS Symposium 3 (14:30-15:00)</td>
<td>Common Concerns: Hepatologists &amp; Surgeons (14:30-15:15)</td>
<td>Asian Forum (Korea-Japan-Taiwan) (14:30-15:15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:00-</td>
<td>KASL-KAHPBS-KLCA-KLCA Joint Symposium: TWIN 2019 Delirium (15:40-16:40)</td>
<td>KAHPBS Symposium 3 (14:30-15:00)</td>
<td>KAHPBS Symposium 3 (14:30-15:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17:00-</td>
<td>Closing &amp; Award Ceremony (16:30-17:00)</td>
<td>KAHPBS Symposium 3 (14:30-15:00)</td>
<td>KAHPBS Symposium 3 (14:30-15:00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## SCIENTIFIC PROGRAM

### ROOM A [1F] 103-105 / 108-110

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-10:00</td>
<td>Symposium 3. Hepatitis C Virus</td>
<td>Masao Omata (Yamanashi Prefectural Central Hospital, Japan), Si Hyun Bae (The Catholic Univ. of Korea)</td>
</tr>
<tr>
<td>09:00-09:20</td>
<td>Long-Term Outcome of Direct-Acting Antiviral Treatment</td>
<td>Jung Il Lee (Yonsei Univ.)</td>
</tr>
<tr>
<td>09:20-09:40</td>
<td>Follow-Up Strategies Following Cure of Hepatitis C Virus Infection</td>
<td>Naoya Sakamoto (Hokkaido Univ., Japan)</td>
</tr>
<tr>
<td>09:40-10:00</td>
<td>Unmet Needs in the Era of Direct-Acting Antiviral Therapy</td>
<td>Ming-Lung Yu (Kaohsiung Medical Univ., Taiwan)</td>
</tr>
<tr>
<td>10:00-10:20</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>10:20-10:50</td>
<td>Special Session. KASL Clinical Practice Guidelines</td>
<td>Kwan Soo Byun (Korea Univ.)</td>
</tr>
<tr>
<td>10:20-10:50</td>
<td>Variceal Bleeding and Hepatic Encephalopathy</td>
<td>Jeong Young Jang (Soochunhyang Univ.)</td>
</tr>
<tr>
<td>10:50-11:20</td>
<td>State-of-the-Art Lecture 2</td>
<td>Jin Mo Yang (The Catholic Univ. of Korea)</td>
</tr>
<tr>
<td>10:50-11:20</td>
<td>Current Understanding of Autoimmune Liver Diseases</td>
<td>Atsushi Tanaka (Tokyo Univ., Japan)</td>
</tr>
<tr>
<td>11:20-12:20</td>
<td>Plenary Session 2</td>
<td>Joong-Won Park (National Cancer Center), Han Chu Lee (Univ. of Ulsan), Myung-Hee Yoon (Pusan National Univ.)</td>
</tr>
<tr>
<td>12:20-13:20</td>
<td>Luncheon Symposium 7 (Yuhan)</td>
<td></td>
</tr>
<tr>
<td>13:20-14:20</td>
<td>Poster Round</td>
<td></td>
</tr>
</tbody>
</table>

### Grand Ballroom [3F]

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:30-15:40</td>
<td>Symposium 4. Cirrhosis</td>
<td>Rino Gani (Univ. of Indonesia, Indonesia), Soon Koo Baik (Yonsei Univ. Wonju)</td>
</tr>
<tr>
<td>14:30-14:50</td>
<td>Mesenchymal Stem Cell Therapy for Liver Cirrhosis (Basic Study and Clinical Application)</td>
<td>Shoji Terai (Nippon Univ., Japan)</td>
</tr>
<tr>
<td>14:50-15:10</td>
<td>The Role of Albumin Related with Systemic Inflammation in Cirrhosis</td>
<td>Paolo Angelii (Univ. of Padova, Italy)</td>
</tr>
<tr>
<td>15:10-15:30</td>
<td>Role of Cytoglobin, a Novel Radical Scavenger in Stellate Cell Activation and Hepatic Fibrosis</td>
<td>Nonifumi Kawada (Osaka City Univ., Japan)</td>
</tr>
<tr>
<td>15:30-15:40</td>
<td>Discussion</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:40-16:40</td>
<td>KASL-KAHBPS-KLCA-KLTS Joint Symposium: The Liver Week 2019 Debrief</td>
<td>Sang Hoon Ahn (Yonsei Univ.), Dong Sik Kim (Korea Univ.), Ji Hoon Kim (Korea Univ.)</td>
</tr>
<tr>
<td>15:40-15:55</td>
<td>Best Presentations of KASL</td>
<td>Jun Yong Park (Yonsei Univ.)</td>
</tr>
<tr>
<td>15:55-16:10</td>
<td>Best Presentations of KAHBPS</td>
<td>Say-June Kim (The Catholic Univ. of Korea), Seo Bysoo Choi (Korea Univ.)</td>
</tr>
<tr>
<td>16:10-16:25</td>
<td>Best Presentations of KLCA</td>
<td>Su Jong Yu (Seoul National Univ.)</td>
</tr>
<tr>
<td>16:25-16:40</td>
<td>Best Presentations of KLTs</td>
<td>Jeong Geun Lee (Korea Univ.)</td>
</tr>
<tr>
<td>16:40-17:00</td>
<td>Closing and Award Ceremony</td>
<td></td>
</tr>
</tbody>
</table>

### ROOM BC [1F] 101-102

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-10:00</td>
<td>KAHBPS Symposium 1. Surgical Research in HBP: Challenges and Barriers</td>
<td>Il-Young Park (The Catholic Univ. of Korea), Koo Jong Kang (Keimyung Univ.)</td>
</tr>
<tr>
<td>09:00-09:20</td>
<td>Surgeon-Scientists: An Endangered Species?</td>
<td>Sundee D. Keswani (Baylor College of Medicine, USA)</td>
</tr>
<tr>
<td>09:20-09:40</td>
<td>Basic/Translational Research (How to Start and Grow)</td>
<td>Say-June Kim (The Catholic Univ. of Korea)</td>
</tr>
<tr>
<td>09:40-10:00</td>
<td>Clinical Research to Reduce Pancreatic Fistula after Distal Pancreatectomy</td>
<td>Monabu Kawai (Wakayama Medical Univ., Japan)</td>
</tr>
<tr>
<td>10:00-10:20</td>
<td>Coffee Break</td>
<td></td>
</tr>
</tbody>
</table>
DAY 3  Saturday, June 22, 2019

SCIENTIFIC PROGRAM

ROOM BC [1F] 101-102

Management of Gallstones and Acute Cholecystitis in Patient with Liver Cirrhosis
Hyung Chul Kim (Soochunhyang Univ.), Young Won Noh (Univ of Ulsan)

10:20:10:35  1] Medical Treatment: Indication and Result of Medical Treatment
Ki Tae Suk (Hallym Univ.)

10:35:10:50  2] Surgical Treatment: What Should We Caution to Consider Surgery?
Shang Yu Wong (Chang-Gung Univ., Taiwan)

10:50:11:05  Clinical Outcomes and Prognosis of Emergency Surgery in Liver Cirrhosis Patient
Fausto Catena (Univ of Bologna, Italy)

11:05:11:20  Elective Cancer Surgery in Patients with Liver Cirrhosis
Sae Byeol Choi (Korea Univ.)

12:20:13:20  Luncheon Symposium 8 [BMS]

13:20:14:20  Poster Round

14:00:14:30  KAHBPS Special Lecture
Hee Chul Yu (Chonbuk National Univ.)

14:00:14:30  The Journey from Scientific Idea to Funded Grant: A Surgeon’s Approach
Sundeep C. Keswani (Baylor College of Medicine, USA)

14:30:15:30  KAHBPS Symposium 3. Focus Review of Advanced Gallbladder Cancer Treatment
Dong Wook Choi (Sungkyunkwan Univ.), Sang-Joo Park (National Cancer Center)

14:30:14:50  The Operative Indication of Advanced Gallbladder Cancer: How Much Advance Is the Limitation?
Masayuki Ohitsuka (Chiba Univ., Japan)

14:50:15:10  Recent Advances in the Chemotherapy in Advanced Gallbladder Cancer: Palliative vs. Neoadjuvant Chemotherapy
Hei-Chul Jeong (Monsel Univ.)

15:10:15:30  Case Presentation
Chi-Yong Jeong (Gyeongsang National Univ.)

ROOM D [1F] 106

10:20:11:20  Special Session, National Health Insurance Big Data Research (R)
Hyung-Soo Kang (National Health Insurance Service), Jeeyoung Cheong (Ajou Univ.)

10:20:10:35  National Health Insurance Big Data Analysis: Process and Example
Seong Yong Park (National Health Insurance Service)

10:35:10:50  National Health Insurance Big Data Research: HCC Surveillance
Yong-Han Park (Sungkyunkwan Univ.)

10:50:11:05  Role of Staging on Development and Progression of Non-Alcoholic Fatty Liver Disease: A Nationwide Nested Case-Control Study
Jung Il Lee (Monsel Univ.)

11:05:11:20  National Health Insurance Big Data Research: Liver Cirrhosis
Dae Won Jun (Hanyang Univ.)


12:20:13:20  Luncheon Symposium 9 [Dong-A ST]

13:20:14:20  Poster Round

14:30:15:40  Common Concerns: Histopathologists and Surgeons (R)
Yung Sang Lee (Univ of Ulsan), Sung Su Yun (Yeungnam Univ.)

14:30:14:45  Assessment of Surgical Risk in Patients with Cirrhosis
Ki Tae Yoon (Pusan National Univ.)

14:45:15:00  Determination of Preoperative Liver Function and Extent of Resection
Bong-Wan Kim (Ajou Univ.)

15:00:15:15  Prophylaxis of Hepatitis B Virus Reactivation after Liver Transplantation
Jae Hyn Han (The Catholic Univ of Korea)

15:15:15:30  Optimal Hepatitis C Virus Treatment Strategy for Patients Waiting for Liver Transplantation
In Hee Kim (Chonbuk National Univ.)

15:30:15:40  Discussion
## SCIENTIFIC PROGRAM

### ROOM D [2F] 205

- **09:00-10:00** KAHBPS-KLTS-KLCA Joint Symposium 1, Unresolved Issues in HCC: Medical and Interventional Radiology  
  Yun Hwan Kim (Korea Univ.), Joonseok Hwang (Keimyung Univ.)
  - **09:00-09:20** Adjuvant Therapy after Curative Treatment: Enough or Still Lacking?  
    Su Jong Yu (Seoul National Univ.)
  - **09:20-09:40** Direct Acting Antiviral and HCC in Chronic Hepatitis C: Friend or Foe?  
    Hyung Joon Kim (Chung-Ang Univ.)
  - **09:40-10:00** How to Overcome Long-Term Decline in Survival of HCC Patients Treated with Ablation  
    Shuichiro Shina (Juntendo Univ., Japan)

- **10:00-10:20** Coffee Break

- **10:20-11:20** KAHBPS-KLTS-KLCA Joint Symposium 2, Unresolved Issues in HCC: Surgical and Radiation Oncology  
  Hee Jung Wang (Ajou Univ.), Jinsoil Seo (Yonsei Univ.)
  - **10:20-10:40** Will Laparoscopic Approach Be Almighty Weapon in Surgery in HCC  
    Jong Man Kim (Sungkyunkwan Univ.)
  - **10:40-11:00** Priority Policy for Patients with HCC Awaiting Liver Transplantation: Unresolved Issue?  
    Dorry L. Segev (Johns Hopkins Univ., USA)
  - **11:00-11:20** Radiation Therapy for Early HCC: Will It Be a Good Option in Practice?  
    Sang Min Yoon (Univ. of Ulsan)

- **11:20-12:30** Luncheon Symposium 10 [Eisai]

- **12:30-14:20** Poster Round

- **14:20-15:40** Asian Forum: Korea-Japan-Taiwan  
  Jin Mo Yang (Korea), Tetsuo Takehara (Japan), Jia-Hong Kao (Taiwan)
  - **14:20-14:35** Current Status and Emerging Issues in Liver Diseases in Japan  
    Hayato Hikita (Osaka Univ., Japan)
  - **14:35-14:50** Current Status and Emerging Issues in Liver Diseases in Taiwan  
    Chun-Jen Liu (National Taiwan Univ., Taiwan)
  - **14:50-15:05** Current Status and Emerging Issues in Liver Diseases in Korea  
    Yoosun Kim (Seoul National Univ.)
  - **15:05-15:20** Cirrhotic Portal Hypertension: From Arterial Vasodilatation to Systemic Inflammation  
    Han-Chieh Lin (National Yang-Ming Univ., Taiwan)
  - **15:25-15:40** Discussion
### DAY 3 Saturday, June 22, 2019

**SCIENTIFIC PROGRAM**

#### ULRASONOGRAPHY (USG) TRAINING COURSE & HANDS-ON COURSE

**ROOM A [2F] 201-202**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-10:00</td>
<td><strong>USG Session 1. Upgrading the USG Education</strong> (K)</td>
<td>Soon Koo Baik (Yonsei Univ, Wonju)</td>
</tr>
<tr>
<td>09:00-09:15</td>
<td>Current Status of USG Education Program and USG Specialist Certificates of KASL</td>
<td>Hyung Joon Yim (Korea Univ)</td>
</tr>
<tr>
<td>09:15-09:35</td>
<td>How Do I Teach Abdominal USG for Trainee?</td>
<td>Yun Soo Kim (Sachon Univ)</td>
</tr>
<tr>
<td>09:35-10:00</td>
<td>How to Perform Contrast-Enhanced USG: Experiences in Japan</td>
<td>Fuminori Moriyasu (Juntendo Univ. of Health and Welfare, Japan)</td>
</tr>
<tr>
<td>10:00-10:20</td>
<td>Coffee Break</td>
<td></td>
</tr>
<tr>
<td>10:20-12:20</td>
<td><strong>USG Session 2. Diversifying the Field of USG for Training</strong> (K)</td>
<td>Won Young Tak (Kyungpook National Univ)</td>
</tr>
<tr>
<td>10:20-10:40</td>
<td>Setting-Up an Abdominal USG Facility and Training Program</td>
<td>In Hee Kim (Chonbuk National Univ)</td>
</tr>
<tr>
<td>10:40-11:00</td>
<td>Tips for Selection and Maintenance of USG Machines</td>
<td>Hyun Joo Kim (GE), Han Jong Yu (Canon)</td>
</tr>
<tr>
<td>11:00-11:20</td>
<td>Assessment of Hepatic Fibrosis with 2 Dimensional Real-Time Shear Wave Elastography</td>
<td>Joo Hyun Sohn (Hanyang Univ)</td>
</tr>
<tr>
<td>11:20-11:40</td>
<td>How to Improve Precision in Targeting Focal Lesion</td>
<td>Shuichi Shina (Juntendo Univ., Japan)</td>
</tr>
<tr>
<td>11:40-12:00</td>
<td>New Insight for Lower Abdomen and Kidney USG</td>
<td>Seong Sook Hong (Soochunhyung Univ)</td>
</tr>
<tr>
<td>12:00-12:20</td>
<td>Present and Future of National Health Insurance System for USG:</td>
<td>Hong Soo Kim (Soochunhyung Univ)</td>
</tr>
<tr>
<td></td>
<td>What Do We Need to Prepare for?</td>
<td></td>
</tr>
</tbody>
</table>

#### ROOM BC [2F] 203-204

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-10:00</td>
<td><strong>USG Trainee Session</strong> (K)</td>
<td>Young Seok Kim (Soochunhyung Univ)</td>
</tr>
<tr>
<td>09:00-09:20</td>
<td>How to Utilize the Various Functions of USG Machine</td>
<td>Moon Young Kim (Yonsei Univ, Wonju)</td>
</tr>
<tr>
<td>09:20-09:40</td>
<td>Basic Liver Scanning and Key Findings</td>
<td>Jeong Eun Song (Daegu Catholic Univ.)</td>
</tr>
<tr>
<td>09:40-10:00</td>
<td>Pancreatobiliary USG Scanning Made Easy</td>
<td>Soon Sun Kim (Ajou Univ)</td>
</tr>
</tbody>
</table>

#### ROOM E [1F] 107

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Tutors</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:20-12:20</td>
<td><strong>Hands-on Course I</strong> (K)</td>
<td>Sae Hwan Lee (Soochunhyang Univ), Won Sohn (Sungkyunkwan Univ), Do Seon Song (The Catholic Univ of Korea), Chung Hwan Jun (Chonnam National Univ), Sung Non Lee (The Catholic Univ of Korea), Sun Hong You (The Catholic Univ of Korea)</td>
</tr>
<tr>
<td>13:20-15:20</td>
<td><strong>Hands-on Course II</strong> (K)</td>
<td>Jae Young Jang (Soochunhyang Univ), Jaeyoun Cheong (Ajou Univ), Yeon Seok Seo (Korea Univ), Song Gyune Kim (Soochunhyang Univ), Moon Young Kim (Yonsei Univ, Wonju), Kj Tae Suk (Hallym Univ)</td>
</tr>
</tbody>
</table>
### Contents

#### DAY 1  Thursday, June 20, 2019

**Basic Forum 1. Hepatitis Virus (K)**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Basis for Cure of Hepatitis B Virus Infection</td>
<td>2</td>
</tr>
<tr>
<td>Kyun-Hwan Kim</td>
<td></td>
</tr>
<tr>
<td>Drug Development for Hepatitis B Virus Treatment</td>
<td>5</td>
</tr>
<tr>
<td>Sung-Gyoo Park</td>
<td></td>
</tr>
<tr>
<td>Identification and Validation of Druggable Targets in the Hepatitis C Virus Life Cycle</td>
<td>7</td>
</tr>
<tr>
<td>Soon Bang Hwang</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C Virus Vaccine Development</td>
<td>8</td>
</tr>
<tr>
<td>Eui-Cheol Shin</td>
<td></td>
</tr>
</tbody>
</table>

**Basic Forum 2. Hepatocellular Carcinoma and Steatohepatitis (K)**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understanding of Immune Checkpoint Inhibitors in Hepatocellular Carcinoma</td>
<td>10</td>
</tr>
<tr>
<td>Su-Hyung Park</td>
<td></td>
</tr>
<tr>
<td>Hepatocarcinogenesis and Animal Model</td>
<td>11</td>
</tr>
<tr>
<td>Weonsang Ro</td>
<td></td>
</tr>
<tr>
<td>Hepatic mGluR5 Signaling in Endocannabinoid-Mediated Alcoholic Steatosis</td>
<td>13</td>
</tr>
<tr>
<td>Won-il Jeong</td>
<td></td>
</tr>
<tr>
<td>Pathogenesis of Non-Alcoholic Steatohepatitis</td>
<td>15</td>
</tr>
<tr>
<td>Sang Geun Kim</td>
<td></td>
</tr>
</tbody>
</table>

#### DAY 2  Friday, June 21, 2019

**Symposium 1. Non-Alcoholic Fatty Liver Disease and Alcohol-Related Liver Disease**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal Microbiota Transplant in Alcoholic Hepatitis</td>
<td>20</td>
</tr>
<tr>
<td>SM Shasthry</td>
<td></td>
</tr>
<tr>
<td>Systemic Manifestation in Non-Alcoholic Fatty Liver Disease</td>
<td>21</td>
</tr>
<tr>
<td>Donghee Kim</td>
<td></td>
</tr>
<tr>
<td>Update on the Management of Non-Alcoholic Fatty Liver Disease</td>
<td>22</td>
</tr>
<tr>
<td>Vincent Wong</td>
<td></td>
</tr>
</tbody>
</table>

**Special Lectures with Debates: Can We Discontinue Hepatitis B Virus Therapy? Pros. vs. Cons.**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside Analogue (NUC) Treatment Can Be Discontinued</td>
<td>24</td>
</tr>
<tr>
<td>Chun-Jen Liu</td>
<td></td>
</tr>
<tr>
<td>NUC Treatment Should Be Continued</td>
<td>25</td>
</tr>
<tr>
<td>Young-Suk Lim</td>
<td></td>
</tr>
</tbody>
</table>

**State-of-the-Art Lecture 1**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B Virus: From Control to Cure</td>
<td>30</td>
</tr>
<tr>
<td>Ja-Hong Kao</td>
<td></td>
</tr>
</tbody>
</table>

**Symposium 2. Hepatitis B Virus**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral Factors for Hepatitis B Virus-Related Hepatocellular Carcinoma</td>
<td>32</td>
</tr>
<tr>
<td>Jeong Won Jang</td>
<td></td>
</tr>
</tbody>
</table>
### Clinical Hepatology Update. Clinical Trials of Management in Chronic Liver Diseases (*K*)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Hepatitis B: Where Are We Now for Functional Cure?</td>
<td>Hyun Woong Lee</td>
</tr>
<tr>
<td>Non-Alcoholic Steatohepatitis: Key Targets and Endpoints</td>
<td>Byoung Kuk Jang</td>
</tr>
<tr>
<td>Cirrhosis: Effort against Fibrosis and Portal Hypertension</td>
<td>Kyung-Ah Kim</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma Treatment Showdown: Mono vs. Combination Therapy</td>
<td>Ju Hyeon Shim</td>
</tr>
</tbody>
</table>

### Hepatology Associates Course (*K*)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of Chronic Hepatitis B and C Virus</td>
<td>Eileen L. Yoon</td>
</tr>
<tr>
<td>Management of Acute Variceal Bleeding</td>
<td>Seung Kuk Shin</td>
</tr>
<tr>
<td>Liver Transplantation: When and How?</td>
<td>Bum-Soo Kim</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma Diagnosis and Tumor Staging</td>
<td>Woo Jin Chung</td>
</tr>
</tbody>
</table>

### The Liver Week Satellite Symposium for Regeneration Medicine

<table>
<thead>
<tr>
<th>Topic</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison of Bone Marrow-Derived Mesenchymal Stem Cells Isolated from Normal and Cirrhotic Patients</td>
<td>Young Woo Eom</td>
</tr>
<tr>
<td>Feasibility of Enhanced PRL-1 in Placenta-derived Mesenchymal Stem Cells by Gene Modification on a Rat Model with Hepatic Failure</td>
<td>Gi Jin Kim</td>
</tr>
<tr>
<td>Vascularized Liver Tissue with Different Types of Endothelial Cells and Recovery Aids for Acute Liver Failure</td>
<td>Jaeseo Lee, DoYeun Park, Soo Hyun Kim</td>
</tr>
<tr>
<td>MicroRNA Profile Analysis in Liver Fibrotic Tissue and Hepatic Differentiated Human Bone Marrow-Derived Mesenchymal Stem Cells</td>
<td>Jung Hoan Cha</td>
</tr>
<tr>
<td>Proteomics Approach for Translational Research, Focusing on Liver Disease</td>
<td>Kyunggon Kim</td>
</tr>
</tbody>
</table>

### KLTS Symposium 1. Conundrum: Transplanted Liver Pathology

<table>
<thead>
<tr>
<th>Topic</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver Allograft Pathology: Developments in Antibody-Mediated Rejection</td>
<td>Christopher Bellamy</td>
</tr>
<tr>
<td>Is a Protocol Biopsy Needed in a Liver Recipient?</td>
<td>Suk Kyun Hong</td>
</tr>
</tbody>
</table>

### KAHBPS-KLTS Joint Symposium. Diagnosis and Management of Combined Hepatocellular Carcinoma (HCC) and Cholangiocellular Carcinoma (CCC)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Point of View of Combined HCC and CCA: What is the Origin and Diagnostic Criteria of Combined HCC and CCA?</td>
<td>Young Nyan Park</td>
</tr>
<tr>
<td>Contents</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Imaging Features of Combined HCC and CCC: What Is the Difference Compared with HCC or CCC?</td>
<td>85</td>
</tr>
<tr>
<td>Chang-Hee Lee</td>
<td></td>
</tr>
<tr>
<td>Surgical Treatment and Prognosis of Combined HCC and CCC</td>
<td>87</td>
</tr>
<tr>
<td>Ryusei Matsuyama, Yasuhiro Yabushita, Yuki Homma, Takefumi Kunamoto, Itaru Endo</td>
<td></td>
</tr>
<tr>
<td>Issues of Combined HCC and CCC in Liver Transplantation</td>
<td>88</td>
</tr>
<tr>
<td>Young Seok Han</td>
<td></td>
</tr>
<tr>
<td><strong>KLTS Special Lecture</strong></td>
<td></td>
</tr>
<tr>
<td>Donation after Circulatory Death Liver Procurement in Real Practice</td>
<td>90</td>
</tr>
<tr>
<td>Koji Hashimoto</td>
<td></td>
</tr>
<tr>
<td><strong>KLTS Symposium 2. Use of Donation after Circulatory Death to Overcome the Decrease of Brain Death Donor (K%)</strong></td>
<td></td>
</tr>
<tr>
<td>Current Status and Problems of Organ Donation in Korea</td>
<td>92</td>
</tr>
<tr>
<td>Won-Hyun Cho</td>
<td></td>
</tr>
<tr>
<td>Current Status of Liver Allocation System</td>
<td>93</td>
</tr>
<tr>
<td>Jae Geun Lee</td>
<td></td>
</tr>
<tr>
<td>Institutional Issue and Limit of Donation after Cardiac Death</td>
<td>94</td>
</tr>
<tr>
<td>Dong-Sik Kim</td>
<td></td>
</tr>
<tr>
<td><strong>KASL-KLTS Joint Symposium: Hepatorenal Syndrome (HRS) (K%)</strong></td>
<td></td>
</tr>
<tr>
<td>HRS: Definition, Pathophysiology, and Medical Management</td>
<td>96</td>
</tr>
<tr>
<td>Yeon Seok Seo</td>
<td></td>
</tr>
<tr>
<td>When to Consider Simultaneous Liver Kidney and How to Prevent Adverse Renal Outcome after Liver Transplantation</td>
<td>100</td>
</tr>
<tr>
<td>Jae Min Chun</td>
<td></td>
</tr>
<tr>
<td>MELD Purgatory in HRS and Allocation Policy: When to Start Renal Replacement Therapy?</td>
<td>102</td>
</tr>
<tr>
<td>Shin Hwang</td>
<td></td>
</tr>
<tr>
<td>When to Start Renal Replacement Therapy for Hepatorenal Syndrome</td>
<td>103</td>
</tr>
<tr>
<td>Hye Ryoun Jang</td>
<td></td>
</tr>
<tr>
<td><strong>KLTS Coordinator Session (K%)</strong></td>
<td></td>
</tr>
<tr>
<td>Recovery Management for Old Age Recipient</td>
<td>106</td>
</tr>
<tr>
<td>Man Ki Ju</td>
<td></td>
</tr>
<tr>
<td>Transplantation Counseling for an Elderly Liver Transplantation Patient</td>
<td>107</td>
</tr>
<tr>
<td>Myung Sook Kim</td>
<td></td>
</tr>
<tr>
<td>Acute Liver Failure</td>
<td>108</td>
</tr>
<tr>
<td>Dong Jin Joo</td>
<td></td>
</tr>
<tr>
<td>Patient Management after Liver Transplantation</td>
<td>110</td>
</tr>
<tr>
<td>Seung Heui Hong</td>
<td></td>
</tr>
<tr>
<td><strong>KLCA Symposium 1. A Developing Strategy to Improve Diagnosis of HCC</strong></td>
<td></td>
</tr>
<tr>
<td>Surveillance for HCC in Patients with Non-Alcoholic Fatty Liver Disease</td>
<td>114</td>
</tr>
<tr>
<td>Vincent Wong</td>
<td></td>
</tr>
<tr>
<td>Are Emerging Biomarkers and Imaging Tools Better than Routine Abdominal Sonography for HCC Surveillance?</td>
<td>115</td>
</tr>
<tr>
<td>Do Young Kim</td>
<td></td>
</tr>
<tr>
<td>Is LI-RADS Better for Diagnosis of HCC?</td>
<td>117</td>
</tr>
<tr>
<td>Jeong Min Lee</td>
<td></td>
</tr>
</tbody>
</table>
## KLCA General Meeting (K)

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>0202 Liver Cancer Day Special Lecture</td>
<td>120</td>
</tr>
<tr>
<td>Hyun Woong Lee</td>
<td></td>
</tr>
</tbody>
</table>

## LCSGJ-KLCA Joint Symposium 1. One Step Forward for Understanding Basic Knowledge

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential of Exosome-Carrying microRNAs in Liquid Biopsy</td>
<td>124</td>
</tr>
<tr>
<td>Takahiro Ochiya</td>
<td></td>
</tr>
<tr>
<td>T Cell Based Adoptive Cell Therapy for Solid Cancers</td>
<td>125</td>
</tr>
<tr>
<td>Tatsuki Kawakami</td>
<td></td>
</tr>
<tr>
<td>Oncolytic Virus-Based Therapy for HCC</td>
<td>126</td>
</tr>
<tr>
<td>Jeong Heo</td>
<td></td>
</tr>
</tbody>
</table>

## LCSGJ-KLCA Joint Symposium 2. Similarities and Differences in Treatment of HCC

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent Trends of Treatment for Intermediate Stage HCC: Japanese Experience</td>
<td>128</td>
</tr>
<tr>
<td>Masatoshi Kudo</td>
<td></td>
</tr>
<tr>
<td>Recent Trends of Treatment for Intermediate Stage HCC: Korean Experience</td>
<td>129</td>
</tr>
<tr>
<td>Ji Hoon Kim</td>
<td></td>
</tr>
<tr>
<td>Recent Trends of Treatment for Advanced Stage HCC: Japanese Experience</td>
<td>130</td>
</tr>
<tr>
<td>Kazumi Uekiya</td>
<td></td>
</tr>
<tr>
<td>Recent Trends of Treatment for Advanced Stage HCC: Korean Experience</td>
<td>131</td>
</tr>
<tr>
<td>Won Young Tak</td>
<td></td>
</tr>
</tbody>
</table>

## KLCA Symposium 2. New and Emerging Systemic Therapies in Advanced HCC

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Line Treatments for HCC</td>
<td>134</td>
</tr>
<tr>
<td>Arndt Vogel</td>
<td></td>
</tr>
<tr>
<td>Second Line Treatments for HCC</td>
<td>135</td>
</tr>
<tr>
<td>Stephen L. Chan</td>
<td></td>
</tr>
<tr>
<td>A Future of Systemic Agents: Emerging Therapies and Strategies</td>
<td>136</td>
</tr>
<tr>
<td>Baek-Yeol Ryoo</td>
<td></td>
</tr>
<tr>
<td>Combination of Interventional and Systemic Therapies for HCC: Current Status and Future Direction</td>
<td>137</td>
</tr>
<tr>
<td>Joong-Won Park</td>
<td></td>
</tr>
</tbody>
</table>

## DAY 3 Saturday, June 22, 2019

### Symposium 3. Hepatitis C Virus

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-Term Outcome of Direct-Acting Antiviral Treatment</td>
<td>140</td>
</tr>
<tr>
<td>Jung Il Lee</td>
<td></td>
</tr>
<tr>
<td>Follow-Up Strategies Following Cure of Hepatitis C Virus Infection</td>
<td>142</td>
</tr>
<tr>
<td>Natsya Sakamoto</td>
<td></td>
</tr>
<tr>
<td>Unmet Needs in the Era of Direct-Acting Antiviral Therapy</td>
<td>143</td>
</tr>
<tr>
<td>Xinyang Li</td>
<td></td>
</tr>
</tbody>
</table>

### State-of-the-Art Lecture 2

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Understanding of Autoimmune Liver Diseases</td>
<td>146</td>
</tr>
<tr>
<td>Atsushi Tanaka</td>
<td></td>
</tr>
</tbody>
</table>
## Contents

### Symposium 4. Cirrhosis

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesenchymal Stem Cell Therapy for Liver Cirrhosis - Basic Study and Clinical Application</td>
<td>150</td>
</tr>
<tr>
<td>Shuji Terai</td>
<td></td>
</tr>
<tr>
<td>The Role of Albumin Related with Systemic Inflammation in Cirrhosis</td>
<td>151</td>
</tr>
<tr>
<td>Paolo Angelé</td>
<td></td>
</tr>
<tr>
<td>Role of Cytoglobin, a Novel Radical Scavenger in Stellate Cell Activation and Hepatic Fibrosis</td>
<td>152</td>
</tr>
<tr>
<td>Norihumi Kawada</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS Symposium 1. Surgical Research in HBP Field – Challenges and Barriers

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgeon-Scientists: An Endangered Species?</td>
<td>154</td>
</tr>
<tr>
<td>Sundeep G. Keswani</td>
<td></td>
</tr>
<tr>
<td>Basic/Translational Research: How to Start and Grow?</td>
<td>155</td>
</tr>
<tr>
<td>Soy-June Kim</td>
<td></td>
</tr>
<tr>
<td>Clinical Research to Reduce Pancreatic Fistula after Distal Pancreatectomy</td>
<td>156</td>
</tr>
<tr>
<td>Masayuki Kawagoe, Seiko Hirono, Kumi Kikada, Motoshi Miyazawa, Kyo Kitahara, Ryohin Kobayashi, Masaki Uema, Shinya Nagami, Miki Yamazaki</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS Symposium 2. Clinical Issues in Non-Hepatic Abdominal Surgery in Patients with Liver Cirrhosis

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of Gallstones and Acute Cholecystitis in Patient with Liver Cirrhosis</td>
<td>158</td>
</tr>
<tr>
<td>- Medical Treatment: Indication and Result of Medical Treatment</td>
<td></td>
</tr>
<tr>
<td>KI Tae Suk</td>
<td></td>
</tr>
<tr>
<td>Management of Gallstones and Acute Cholecystitis in Patient with Liver Cirrhosis</td>
<td>161</td>
</tr>
<tr>
<td>- Surgical Treatment: What Should We Caution to Consider Surgery?</td>
<td></td>
</tr>
<tr>
<td>Shang Yu Wang</td>
<td></td>
</tr>
<tr>
<td>Clinical Outcomes and Prognosis of Emergency Surgery in Liver Cirrhosis Patient</td>
<td>162</td>
</tr>
<tr>
<td>Fausto Catena</td>
<td></td>
</tr>
<tr>
<td>Elective Cancer Surgery in Patients with Liver Cirrhosis</td>
<td>163</td>
</tr>
<tr>
<td>Sae Byol Choi</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS Special Lecture

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Journey from Scientific Idea to Funded Grant: A Surgeon's Approach</td>
<td>166</td>
</tr>
<tr>
<td>Sundeep G. Keswani</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS Symposium 3. Focus Review of Advanced Gallbladder Cancer Treatment (*K)

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Operative Indication of Advanced Gallbladder Cancer: How Much Advance Is the Limitation?</td>
<td>168</td>
</tr>
<tr>
<td>Masayuki Ohnoke, Hideyuki Yoshimi, Katsunori Furukawa, Tsukasa Takeshita, Satoshi Kuboki, Shigetsugu Takano</td>
<td></td>
</tr>
<tr>
<td>Recent Advances in the Chemotherapy in Advanced Gallbladder Cancer: Palliative vs. Neoadjuvant Chemotherapy</td>
<td>169</td>
</tr>
<tr>
<td>Hei-Chul Jeong</td>
<td></td>
</tr>
<tr>
<td>Case Presentation</td>
<td>170</td>
</tr>
<tr>
<td>Oh-Young Jeong</td>
<td></td>
</tr>
</tbody>
</table>

### Special Session. National Health Insurance Big Data Research (*K)

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Health Insurance Big Data Analysis: Process and Example</td>
<td>172</td>
</tr>
<tr>
<td>Seong Yong Park</td>
<td></td>
</tr>
<tr>
<td>National Health Insurance Big Data Research: HCC Surveillance</td>
<td>173</td>
</tr>
<tr>
<td>Yong-Han Park</td>
<td></td>
</tr>
<tr>
<td>Role of Statins on Development and Progression of Non-Alcoholic Fatty Liver Disease: A Nationwide Nested Case-Control Study</td>
<td>174</td>
</tr>
<tr>
<td>Jung Il Lee, Hyun Woon Lee, Kwan Sik Lee, Nye San Lee, Ju-Young Park</td>
<td></td>
</tr>
</tbody>
</table>

www.theliverweek.org  xxiii
### Common Concerns: Hepatologists and Surgeons (*K*)

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of Surgical Risk in Patients with Cirrhosis</td>
<td>180</td>
</tr>
<tr>
<td>Ki Tae Yoon</td>
<td></td>
</tr>
<tr>
<td>Determination of Preoperative Liver Function and Extent of Resection</td>
<td>183</td>
</tr>
<tr>
<td>Bong-Wan Kim</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis of Hepatitis B Virus Reactivation after Liver Transplantation</td>
<td>184</td>
</tr>
<tr>
<td>Jae Hyun An</td>
<td></td>
</tr>
<tr>
<td>Optimal Hepatitis C Virus Treatment Strategy for Patients Waiting for Liver Transplantation</td>
<td>185</td>
</tr>
<tr>
<td>Ih Hee Kim</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS-KLTS-KLCA Joint Symposium 1. Unresolved Issues in HCC: Medical and Interventional Radiology

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant Therapy after Curative Treatment: Enough or Still Lacking?</td>
<td>196</td>
</tr>
<tr>
<td>Su Jong Yu, Yun Bin Lee, Eun Ju Cho, Jeong Hoan Lee, Yoon Jun Kim, Jung Hwan Yoon</td>
<td></td>
</tr>
<tr>
<td>Direct Acting Antiviral and HCC in Chronic Hepatitis C: Friend or Foe?</td>
<td>197</td>
</tr>
<tr>
<td>Hyung Joon Kim</td>
<td></td>
</tr>
<tr>
<td>How to Overcome Long-Term Decline in Survival of HCC Patients Treated with Ablation</td>
<td>199</td>
</tr>
<tr>
<td>Shuichiro Shiina</td>
<td></td>
</tr>
</tbody>
</table>

### KAHBPS-KLTS-KLCA Joint Symposium 2. Unresolved Issues in HCC: Surgical and Radiation Oncology

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will Laparoscopic Approach Be Almighty Weapon in Surgery of HCC?</td>
<td>202</td>
</tr>
<tr>
<td>Jong Man Kim</td>
<td></td>
</tr>
<tr>
<td>Priority Policy for Patients with HCC Awaiting Liver Transplantation: Unresolved Issue?</td>
<td>204</td>
</tr>
<tr>
<td>Dorry L. Segev</td>
<td></td>
</tr>
<tr>
<td>Radiation Therapy for Early HCC: Will It Be a Good Option in Practice?</td>
<td>205</td>
</tr>
<tr>
<td>Sang Min Yoon</td>
<td></td>
</tr>
</tbody>
</table>

### Asian Forum: Korea-Japan-Taiwan

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Status and Emerging Issues in Liver Diseases in Japan</td>
<td>208</td>
</tr>
<tr>
<td>Hayato Hikita</td>
<td></td>
</tr>
<tr>
<td>Current Status and Emerging Issues in Liver Diseases in Taiwan</td>
<td>210</td>
</tr>
<tr>
<td>Chun-Jen Lu</td>
<td></td>
</tr>
<tr>
<td>Current Status and Emerging Issues in Liver Diseases in Korea</td>
<td>211</td>
</tr>
<tr>
<td>Yoon Jun Kim</td>
<td></td>
</tr>
<tr>
<td>Cirrhotic Portal Hypertension: From Arterial Vasodilatation to Systemic Inflammation</td>
<td>212</td>
</tr>
<tr>
<td>Han-Cheh Lin</td>
<td></td>
</tr>
</tbody>
</table>

### USG Session 1. Upgrading the USG Education (*K*)

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Status of Ultrasonography Education Program and Ultrasonography Specialist Certificates of KASL</td>
<td>214</td>
</tr>
<tr>
<td>Hyung Joon Yim</td>
<td></td>
</tr>
<tr>
<td>How Do I Teach Abdominal USG for Trainee?</td>
<td>215</td>
</tr>
<tr>
<td>Yun Soo Kim</td>
<td></td>
</tr>
<tr>
<td>How to Perform Contrast-Enhanced USG: Experiences in Japan</td>
<td>219</td>
</tr>
<tr>
<td>Fumio Moriyasu</td>
<td></td>
</tr>
</tbody>
</table>
Contents

USG Session 2. Diversifying the Field of USG for Training (*K)

Setting-Up an Abdominal USG Facility and Training Program ................................................................. 222
In Hee Kim

Tips for Selection and Maintenance of USG Machines ................................................................................. 227
Hyun Joo Kim, Han Jong Yu

Assessment of Hepatic Fibrosis with 2-dimensional Real-Time Shear Wave Elastography (SWE) .............. 228
Joo Hyun Sohn

How to Improve Precision in Targeting Focal Lesion ................................................................................ 236
Shuichiro Shiina

New Insight for Lower Abdomen and Kidney USG ...................................................................................... 237
Seong Sook Hong

Present and Future of National Health Insurance System for USG: What Do We Need to Prepare for? .............................................................. 241
Hong Soo Kim

USG Trainee Session (*K)

How to Utilize the Various Functions of USG Machine ................................................................................. 244
Moon Young Kim

Basic Liver Scanning and Key Findings ........................................................................................................ 254
Jeong Eun Song

Pancratobiliary USG Scanning Made Easy .................................................................................................. 260
Soon Sun Kim
Plenary Session 1

PS 1-1 The Discontinuation of Nucleos(t)ide Analogue Treatment Is Not Associated with Higher Risk of HBsAg-Seroreversion after Antiviral-Induced HBsAg-Seroclearance: A Multicenter Cohort Study

PS 1-2 Gender Differences in the Association of Adipose Tissue and Sarcopenia in Patients with Cirrhosis

PS 1-3 Ephrin-A3 (EFNA3) Is a Key Player in Hypoxic Microenvironment of Hepatocellular Carcinoma

PS 1-4 Individualized Optimization of Posttransplant Hepatitis B Prophylaxis with Hepatitis B Immunoglobulin Using Half-Life Simulation

Plenary Session 2

PS 2-1 Novel SNPs for Screening of Nonalcoholic Fatty Liver Disease: A Korean Population-Based Study

PS 2-2 Statin Use and the Risk of Hepatocellular Carcinoma in Patients with Chronic Hepatitis B

PS 2-3 Robotic Major Liver Resections: Surgical Outcomes Compared with Open Major Liver Resections

PS 2-4 Early Reduction of Regulatory T Cells by Calcineurin Inhibitor Is Associated with Acute Rejection in Liver Transplantation

Free Paper Session

1. HBV

O-001 Regular Follow-Up and Mortality in Patients with Chronic Hepatitis B: A National Health Insurance Cohort Study

O-002 Bone and Renal Safety Improvements in CHB Patients Switched to Tenofovir Alafenamide (TAF) after Tenofovir Disoproxil Fumarate (TDF) Treatment

O-003 A Phase 3, Stable Switching from Tenofovir Disoproxil Fumarate (TDF) to Tenofovir Alafenamide (TAF) in Chronic Hepatitis B (CHB) Patients: 48w Results

O-004 Tenofovir Disoproxil Fumarate Directly Regresses Liver Fibrosis by Inducing Hepatic Stellate Cell Apoptosis

O-005 Risk of Hepatocellular Carcinoma in Patients with Immune-Tolerant Chronic Hepatitis B

O-006 Detection of HBV Integration in the Human Genome Using High-Throughput Targeted Sequencing

2. ALD & NAFLD

O-007 Incidence and Risk Factors Analysis of Liver Cancer in Patients with Alcoholic Liver Disease: Retrospective Cohort Analysis of 5,160 Patients

O-008 Algorithms Using Noninvasive Tests Can Accurately Identify Patients with Advanced Fibrosis Due to NASH: Data from the STELLAR Clinical Trials

xxvi June 20-22, 2019 | BEXCO, Busan, South Korea
6. Liver Cancer

O-031  Tumor Marker-Based Characterization of Patients with Intermediate-Stage Hepatocellular Carcinoma Deemed to Have a Grave Prognosis ................................................................. 298

O-032  Hepatocyte-Specific MRI-Based Assessment of Indeterminate Hepatic Nodules in the Liver Transplant Evaluation of Cirrhotic Patients ................................................................. 298
  Ha Il Kim Jong Seok Kang, Jun Jong Park, Dong Young Park, Sang Hoon Ahn, Kwang-Hyub Han, Cheol-Hyung Lee, Jun Hyuk Kang, Joong-Won Park, Minjong Lee, Bo Hyun Kim

O-033  Response to Sorafenib in Patients with Advanced Hepatocellular Carcinoma: Predictive Analytics Using Machine Learning with a Neighborhood-Group Detection Method ................................................................. 299
  Jun Hyuk Kang, Jeong-Won Park, Minjong Lee, Bo Hyun Kim

O-034  A Multi-National, Multi-Institutional Study of Comparing an Efficacy of Stereotactic Body Radiation Therapy and Radiofrequency Ablation for Hepatocellular Carcinoma ................................................................. 299
  Nalee Kim, Jason Cheng, Wen-Yen Huang, Tamaki Kimura, Victor Hie Lee, Zhao Cheng Zeng, Chul Seong Kay, Jinal Seong

O-035  Practice Patterns, Radiologic Tumor Response, and Deterioration of Liver Function after Transarterial Chemoembolization (TACE): Final Analysis of OPTIMIS in Korea and Rest of Asia ................................................................. 300
  Jeong Hee Ann-Liu Cheng, Jean-Luc Raul, Markus Pertk-Radosavljevic, Masatoki Kudo, Keiko Nakajima, Inga Bay, Sh-Ming Lin, Nan Chu Lee

O-036  Distinct Mutational and Molecular Patterns Associated with Family History in Hepatocellular Carcinoma ................................................................. 301
  Jeong An, J-Hye Oh, Ho Y Kim, Seheon Chang, Chang-Duk Song, Nam Chu Lee, Ju Hyun Shin

7. Surgery, Biliary

O-037  Management of Pancreaticojejunostomy Stricture after Pancreaticoduodenectomy ................................................................. 301
  Xu'an WANG, Wenge Wang, Hao WANG, Xueping ZHOU, Liang CHEN, Xuefeng WANG, Yingbin LIU

O-038  A Inverted Mattress Technique of Pancreaticojejunostomy for Laparoscopic Pancreatoduodenectomy ................................................................. 301
  Hyung Jun Kwon, Sang Goo Kim, Yun Jin Hwang

O-039  New Onset Diabetes and Reduction of Pancreatic Volume in Laparoscopic versus Open Pancreatoduodenectomy ................................................................. 302
  Sung Hoon Cho

O-040  Preoperative Serum Glucose to Lymphocyte Ratio as an Independent Prognostic Factor: Developing 3-Scored Survival Estimating System in Resected Pancreatic Ductal Adenocarcinoma ................................................................. 302
  Incheon KANG, Chang Moi KANG

O-041  Development and Validation of a Novel Topical Agent for Gallstone Dissolution ................................................................. 303
  Say-June KIM, Kee Hwan KIM

O-042  Robotic Surgery for Gall Bladder Cancer: Operative Technique and Early Outcomes ................................................................. 303
  Shedada Fatouk, Kunal Khandogar, Sagar Kurunkar, Mahesh Goel, Ragopal Acharya

O-043  Laparoscopic Pancreatoduodenectomy: CUSUM Analysis in a Developing Single Surgeon ................................................................. 303
  Jung Hwa Lee, Dong Hyun Kim, Jung Y Kim, Nae Young Kim, Jung Ho Park

O-044  Upfront vs. Delayed Laparoscopic Assisted Necrosectomy for Infected Pancreatic Necrosis ................................................................. 304
  Feng CAO, Fei LI
## Contents

### 8. Surgery, Technical Issues

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-045 Parietal Peritoneum as an Autologous Substitute for Middle Hepatic Vein Reconstruction during Living-Donor Liver Transplantation</td>
<td>304</td>
</tr>
<tr>
<td>Byun, Eun Yeon, Do-Sun Lim, Kwan Soo Byun, Soon Ho Um</td>
<td></td>
</tr>
<tr>
<td>O-046 Prospective Multicenter Study for Robotic Anatomic Major Liver Resection</td>
<td>304</td>
</tr>
<tr>
<td>Han, Dal Hoeon, Han, Sung Hoan CHO, Jin Ho Lee, Gi Hon CHO, Yoo Ki Cho, Jin Hoon LEE</td>
<td></td>
</tr>
<tr>
<td>O-047 Selective Occlusion of the Hepatic Artery and Portal Vein Improves Liver Hypertrophy for Staged Hepatectomy</td>
<td>305</td>
</tr>
<tr>
<td>Na, Changku</td>
<td></td>
</tr>
<tr>
<td>O-048 The Anatomical Characteristics of Patients with Posterior Bile Duct Stricture after a Liver Resection Including Anterior Section</td>
<td>305</td>
</tr>
<tr>
<td>Kim, Kyung Chul YOON, Woo-Hyoung KANG, Hye-Sung KOO, Dong-Won YU, Dong-Sik KIM</td>
<td></td>
</tr>
<tr>
<td>O-049 Clinical Outcomes of Laparoscopic Living Donor Right Hepatectomy without Pringle's and Hanging Maneuver</td>
<td>305</td>
</tr>
<tr>
<td>Han, Young Seok HAN, Ja Ryung HAN, Heon Tak HA, Jin Min CHUN, Yoon Jin HWANG</td>
<td></td>
</tr>
<tr>
<td>O-050 Right and Ventral Margins of Para-caval Portion of Caudate Lobe: Studies from Cadaveric Dissection and 3D Reconstruction</td>
<td>306</td>
</tr>
<tr>
<td>Byun, Xue-Yin SHI, Sang-Heon HONG, Xu-Guang HU, Mi-Na KIM, Bong-Wan KIM, Hee-Jung WANG</td>
<td></td>
</tr>
<tr>
<td>O-051 Short Term Result of Parenchymal Sparing Anatomical Liver Resection Based on Portal Ramification of the Right Anterior Section: A Single Center Experience</td>
<td>306</td>
</tr>
<tr>
<td>Byun, Giang NGUYEN, Anh PHAM, Ho NGIEM, Hung NGUYEN, Duc PHAM</td>
<td></td>
</tr>
<tr>
<td>O-052 Improved Outcomes of Laparoscopic Liver Resection for Hepatocellular Carcinoma Located in Posterosuperior Segments of the Liver</td>
<td>307</td>
</tr>
<tr>
<td>Kim, Yujin Kwon, Jin Young CHO, Ho-Seung KIM, Yoo-Seek YOON, Young Rok Choi, Bum-A Lee</td>
<td></td>
</tr>
</tbody>
</table>

### 9. ALD & NAFLD

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-053 Combinatorial Effect of Etizimibe and Empagliflozin on NAFLD in Choline Deficient High Fat Diet-Induced Murine Model</td>
<td>307</td>
</tr>
<tr>
<td>Byun, Dong YUN, Kim, Kyu Sik CHANG, Chun, Heon Young GEE, Jun Yong Park</td>
<td></td>
</tr>
<tr>
<td>O-054 Nicotinamide Riboside Does Not Attenuate Steatosis but Improve Inflammation in Non-Alcoholic Steatohepatitis Induced by Methionine-Choline Deficient Diet</td>
<td>308</td>
</tr>
<tr>
<td>Lee, Soon Sun, Kim, Hye Eun BURAN, Jung Min KIM, Eun Jung WOO, Chun, JIN HEE CHEONG, Young Hwan ALRE, Hye Jung CHA, Young Sun, AND JONG Won CHO</td>
<td></td>
</tr>
<tr>
<td>O-055 PNPLA3 Genetic Polymorphisms Associated with the Development of Non-Alcoholic Fatty Liver Disease in Korea Biobank Network</td>
<td>308</td>
</tr>
<tr>
<td>Byun, Sooyeon, Oh, Keong Won HONG, Eun JI CHANG, Seong Gu HuNG, Joo Ho Lee, Sang Woon Cho</td>
<td></td>
</tr>
<tr>
<td>O-056 Gut-Microbiome Taxonomic Profiling as Non-Invasive Biomarkers for the Early Detection in Alcoholic Hepatocellular Carcinoma</td>
<td>309</td>
</tr>
<tr>
<td>Byun, Hanjiyou Gupta, Min, Jeon Shin, Gui Soo Yoon, Sang Jun Yoon, Dae Hee PARK, Nayeong Lee, Dong Joong Kim, Ki Tae Suk</td>
<td></td>
</tr>
<tr>
<td>O-057 Serum MFG-E8 Level as a Potential Biomarker for the Evaluation and Prediction of the Metabolic Syndrome</td>
<td>310</td>
</tr>
<tr>
<td>Byun, Han Ah Lee, Hyung Won Hong, Jong Seok KIM, Young Ji CHANG, Jun Young Park, Ki-Tae Yoo</td>
<td></td>
</tr>
<tr>
<td>O-058 Long-Term Risk of a Non-alcoholic Fatty Liver after Tamoxifen Use in Breast Cancer: Propensity Score Matching Analysis</td>
<td>310</td>
</tr>
<tr>
<td>Byun, Jeong-Joo Lee, Sang Gyuane Kim, Young Seok Kim, Seong Min Jeong, Jae Young Jang, Jang Min Hwan, Hong Soo Kim, Bae Suk Gyoo, Jae Yong Kim, Jeon Jhin Cheon</td>
<td></td>
</tr>
<tr>
<td>O-059 Combined Use of Rosuvastatin and Etizimibe Improves Hepatic Steatosis in Patients with Dyslipidemia</td>
<td>310</td>
</tr>
<tr>
<td>Byun, Won Dong Lee, Beom Kyung KIM, Jae Yong Park, Do Yong Kim, Sang Hoon ALRE, Ki-Yong Hyub HAN, Seung Up KIM</td>
<td></td>
</tr>
<tr>
<td>O-060 Weight Change and Resolution of Fatty Liver in Normal Weight Individuals with Non-Alcoholic Fatty Liver Disease</td>
<td>311</td>
</tr>
<tr>
<td>Byun, Joo Hyun CHI, Tae Jin KIM, Dong-Hyun SHIN, Danhee KANG, Soo In CHO, Seung Woon Park, Dae Sung KOO, Jhee Lee, Geun-Youn Guak</td>
<td></td>
</tr>
</tbody>
</table>

### 10. Liver Transplantation

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-061 Risk Factors for Long-Term Mortality in Live Liver Donors</td>
<td>312</td>
</tr>
<tr>
<td>Byun, Suk Kyun HWONG, Sunho CHO, Nam-Ioon YI, Ansum SHIN, Eun-Kyung CHOE, Kyung Chul YOON, Jae-Hyung CHO, Jeong-Moo LEE, Kwang-Woong LEE, Kyung-Suk SHIN</td>
<td></td>
</tr>
<tr>
<td>O-062 Gene Expression of STAT3 and IL-17-Pathway Decrease in Tolerance Patients Compared to Non-Tolerance after Tapering Immunosuppressants in Liver Transplantation</td>
<td>312</td>
</tr>
<tr>
<td>Byun, Soon Kye Lee, Jung Young CHOI, Jung Hyun KWAN, Jung Won JANG, Chang Woak MIN, SI Hyeon BAE, Seung Kwee YOON, Ho Jeong CHOI, Young Kyung YOI, Dong Geom KIM, Mi-La CHOI</td>
<td></td>
</tr>
<tr>
<td>O-063 Silent Allograft Fibrosis in 10-Year Post-Transplantation Histology of Pediatric Liver Transplantation: Is It Really Silent?</td>
<td>313</td>
</tr>
<tr>
<td>Byun, Jaeso RHL, Suki KOO LEE, Sanghoon LEE, Jong Eun KIM, Gyu Seong CHOE, Jee-Wan XOH</td>
<td></td>
</tr>
<tr>
<td>O-064 Clinical Features and Prognosis of DILBS (Diffuse Intrahepatic Biliary Stricture) after Adult ABO-Incompatible Living Donor Liver Transplantation</td>
<td>313</td>
</tr>
<tr>
<td>Byun, Jae Hyun KIM, Gi-Won SONG, Shin NHANG, Ki Hun KIM, Chul Soo AHN, Deok-Bang MOON, Tae Yong HA, Dong-Hwan JUNG, Gi-Chun PARK, Young-In YOON, Hwa-Dong CHOI, Yong-Kyu CHANG, Sang-Hyun KANG, I-S JEONG, Jin Ho CHOI, Sung Guy LEE</td>
<td></td>
</tr>
</tbody>
</table>
0-065  Impact of the Baseline Anti-A/B IgG Titer on the Clinical Outcome in ABO-Incompatible Liver Transplantation  ................................................................. 313
   Juhan Lee, Deok Geon Kim, Jeon Yoon Lee, Seok Jong Yang, Jae Geon Lee, Myoung Soo Kim, Soon Il Kim, and Dong Jin Joo

0-066  Comparative Analysis of Bile Microbiology and Antibiotic Susceptibilities between Liver Transplant Recipients and Normal Population: Multicenter Cohort Study ................................................................. 314
   Suk-Won Suh, Seung Eun Lee, Yoo-Shin Choi, YoungRok Choi, JaeHyeong Jeong

11. HBV

0-067  Dynamics of Transient Elastography-Based Risk Prediction Model for Hepatocellular Carcinoma during Antiviral Therapy in Patients with Chronic Hepatitis B: A Nation-Wide Multi-Center Retrospective Cohort Study ........................................................................................................ 314
   Hyo Joon Chun, Yeon Seok Seo, Young Il Lee, Byung Suk Kim, Byoung Kuk Jung, Sang Gyu Lee, Ki Tae Suk, In Hee Kim, Jin-Woo Lee, Moon Young Kim, Seong Won Jeong, Han Ah Lee, Sun Young Yi, Soon Ho Uhn, Hwan Woong Lee, Kwan Sik Lee, Jeong Eun Song, Chang Hyang Lee, Won Hyung Chung, Jae Seok Hwang, Jeong Soo Hwa, Young Seok Kim, Dong Joon Kim, Chang Hun Lee, Jung Ho Yu, Young Eun Cho, Jeong Yung Ho, Mi Na Kim, Jo Ho Lee, Seong Gyu Haeng, Seong Hee Jung, Soon Koo Bak, Jae Young Jung, Sang Jun Suh, Young Kuk Jung, Beom Kun Jung, Jun Yang Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Hwan Joon Yi, and Seung Up Kim

0-068  Increased Clinical and Economic Burden of Chronic Hepatitis B (CHB) Patients Compared to Non-CHB from 2007 to 2016 in Korea .................................................................................................................. 315
   Dae Won Jun, Hyoung Oh, Hyun Jung Ahn, Boo Il Kim, Mindie H. Nguyen

0-069  Comparison of Tenofovir and Entecavir on the Risk of Hepatocellular Carcinoma and Liver-Related Events in Patients with Chronic Hepatitis B: A Propensity Score Analysis ........................................................................................................ 316
   Sung Woon Lee, Jung Hyun Kwon, Han Eun Lee, Sun Hong Yoo, Hee Chul Nam, PI Soo Song, Soon Woo Nam, Si Hyun Bae, Jong Young Choi, Seong Kwee Yoon, Nam Ik Han, Jeong Won Jung

0-070  The Risk of Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Who Received Tenofovir vs. Entecavir Treatment ........................................................................................................ 316
   Terry Cheuk-Fung Yip, Vincent Wai-Sun Wong, Henry Lia-Yuen Chan, Yee Kit Tse, Grace Leung Wai Wong

0-071  Hepatitis B Immunology ......................................................................................................................................................................................... 317
   Ashok Kumar Vyas, Pooja Negi, Sharda Patha, Jaswinder Singh Makas, Shikumar Sarin, Neeraj Verma

0-072  Sustained Response without Nucleos(t)ides after Pegylated Interferon Represent Favorable Outcome: Up to 13 Years Follow-Up .................................................................................................................. 317
   Soon Koo Lee, Jung Hyun Kwon, Jeong Won Jung, Sung Ju Lee, Soon Wook Yi, Si Hyun Bae, Jong Young Choi, Seong Kwee Yoon

12. Liver Cancer, Clinical

0-073  Novel Deep Neural Network-Based Liver Transplantation Criteria for Hepatocellular Carcinoma: A Multicenter Study ................................................................................................................................. 318
   Jong Hee Nam, Jeong-Hoon Lee, Junbae Bae, Young Chang, Yuli Choi, Hwi Young Kim, Dong Hyun Shin, Bo Hyun Kim, Seong Ho Yoon, Nam-Soon Yi, Kwang-Woong Lee, Jong Man Kim, Jong Woon Park, Tae Hun Kim, Yoon Jun Kim, Jung-Hwan Yoon, Jee Won Jo, Kyung-Sa Suh, and Kwon Yoo

0-074  Bioelectrical Impedance Analysis for Predicting Postoperative Complications and Survival after Liver Resection for Hepatocellular Carcinoma .......................................................................................... 319
   Gil Hoon Lee, Hye Jung Cha, Garam Lee, Han Gyoon Kim, Hwi Young Jung, Sang Woon Kim, Mi Young Lee, Jeong Heung Cheong, Young Hwan Ahn, So Young Yi, Choong Kyun Noh, Chul Wan Suh, Jung Eun Eun, Jee Young Cheong, Sung Won Cho, and Soon Sun Kim

0-075  Laparoscopic Resection vs. Percutaneous Radiofrequency Ablation for Small HCC: Comparison of Clinical Outcome ................................................................................................................................. 319
   Dong Ho Lee, Jin Wook Kim, Jeong Min Lee, Jong Man Kim, Chin Wook Lee, Hyoung Hwee, Hyoung Son Suk

0-076  Factors and Models for Predicting Liver-Related Morbidity in Patients Undergoing Hepatic Resection for Hepatocellular Carcinoma ........................................................................................................ 320
   Jonggi Choi, So-Hyun Kim, Seung Hwan Kim, Dae Heum Lee, Ju Hyun Shin, Young Suk Lim, Han Chu Lee, Young Hwa Chung, Sung-Gyu Lee, Sang Gyu Lee, Ki Hun Kim, and Kang Mo Kim

0-077  Regorafenib versus Nivolumab for Hepatocellular Carcinoma Patients Who Experienced Sorafenib Treatment Failure: A Propensity Score Analysis .............................................................................. 320
   Choil-Hyun Lee, Yoon Bin Lee, Minsook Albert Kim, Heejoon Jung, Sun Woong Lee, Eun Ju Cho, Kyung Hoon Lee, Jong Myung Yoo, Ju Sung Yu, Tae Youn Kim, Yoon Jun Kim

0-078  The Effect of Urea Cream on Sorafenib-Associated Hand-Foot Skin Reaction in Patients with Hepatocellular Carcinoma: Multicenter, Prospective Randomized Double-Blind Controlled Study ................................................................................................................................. 321
   Young Sun Lee, J Hoon Kim, Do Young Kim, Moon Young Kim, Hyung Joan Kim, Yoon Seok Seo, Ki Tae Yoon, Jeong Hoon Lee, Hyun Woon Lee, Young Kuk Jung, Hyong Joan Yim, Byoung Jung Kuk, Eun Sun Jung, Jae Young Jung, Sung Bum Cho, Seong Yoon Hwang

13. Cirrhosis & Liver Failure

0-079  Validation of the Updated Version of Korean Stroop Test in the Screening of Minimal Hepatic Encephalopathy ........................................................................................................................................................................ 322
   Eileen L. Yoon, Dae Won Jun, Eun Chul Jung, Jae Yoon Jeong, Do Seon Song, Sang Bang Ahn, Hye Yoon Kim, Sung Eun Kim, Hyeong Su Kim, Seong Won Jeong, Sang Gyu Lee, Tae Hee Lee, Yong Crang Cho

0-080  Validation of Asian Pacific Association for the Study of the Liver Acute-on-Chronic Liver Failure (ACLF) Research Consortium (AARCC) ACLF Score in Korean ACLF Cohort ........................................................................................................................................................................ 322
   Do Seon Song, Hye Yoon Kim, Young Joo Joo, Dong Hyun Sinn, Eileen L. Yoon, Chang Woob Kim, Young Kuk Jung, Ki Tae Suk, Sang Soo Lee, Hwan Hyeong Lee, Hwi Young Kim, Tae Hun Kim, Eun Ji Lee, Hyung Joan Yim, Sung Eun Lee, Sung Won Lee, Jung Hyun Kwon, Seong Hee Jung, Soon Koo Bak, Byung Seok Lee, Jae Young Jung, Jong Il Suh, Hyung Soo Nam, Hyeok Choon Kwon, Young Seok Kim, Sang Gyu Lee, Hwi Bok Chae, Jin Mo Yang, Joo Hyun Sohn, Joon Gil Park, Heon Ju Lee, Yoon Jun Kim, In Hee Kim, Ju Yoon Cho, Min Woo Kim, Sang Yyoung Nam, Won Kim, Dong Soo Kim, on behalf of the Korean Acute-on-Chronic Liver Failure (KACLF) Study Group
Contents

14. Liver Cancer, Clinical

O-085 A Significant Diagnostic Role for Discrimination of Malignancy of Contrast Enhanced Ultrasound for Portal Vein Thrombosis in HCC Patients .......................................................... 325
Yu Ri Shin, Jung Hyun Kwak, Yoon Jung Kim, Sun Ho Lee, Soon Hoo Nam

O-086 Comparison between Stereotactic Body Radiotherapy and Radiofrequency Ablation as First Therapy for Small Hepatocellular Carcinoma .......................................................... 326
Soo Young Chai, Bong Gu Jun, Young Won Kim, Gab Jun Chen, Jeong Jeu Yoo, Sang Gun Lee, Young Seok Kim, Sang-Won Jeong, Jae Young Jung, Hyung Soo Kim, Sang Ho Lee

O-087 Prognostic Factors for Survival in Patients with Hepatocellular Carcinoma Treated by Trans-Arterial Radioembolization.......................................................... 327
Hye Chul Nam, Pil Soo Sung, Jong Won Jang, Ho Jong Chun, Si Hyun Bae, Jong Young Choi, Seung Kew Youn

O-088 Prediction of Overall Survival after Resection or Radiofrequency Ablation Using Surrogates for Clinically Significant Portal Hypertension in Patients with Early Hepatocellular Carcinoma .......................................................... 327
Jae Seok Bae, Dong Hee Lee, Ji Koo Nam

O-089 Clinical Significance of the Thioredoxin System and Thioredoxin Domain Containing Protein Family in Hepatocellular Carcinoma .......................................................... 328
Sang Yeon Cho, Sung Ju Kim, Myung Soo Park, Woo Sun Rou, Seok Hyun Kim, Suk Hyo Eun, Byung Seok Lee

O-090 Contrast-Enhanced Ultrasound with Perfluorobutane for Hepatocellular Carcinoma Surveillance: A Multicenter Diagnostic Trial (SCAN) .......................................................... 328
Ji Hong Park, Mi Suk Joung, So Jung Lee, Won Kyung Jeong, Jae Young Lee, Min Jung Park, Sung Soo Lee, Kyung Hwa Han, Chung Mi Nam, Seong Ho Park, Kyung Ho Lee

15. Liver Cancer, Clinical

O-091 Redeclassification of Microvascular Invasion in Hepatocellular Carcinoma According to Its Anatomical Location .......................................................... 329
Incheon Kang, Gil Hong Choi

O-092 The Clinical Impact of Applying BCLC Guideline for the Treatment of Recurrent Intrahepatic Single and Small Sized Hepatocellular Carcinoma .......................................................... 329
Hyun-Sin Kim, Nam-Joon Yoon

O-093 Chronological Improvement in Long-Term Outcomes of Surgical Resection for Patients with Hepatocellular Carcinoma: Two Large-Volume Center Study .......................................................... 330
Yun Bin Lee, Jeong Hoop Lee, Hyo Young Lee, Cheol-Hyung Lee, Minseok Albert Kim, Heejong Jang, Sun Woong Kim, Suk Kwan Hong, Eun Ju Cho, Su Jong Yu, Nam-Joon Yoon, Kwang-Woong Lee, Jong Man Kim, Je-Won Jo, Yeonjun Kim, Kyung-Suk Suh, Jung Ho Lee

O-094 Is Liver Resection Justified for Multinodular Hepatocellular Carcinoma in Patients with Cirrhosis? A Multicenter Analysis of 1,066 Patients .......................................................... 330
Zhen Li Li, Xian-Hai MAO, Ting-Hao CHEN, Jun Wu GUO, Wei-Min GIU, Ya-Nao ZHOU, Hong WANG, Wan-Guang ZHANG, Timothy M. PAWLIK, Wan Yee LAU, Lei LIANG, Feng SHEN, Tian YANG

O-095 Change in the Recurrence Pattern and Risk Factors over Time after the Complete Cure of Hepatocellular Carcinoma: Ten-Year Follow-Up Study .......................................................... 331
Han Ah Lee, Seung Up Kim, Hyun Gil Goo, Tae Kyung Kim, Sun Young Yim, Young Soon Lee, Sang Jun Shin, Young Kui Jung, Ji Hong Park, Yeon Jeong Seo, Hyung Soo Kim, Hyung Ju Kim, Jang Eun Yoon, Kwang Soon Byun, Soon Ho Um

O-096 Surgical Resection Should Be Considered in Resectable Solitary Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis of Patients with Child A: A Two Large-Volume Center Study .......................................................... 332
Jong Man Kim, Sang Ho Kim, Seo Hae Lee, Gyu-Geun Choi, Jae-Won Jo

16. Basic & Others

O-097 Serine Protease Htra2/Omi Deficiency Impairs Mitochondrial Homeostasis and Promotes Liver Fibrosis .......................................................... 332
Wonhee Hur, Byung-yeon Kang, Sung Min Kim, Gil Won Lee, Min-Kyung Nam, Hyungshik Ram, and Seung Kwe Youn
O-098 Glutamate/mGluR5 Signaling in Stellate Cells Drives Endocannabinoid-Mediated Alcoholic Steatosis
Won-Mook Choi, Myung-Ho Kim, Raoult Cizeron, Bae Gae, Hyuk Soo Eun, Young-Sun Lee, Won-Kim, Gyung-Kun, and Won-D Jeong

O-099 Src Inhibition Attenuates Liver Fibrosis by Downregulating CTGF and Phospho-Smad3
Hye-Young Seo, So-Hye Lee, Ji-Ha Lee, Jae Seok Jang, Myoung-Kim, Byoung-Kuk, and Jang

O-100 Correlation of Infiltration by T Cells and Macrophages with the Severity of Liver Damage in Drug-Induced Liver Injury: Implications in Responsiveness to Steroid Therapy
Hye-Young Seo, P.J. Soo Song, Kwon Yong Tak, Jae Jun Lee, Hye Chul Nam, Jeong Won Jang, Si Hyun Bae, Jung Young Choi, Seung Kew Yoon, Eun Sun Jung, Sang Wook Choi

O-101 Liver Enzyme Variability and the Risk of Heart Diseases and Mortality: A Nationwide Population-Based Study of 6.5 Million Subjects
Eun Ju Cha, Kyung-Soon Han, Dong Wook Shin, Su Jong Yu, Yun Bin Lee, Hyeong-Hoon Lee, Seung-Pyo Lee, Yoon Jun Kim, Jung-Hwan Yoon

O-102 Increased Annual Incidence of Pyogenic Liver Abscess and Its Risk Factors: An Analysis from HIRA-NPS of South Korea, 2012-2016
Jeong-Ju Yoo, Sang-Gyu Jang, Jeong-Soo Park, Seung-Won Lim, Jae Young Jang, Sae Hwan Lee, Hyeong-Soo Kim, Baek Gu Je, Young Don Kim, Gab Jin Cheon

Oral Poster Presentation
ALD & NAFLD

OP-001 Exosomal Double-Stranded RNA Promotes Interleukin-1β Production in Kupffer Cells via Toll-Like Receptor 3 in Alcoholic Liver Injury
Jun-Hee Lee, Young-Ri Shin, Won-Soo Seo, Won-Jeong, Myung-Ho Kim, Il-eun Kim, Tom Ryu, Kangming Yang

OP-002 Gut-Microbiome Composition and Diversity According to the Progression of Alcoholic Liver Disease
G Solo Yuan, Min Jea Shin, Nanpya Gupta, Dae Hee Han, Sang Jun Yoon, Na Young Lee, Dong June Kim, Ki Tae Sook

OP-003 Prospective Association of Soybean Products on the Risk of Non Alcoholic Fatty Liver Disease: A Nationwide Population-Based Study
Youn I Cha, Yun Soo Kim, Oh Sang Kwon, Hyeong-Hoon Lee, Seung Kew Yoon, and Dong Kyun Park

OP-004 Evolution of Hepatic Fibrosis and Steatosis during the Long-Term Use of Metformin in Patients with Type 2 Diabetes
Ji Hye Kim, Hye-Won Lee, Beom Kyung Jun, Chang Park, Do Young Kim, Sang Hoong Ahn, Kwang-Hyun Han, and Seung Up Kim

OP-005 Low Psoas Muscle Mass Is Associated with Advanced Fibrosis in Patients with Biopsy-Proven Non-Alcoholic Fatty Liver Disease
Min Kyu Kang, Jehun Baek, Jung Gil Park, Soon Young Park, Won Young Tak, Young Oh Kweon, Se Young Jang, Yu Rim Lee, Koon Ho

OP-006 Alanine Aminotransferase 37.5% of Metabolic Disease in Metabolically Healthy Population: A Nationwide Claim Data Study
Heejoon Jang, Jeong-Hoon Lee, Seokhun Kim, Si Hyun Bae, Dong Sup Seo, Jong Young Choi, Seung Kew Yoon, and Dong Kyun Park

Basic

OP-007 Valine and Leucine Suppresses Hepatic Stellate Cells Activation via TGF-β Signaling Inhibition
Sung Wael Cho, Jung Hoon Cha, Na-Ri Park, Hee Lim Lee, Jung Young Choi, Seung Kew Yoon, Si Hyun Bae

OP-008 Molecular Diagnosis of Glycogen Storage Disease Type IX Using GSD Gene Panel
Tae Hyung Kim, Kwang Yeon Kim, Moon-Woo Seong, Sung Soo Park, Jin Soo Moon, Jae Sung Koo

OP-009 A Coagulation Factor IX-Deficient Rat as a Translational Pre-Clinical Model of Severe Hemophilia B
Jae Young Lee, Hyeok Bae, Sun-Hyung Joo, Hyeong-Hoon Lee, Kyung-Min Kim, Dong Wook Song, Ungki Kim Goo Jang, Jung Min Lee

OP-010 MicroRNA-101-3p Suppresses Hepatic Stellate Cell Activation and Promotes the Hepatic Differentiation of Human Bone Marrow-Derived Mesenchymal Stem Cells
Jung Hoon Cha, Na-Ri Park, Sung Wael Cho, Jung Young Choi, Seung Kew Yoon, Si Hyun Bae

OP-011 Effect of Sirtuin Peptide in Animal Models of Non-Alcoholic Steatohepatitis (NASH)
Hyen Tae Kang, Na Gyung Choi, Da Won Jun, Jin Hea Park, Dae Hyun Lim, Won-Woo Seo, Ji Hyun Yoo, Jeong-Hoon Lee, Hyeong-Hoon Lee, Chang-Lak Lee, Oh Young Lee, Byung Chul Yoon, and Ho Soo Choi

OP-012 Amino acid Induced Histopathological Changes in the Liver and Other Organs of Albino Rats
Sabita Paudel, Bijay Aryal, Surendra Ramabhadra, Bhikhu Malle

HBV

OP-013 Comparative Ex Vivo Analyses of Hepatitis B Virus-Specific CD8+ T Response between Patients Considered Immune Tolerant and Patients on Antiviral Treatment
P.I Soo Song, Dong Jun Park, Jung-Hee Kim, Ji Won Han, Eun Byul Lee, Gi Woon Lee, Hee Chul Nam, Jeong Won Jang, Si Hyun Bae, Jung Young Choi, Eui-Cheol Shin, So-Hyung Park, Seung Kew Yoon
Contents

OP-014 Extremely Low Risk of Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients with Immune Tolerant Phase: A Multicenter Retrospective Cohort Study .................................................. 344
Soo Young Park, Hyun Woon Lee, Dong Hyun Sim, In Hee Kim, Hyung Joosim, Jeong Woon Yoo, Young Hyun Tak, Young Oh Kwon, Jeong Jee Sung, Ki Joon Jang, Jin Wook Lee, Han Ah Lee, Sung Jin Yim, Soon No Han, Beem Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Youn Seok Seo, Seung Up Kim

OP-015 Three Year Efficacy and Safety of Tenofovir Alafenamide (TAF) Compared to Tenofovir Disoproxil Fumarate (TDF) in Chronic Hepatitis B (CHB) Patients .................................................. 345
Hyung Joosim, Henry Li, Yuan Chang, Young Suk Lim, Wai Kay Walter Sze, Kosh Agarwal, Maria Cecilia R. Brunetto, Hary L.A. Janssen, Rafik Canara, Tatjana Stupancova, Owen Tsang, Hiroshi Tamakoshi, Won Young Tak, Choi Hyun Che, Mustafa Celen, Erinika Sori, John F. Flaherty, Langa Liu, Andrea Cathcart, Anu Gaggar, Calvin Q. Pan, Shalimac, Maria Balu

OP-016 Predictive Score for Hepatocellular Carcinoma after Hepatitis B E Antigen Loss in Patients Treated with Entecavir or Tenofovir Disoproxil Fumarate .................................................. 346
Tae Seok Lim, Hun Woon Lee, Kwan Sik Lee, Jang Hoon Lee, Byung Kuk Kang, Woon Jin Chong, Hyung Joosim, Young Wook Kim, Seung Ok Lee, Soo Teik Lee, and In Hee Kim

OP-017 Establishment of HBV-Replicating Mice Model from a Korean HBV Genome with Defective HBV-Specific T Cell Responses .................................................. 346
Dong Jun Park, Park Soo Sung, Jung Hye Kim, Gil Woon Lee, and Seung Kew Yoon

OP-018 Entecavir versus Lamivudine as Antiviral Prophylaxis for Patients with Hepatitis B Infection Undergoing Anticancer Cytotoxic Chemotherapy: A Randomized, Multicenter Clinical Trial .................................................. 347
Won Kim, Jeong Hee Kim, Bo Hyun Kim, Young Seok Kim, Hae Young Kim, Soheer Oh, Sook Hyang Jeong

Cirrhosis & Liver Failure

OP-019 Low Apoprotein A1 as an Indicator of Poor Prognosis in Patients with Liver Cirrhosis .................................................................................................................. 348
Chang Hun Lee, Hee Chan Yang, Sung Kyun Yim, Seong Young Seo, Sang Hun Kim, Sang Wook Kim, Seung Ok Lee, Soo Teik Lee, and In Hee Kim

OP-020 Adipose Tissue Distribution in Relation to Insulin Resistance in Patients with Cirrhosis .................................................................................................................. 348
Seong Hee Kang, Hyunil Kim, Jin Sook Lee, Soon Koo Bakk, Moan Young Kim

OP-021 Efficacy of Thromboelastography for Predicting Prognosis of Korean Patients with Cirrhosis .................................................................................................................. 349
Tae Hung Kim, Soon Ho Han, Hyun Gil Goh, Han Ah Lee, Sung Young Yim, Young Sun Lee, Sung Jun Suh, Young Ki Jung, Yeon Seok Seo, Joon Hang Kim, Hyung Joosim, Jang Eun Yoon, Kwan Soo Byun

OP-022 Validation of the Animal Naming Test in the Screening of Minimal Hepatic Encephalopathy .................................................................................................................. 349
Eileen L. Yoon, Daee Won Jun, Sung Eun-Chul, Jae Yoon Jeong, Do Seon Song, Sang Bong Ahn, Hee Yeon Kim, Sang Eun Kim, Hyung Ju Sim, Soong Won Jeong, Sang Gyune Kim, Jee Hee Lee, Yong Kyo Cho

OP-023 Direct Bilirubin is More Valuable for Predicting Prognosis in Patients with Liver Cirrhosis .................................................................................................................. 350
Joan Young Jung, Hyun Gil Goh, Han Ah Lee, Tae Hyung Kim, Sung Yoon Sun, Young Sun Lee, Sung Jun Suh, Young Ki Jung, Joon Hang Kim, Yeon Seok Seo, Hyung Joosim, Jang Eun Yoon, Kwan Soo Byun, Soon Ho Han

OP-024 Impact of Relative Adrenal Insufficiency in Alcoholic Hepatitis (RAIAH) .................................................................................................................. 350
Hyunil Kim, Seong Hee Kang, Soon Koo Bakk, Moan Young Kim

HCV

OP-025 Regression of Liver Fibrosis Assessed by Transthyretinraesthesia after Daclatasvir and Asunaprevir Combined Treatment in Patients with Chronic Hepatitis C with Genotype 1b Infection: Prospective Cohort Study (RELIF-C) .................................................................................................................. 351
Hae Won Yoo, Jin Yong Park, Sang Gun Yim, Se Hwan Lee, Young Ki Jung, Moon Young Kim, Daee Won Jun, Jee Young Jung, Jin Wook Lee, Oh Sang Kwon

OP-026 SVR Following Treatment with Direct Acting Antiviral Regimens Is Durable in More than 6,600 Patients: The Gilead SVR Registry Study .................................................................................................................. 351

OP-027 Treatment with Sofosbuvir-Ledipasvir for Patients with HCV Genotype 2 Infection: A Real-World Experience of Six Hospitals in Taiwan .................................................................................................................. 352
Ro-Yuen Chen, Ching-Chu Lu, Ji-You Chen, Chao-Hung Hung, Chii-Yi Chen, Shih-Je Hsu, Kuo-Chih Tseng

OP-028 Substitution Mutations at Cys 316 of NS5B Affect Treatment with Sofosbuvir by Enhancing Replication of Genotype 1b Hepatitis C Virus .................................................................................................................. 352
Yechan Jung, Bora Mo, Hye Jung Park, Hye Woon Lee, Kwang-Hyud Han, Sang Hoon Ahn, and Seongtaek Kim

OP-029 Efficacy and Safety of 8-Weeks of Glecaprevir/Pibrentasvir in Treatment-Naive Adults with HCV Genotype 1-6 and Aspartate Aminotransferase to Platelet Ratio Index (APRI) ≤ 1 .................................................................................................................. 353

OP-030 Efficacy and Safety of Grazoprevir/Elaovlasir for Korean Patients with Chronic Hepatitis C Virus Infection: A Retrospective, Nationwide, Real-World Study .................................................................................................................. 354
Eun Sun Jang, Hyung Ah Kim, Young Seok Kim, In Hee Kim, Byung Seok Lee, Joon Jae Lee, Woo Jin Chung, Sook Hyung Jeong
<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP-032</td>
<td>Clinical Indication and Safety of Liver Biopsy in the Era of Noninvasive Assessment of Liver Fibrosis</td>
<td>Jun B Kim, Chun Bae Lee, Jeong-Ju Yo, Sung-Gyu Kim, Young Seok Kim, Soong Won Jeong, Jae Young Jang, Sei Hwan Lee, Hong Soon Kim, Bae Gyu Jun, Young Don Kim, Gah Joon Cheon</td>
<td>355</td>
</tr>
<tr>
<td>OP-033</td>
<td>Plasma Levels of Soluble Programmed Death-1 and Programmed Death-Ligand 1 in the Patients with Autoimmune Hepatitis and Primary Biliary Cholangitis</td>
<td>Bong-ik Jang, Gwang Hyun Choi, Yun Suk Choi, Do Woon Jeong, Jae Kyun Choi, Si Hyun Nam, Kang Young Han, Eun Sun Jang, Jin-Wook Kim, Soo-Hyun Jeong</td>
<td>356</td>
</tr>
<tr>
<td>OP-034</td>
<td>Clinical Characteristics of Liver Cirrhosis and Hepatocellular Carcinoma Occurring after Fontan Operation</td>
<td>Jun Sa Yo, Dong Ho Lee, Eun Ju Cho, Mi Kyung Song, Young Hun Cho, Gi Beom Kim, Yun Bin Lee, Jeong-Hoon Lee, Si Jung Ta, Yoon Jun Kim, Jung-Hwan Yoon, Eun Jung Bae</td>
<td>361</td>
</tr>
<tr>
<td>OP-035</td>
<td>The Validity of Two-Dimensional Shear Wave Ultrasound for Assessing Fibrosis Stage in Patients with Chronic Liver Disease: Comparison with Transient Elastography</td>
<td>Hae Won Yo, Sung Gyu Kim, Jeong Ju Yo, Young Seok Kim, Soong Won Jeong, Jae Young Jang, Sei Hwan Lee, Hong Soon Kim, Young Don Kim, Gah Joon Cheon, Bao Sung Kim</td>
<td>362</td>
</tr>
<tr>
<td>OP-036</td>
<td>Proposal of a Cut-off for the Computed Tomography-Assessed Lumbar Skeletal Muscle Index for Diagnosing Sarcopenia in Asian Populations</td>
<td>Seo Yeon Gwak, Min Je Sung, Ta Seop Lim, Mi Young Jeon, Hye Won Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Seung Up Kim</td>
<td>357</td>
</tr>
</tbody>
</table>

**HBV & Others**

| OP-037  | Treatment Response of Noninvasive Fibrosis Markers Predicts Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients | Hee Chul Nam, Si Hyun Bae, Jong Young Choi, Seung Kiwon Yoon, Jeong Won Jang | 357  |
| OP-038  | Anti-Hbc IgG Level in Prediction of HBsAg Seroclearance in Chronic Hepatitis B Patients with Nucleos(t)ide Analogue induced HBeAg Seroclearance | Hyun Wook Lee, Seo In Kim, Seung Kyung Kim, Jung Il Lee, Hye Young Chung, Doh Kyun Kim, Seok Hoon Jeong, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang Hyub Han, Kwan Sa Lee | 358  |
| OP-039  | Maximal Diameter of Hepatic Abscess Independently Predicts Prolonged Hospitalization and Poor Prognosis in Patients with Pyogenic Liver Abscess | Chang Hun Lee, Gun Soo Lim, Myoung Soo Ha, Seung Yeon Ryu, Hee Chan Yang, Song Kyun Kim, Seung Young Seo, Sung Min Kim, Seung Wook Kim, Seung Ok Lee, Sso Teck Lee, and In Hee Kim | 359  |
| OP-040  | Comparative Analysis of Intrahepatic Infiltration of Activated T Cells and Macrophages between Autoimmune Hepatitis and Drug-Induced Liver Injury | P H Soo Sung, Hyeon Yang, Jae Jun Lee, Kwon Yang Tae, Hee Chul Nam, Jeong Won Jang, Si Hyun Bae, Jong Young Choi, Seung Kiwon Yoon, Eun Sun Jang, Sang Wook Choi | 359  |
| OP-041  | Positive Rate of Anti-Mitochondrial M2 Antibody and Anti-Soluble Liver Antigen Antibody in the Patients with Primary Biliary Cholangitis and Autoimmune Hepatitis in South Korea | Jae Kyun Choi, Boo-ik Jang, Yun Suk Choi, Do Woon Jeong, Si Hyun Nam, Kang Young Han, Gwang Hyun Choi, Eun Sun Jang, Jin-Wook Kim, Soo-Hyun Jeong | 360  |
| OP-042  | Prevalence of Antimitochondrial Antibody and Primary Biliary Cholangitis in Korea: A Single Center Study | Yang Jae Yoo | 361  |

**Liver Transplantation**

| OP-043  | Liver Transplantation for Patients with Pre-Existing Portal Vein Thrombosis: A Single-Center Experience | Tai Soo Kim, Keun Soo Ahn, Yong Hoon Kim, Hyesung Tae Kim, Koo Jeong Kang | 361  |
| OP-044  | Accuracy of Noninvasive Methods to Estimate Hepatic Steatosis in Living Liver Donors | Joseph Ahn, Ho Jong Choi, Tae Jun Lee, Bang Jun Kwak, Tae Ho Hong, Young Kyung You, Dong Goo Kim | 361  |
| OP-045  | Neutrophil-to-Lymphocyte Ratio Predicts Acute Cellular Rejection in Living Donor Liver Transplantation | Boram Lee, Young Hae Cho, Jae Young Cho, Ho-Seong Han, Tae Suk Youn | 362  |
| OP-047  | Living Liver Donor Surgical Complication: Single Center Experience with 512 Cases | Eun Hye Jung JWA, Dong-Luk CHO, Soo Dong KIM | 356  |
| OP-048  | Right Anterior Section Graft for Living-Donor Liver Transplantation | Jonathan NAVARRO, Gi Hong CHO, Myoung Soo Kim, Yoon Bin KANG, Jae Geun LEE | 363  |
Biliary and Pancreatic Disease

OP-049 Propensity-Score Matching Analysis of Postoperative Outcome Including Quality of Life after Single Incision Versus Multiport Laparoscopic Cholecystectomy: A Nationwide Prospective Multicenter Study in Korea ........................................................................................................... 363
Dae Joong PARK, Ji Wonkyung HAN, Heon Seok KOH, Hye Seong LEE, Seong K Min, Sun Woon KIM, Yi Young JANG, Kwang Min PARK, Ji Eun CHO, In Seek CHOE, Dongsik CHOI, Seung Ho CHOI, Ho Seong HAN, Ji Young CHOI, Yoo Seok YOON, Kwang Yoo PARK, Woo Jung LEE, Dong Sup YOON, Sol Ji CHO

OP-050 Laparoscopic Total Pancreatectomy in Benign and Borderline Malignant Tumor of the Pancreas: Perioperative Outcomes and Quality of Life ........................................................................................................... 364
Jin Ho Lee, Chang Moo Kang

OP-051 BMP2 Promotes Pancreatic Cancer Proliferation via the GRB2-Mediated PI3K-Akt-mTOR Pathway ........................................................................................................... 364
Haohao GAO, Yashhu WANG, Zhongkui ZHANG, Minjie LI, Qi WANG, Kai ZHANG, Xiaodong TIAN, Yimao YANG

OP-052 Pre-Drainage and Post-Drainage Prognostic Nomograms to Predict Outcome of Percutaneous Drainage in the “Step-Up Approach” for Necrotizing Pancreatitis ........................................................................................................... 364
Rajesh GUPTA, Aditya KULKARNI, Raghuveerendra BABUR, Sunil SHENVI, Rahul GUPTA, Rohit MMSE, Gopal SHARMA, Preetesh VASWAN, Srimati DEVAGIRAMANI, Mandeep KANG, Haryesh SINGH, Vishal SHARMA, M. Poojen KUMAR, Deepak BHATN, Suneeth RAJAN

OP-053 Comparison of the Prognostic Impact and Combination of Preoperative Inflammation-Based and/or Nutritional Markers and 18F-FDG-PET/CT-Derived Markers of Tumor Metabolism in Patients with Bile Duct and Pancreatic Cancer ........................................................................................................... 365
Min-Su Park

OP-054 Risk of Atherosclerotic Cardiovascular Diseases in Patients with Pancreatitis: A Retrospective Cohort Study ........................................................................................................... 365
Yi-Chun Chou, Si-Liang Chen, Chien-Chang Liao

HBV

OP-055 The Significance of Early Virological Response in the Patients with Prolonged Antiviral Treatment for Chronic Hepatitis B ........................................................................................................... 366
Sun Hong Yoo, Soon Hoo Nam, Yoon Jung Kim, Sung Won Lee, Hae Lim Lee, Jeong Won Jang, Shi Hyun Bae, Jong Young Choi, Seung Kew Yoon, Jong Hyun Kwon

OP-056 No Resistance to Tenofovir Alafenamide (TAF) Detected through 144 Weeks of Treatment in Patients with Chronic Hepatitis B (CHB) ........................................................................................................... 366
Ki Tae Yoon, Young-Suk Lim, Yang Liu, Bandita Parhy, Silvia Chang, Ross Martin, Becket Feierbach, Hongmei Mo, Anuj Gaggar, John F Flaherty, Henry LY Chan

OP-057 Low-Level Viremia and Cirrhotic Complications in Chronic Hepatitis B Patients with Good Adherence to Entecavir ........................................................................................................... 367

OP-058 Tenofovir Disoproxil Fumarate on the Risk of Hepatocellular Carcinoma in Chronic Hepatitis B Patients with Failure to Preceding Treatments ........................................................................................................... 367
Gi-Ae Kim, Young-Suk Lim

OP-059 Development of a Mathematical Modeling of HBsAg Kinetics during Long-Term Antiviral Treatment: A Pilot Study ........................................................................................................... 368
Hwi Young Kim, Tar Soo Yang, Hee-Dae Kwon, Joo Ho Lee

OP-060 ALT Normalization after Entecavir and Tenofovir Correlated with Reduction of Development for HCC ........................................................................................................... 368
Seohwa Kim, Sung Won Chang, Na Seok Lee, Min-Ji Lee, Young-Sun Lee, Sung Jun Sul, Ji Hoon Kim, Yeon Seok Seo, Hyung Joan Yim, Jung Eun Yoon, Soon Ho Um, Kwan Sook Byun

Cirrhosis & Liver Failure

OP-061 Effects of Atorvastatin in Lowering Portal Hypertension in Patients with Cirrhosis ........................................................................................................... 369
Le Thi Thu Hien, Le Quoc Tang

OP-062 Low-Dose Propranolol as a Secondary Prophylaxis for Variceal Bleeding Decreases Mortality and Rebleeding Rate in Patients with Tense Ascites ........................................................................................................... 369
Jin Hwa Park, Dae-Won Jun, Dae Hyun Lim, Won Woo Seo, Ji Hyun Yoo, Na Ryung Choi, Ja Hoon Yoon, Kang Nyensong Lee, Hui Sook Lee, Do Young Lee, Byung Chul Yoon, and Ho Soon Choi

OP-063 Endoscopic Variceal Obturation versus Retrograde Transvenous Obliteration for Fundal Variceal Bleeding ........................................................................................................... 370
Hyun Gil Goh, Nan-A Lee, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Sang Jun Sul, Young K Jung, Ji Hoon Kim, Yeon Seok Seo, Hyung Joan Yim, Jung Eun Yoon, Kwan Soo Byun, Soon Ho Um

OP-064 Effect of Acute Kidney Injury on Long-Term Outcomes of Spontaneous Bacterial Peritonitis in Cirrhosis Using ICA-AKI Criteria ........................................................................................................... 370
Won Sohn, Jung Hee Kim, Ju-Yeon Cho

OP-065 Severity Changes of Cirrhotic Patients during Seven Years Period in South Korea: A Multicenter Retrospective Study from 2008 to 2014 ........................................................................................................... 371
Jeong Han Kim, Eileen L. Yoon, Chang Hoon Jun, Jae Hyun Yoon, Byung Seok Kim, Jeong Eun Song, Ki Tae Suk, Moon Young Kim, Seong Hye Kang

OP-066 Clinical Features and Prognosis of the Patients with Chronic Liver Disease Hospitalized with Variceal Bleeding ........................................................................................................... 371
Jung Hwan Yu, Hyeong-In Jo, Jangdoyeon Shin, Jin-Woo Lee, Young-Ki Jung, Hyung Joan Yim, Jin Ho Yoo, Do Seon Song, Young Seok Kim, Sang Guyeon Kim, Dong Jeon Kim, Ki Tae Suk, Eileen Yoon, Sang Soo Lee, Chang Wook Kim, Hee Yeon Kim, Jae Young, On Behalf of the Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group
NAFLD

OP-067  Nonalcoholic Fatty Liver Disease and the Incidence of Myocardial Infarction: A Cohort Study  .......................................................... 372
Jae Na, Dong Hyeon Sim, Dancer Kang, Yosoo Chang, Seungho Ryu, Soo Jin Cha, Seung Moon Pak, Young Bin Song, Roberto Pastor-Barriuso, Eladio Guallar, Juhun Cha,
Geum-Yoon Gweak

OP-068  Association between Body Size-Metabolic Phenotype and Nonalcoholic Steatohepatitis and Significant Fibrosis  .................................................. 372
Seokyung Joo, Donghyeon Kim, Dongsu Lee, Yong-Jin Jung, Byoung Soon Kim, Won Kim

OP-069  Development of Machine Learning Model to Predict the 7-Year Risk of the Non-Alcoholic Fatty Liver Disease (NAFLD) among General Korean Population: A Nationwide Population-Based Study .......................................................... 373
Youn/J Cha, Jinsoo Kim, Oh Sang Ikwon, Ju Hyun Kim, Seung Ki Shin, and Dong Hwan Park

OP-070  Prevalence and Incidence of Tameoxifen-Related Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis  .................................................. 373
Cheon-Bom Lee, Jeong-In Jou, Sung-Gyu Kim, Young Seok Kim, Seong Won Kang, Je Young Jung, Se-Heon Han, Hong Soo Kim, Bank Gun Jun, Young Don Kim,
Gal Jin Cheon

OP-071  Exosomal miRNA Analysis for Classifying Severity of Disease in Biopsy-Proven NAFLD Patients  .................................................................................. 374
Young-Sun Lee, Min-Jin Lee, Seo-Hwa Kim, Ha Seok Kim, Sung-Won Chang, Sang Jun Soo, Ji Hoon Kim, Yun Seok Seo, Hong-Joon Yim, Jong Eun Yeon, Kwan Seo Byun

Liver Cancer, Basic

OP-072  Updated Study on Action Mechanisms of Cereblon as a Novel Prognostic Biomarker for Hepatocellular Carcinoma  .................................................. 375
Shin Hwang, Kyung Jin Lee, Gi-Won Song, Yun-Gyu Kim

OP-073  HKR3 Regulates Cell Cycle through the Inhibition of HTER1 in Hepatocellular Carcinoma Cells  .................................................................................. 375
Sung-Hoon Cha, Sung Hee Yen, Bon Ji, Kyung Joo Cha, Hy Young Lee, Simon Wu Yu, Do Young Kim, Seung-Hoon Ahn, Kwang-Hyub Han, Jun Yang Park

OP-074  Circulating Exosomal microRNA-125b Inhibits Metastasis in Hepatocellular Carcinoma  .................................................................................. 375
Hye Seon Kim, Je Sun Seok, Won Hyeok Hye, Cho Reum Nam, Ph Sung Soo, So Hyun Bae, Jong Young Cho, Seung Kweon Yoon, Jeong Won Kang

OP-075  Gut Microbes May Enhance the Efficacy of ImmunoTherapy in the Murine Metastatic Liver Cancer Model  .................................................................................. 376
Hyunsuk Oh, Minseok Albert Kim, Su Jung Yu, Hye Jin Naik, Hee Sook Jang, Sun Woon Kim, Cheol-Hyung Lee, Yun Bin Lee, Eun Joo Cho, Jeong-Hoon Lee, Yoon Jun Kim, Jung-
Hee Yoon

OP-076  TEAD2 as a Novel Prognostic Factor for Hepatocellular Carcinoma  .................................................................................. 377
Jung Seok Ju, Woon Sun Ryu, Hyuk Soo Seo, Seok Hyun Kim, Byoung Seok Lee

OP-077  Hsa_circ_0005986 as a Prognostic Biomarker in Hepatocellular Carcinoma  .................................................................................. 377
Se Young Song, Gyungmhe Kim, Soo Young Park, Young Oh-Hee, Yu Bin Lee, Jongwon Seo, Young Seok Kim, I-Jhyung Han, Keun Tak Ha, Jae Min Chun, Eunhye Lee, Sun Min
Kim, Jae-Kyeong Seo, Jung Gil Park, Hyo Won Lee, Won Young Tak, and Kun Ho

Liver Cancer, Clinical

OP-078  Prognostic Value of Alpha-Fetoprotein in Patients Who Achieved Complete Response to Transarterial Chemoembolization for Hepatocellular Carcinoma  .......................................................... 378
Jae Seung Lee, Wansook Kang, Dong-Hyun Sim, Mmoon Seok Chi, Geum-Yoon Gweak, Yong-Han Pak, Ioon Hyeok Lee, Kwang Cheol Koh, Seung Moon Pak, Hae Young Kim, Zae
Hun Kim, Kwon Soo, Young Sung Cho, Yoon Jun Kim, Joo Hae Lee, Soo Jin Cha, Seung Gun Hwang, Song Seok Kim, Hee Jang, Jae-Heon Cheong, Sung Won Cho, Seong Ha Park,
Nee-Joon Ha, Young Mi Hong, Ki Tae Young, Moon Cha, Jung Gil Park, Mi Kyu Kang, Soo Young Park, Young Oh Kimseon, Won Youg Tak, Se Young Jung, Beom Kyoung Jung, Jun
Yong Park, Do Young Kim, Seung Hoon Ahn, Kwang-Hyub Han, Seung Up Kim: The KOREAN TACE Study Group

OP-079  Undetectable Viral DNA after Curative Surgery Predicts Favorable Surivals in Patients with Hepatitis B-Related Hepatocellular Carcinoma  .......................................................... 379
Ph Sung Soo, Jeong-Won Kang, Hyoung Sung Park, Hye Cheol Nam, Si Hyun Bae, Jong Young Cho, Seung-Kee Yoon, Sang-Whel Cho, Young Kyung Yoo, Dong Goo Kim,
Sang-Whel Choo

OP-080  Prognosis and Survival Outcomes According to Body Mass Index in Hepatocellular Carcinoma Patients: An Analysis of a Nationwide Cancer Registry Database  .......................................................... 379
Boram Cho, Jang Hwan Yu, Young Ju Suh, Be-Hyeong Song, Yang-Joo In, Jin-Woo Lee

OP-081  Availability of Tumor Markers in Patients with Pretreatment State of Hepatocellular Carcinoma  .................................................................................. 380
Seokm Kang, Seongwoon Nam, Hyo-Joon Ahn, Yong-Jong Cho, Jiaowen Chung, Jung Shin, Seun Kim

OP-082  Validation of AJCC 8th Staging System in Patients with Resected Hepatocellular Carcinoma  .................................................................................. 380
Sun Young Yi, Eun-Jin Lee, Tae Seok Kim, Young Sun Lee, Sang Jun Soo, Na Yeon Han, Yeon Seok Seo, Ji Hoon Kim, Hyo Jung Yim, Dong Sik Kim, Soon Ho Um

OP-083  HCV Eradication Using Direct-Acting Antivirals Improve Treatment Outcomes in Patients with HCV-Related HCC Treated with TACE: A Multi-Center Retrospective Cohort Study  .......................................................... 381
Seung Up Kim, Eun Joo Cho, Soo Young Park, Young Mi Hong, Soo Sun Kim, Hae Young Kim, Nee-Joon Ha, Young Jung Young, Jung Gil Park, Beom Kyoung Jung, Jun Young Park, Do Young Kim, Seung Hoon Ahn, Kwang-Hyub Han, Jeong-Hoon Lee, Su Jung Yu, Yoon Jun Kim, Jung-Mwan Yoon, Won Young Tak, Young Oh Kwion, Nee Tae Young, Mong Cho, Jae Min Chun, Seong Hyeon Ha Park: The KOREAN TACE Study Group

xxvi  June 20–22, 2019 | BEXCO, Busan, South Korea
Surgery, Technical Issues

OP-102 Oncologic Outcome of Two Stage Hepatectomy in Patients with Bilobar Multiple Colorectal Liver Metastases
Jin Hong Lim, Sung Wihan Cho, Dae Ho Han, Gi Hong Choi, Dong Sup Yoon, Jin Sub Choi

OP-103 Surgical Tips of Pure Laparoscopic Donor Right Hepatectomy for Donors with Portal Vein Anatomical Variations
Jeong-Moo Lee, Kiun-Woong Lee, Ahmed Shehata, Suk Kyung Hwang, Jae-Nyung Cho, Nam Joong YI, Kyung-Suk Suh

OP-104 Subtotal Hepatectomy: Pig Models for the Study of Post-Hepatectomy Liver Failure
Yoon Young Choi, Kyung Chul Yoon, Hye Sung Ju, Jin Seok, Dong-Sik Kim

OP-105 Choice the Optimal Surgical Treatment Strategy for Liver Alveococcosis
Kiselev Nikolai Michailovich, Rykhtik Pavel Ivanovich, Bobrov Nikolay Viktorovich, Zagainov Vladimir Evgenievich

OP-106 Robotic Hilar Cholangiocarcinoma Radical Resection Compared with Laparotomy in Prognosis
Sai CHOU, Zheng-Yao CHANG, Guo-Dong ZHAO, Rong LIU

OP-107 Robotic Anatomical Hepatectomies for Difficult Segments
Sung Hoon Choi

Poster Exhibition

Alcoholic Liver Disease

PE-001 Randomized Controlled Trial of Lactulose and Lactulose with Probiotic in the Treatment of Minimal Hepatic Encephalopathy in Chronic Liver Disease
Durga Bhandari, Denish Peeyush

PE-002 Peptic Ulcer Disease in Cirrhosis
Denish Peeyush

PE-003 Beneficial Effects of Cisplatin on Liver Fibrosis in a Non-Alcoholic Steatohepatitis (NASH) Rodent Model
B.L Gupta, Arun Kumar Rao

PE-004 Preclinical and Clinical Study in Alcohol Dependence Syndrome Patients with Lipid Profile and Cardiac Markers to Correlate Occurrence of Cardiovascular Disease
Hari Prasad Dolal

PE-005 Unexpected Improvement of Liver Function by Intravenous Immunoglobulin in a Steroid-Experienced Severe Alcoholic Hepatitis
Kwon Yong Tak, Pil Soo Sung, Hee Chul Nam, Jeong Won Jang, Jong Young Choi, Seung Kew Yoon

PE-006 A Case of Pneumocystis Pneumonia after Use of Glucocorticoids in Severe Alcoholic Hepatitis
Min-Woo Chung, Chang Hwan Jun, Sung Bum Cho, Seon Young Park, Chang Hwan Park, Huan Soo Kim, Sung Kyu Choi, and Jong Sun R.ew

PE-007 Essential Amino Acid Supplementation Decreases Liver Damage Induced by Chronic Ethanol Consumption in Rats
Bauyrzhan Darzilgengov, Darkhan Kopzhassaruly

PE-008 Types and Pattern of Alcoholic Drinks Consumption and the Knowledge of Liver Cirrhosis and Alcohol Related Health Hazards among Selected Nepalese People
Nawadatta Sudevi

PE-009 Study of Biochemical and Haematological Parameters of Alcoholic Liver Disease Patients
Padam Bahadur Khadka, Mukunda Raj Kalouni

PE-010 Alcoholic Hepatitis Initial Recovery Is Complicated by Second Hit Drug Induced Liver Injury by Ayurvedic Medicines in India and Is Associated with Bad Prognosis
Bhavin VASAVAD, Hardik PATEL

Bimala Sharma, Bishnu Raj Tiwari, Song Geurum, Eun Woo Nam

Autoimmune Liver Disease

PE-012 Seroprevalence of Anti-Hepatitis E Virus in the Patients with Autoimmune Hepatitis and Primary Biliary Cholangitis in South Korea
Jae Kyun Choi, Biao-chi Jang, Yun Suk Choi, Da-woon Jeong, Si Ho Kim, Kyunghan Lee, Giwang Hyeon Choi, Eun Sun Jang, Jin-Wook Kim, Sook-Hyoung Jeong
PE-014 Histopathological Analysis and Validation of Different Scoring Systems for Autoimmune Hepatitis: Experience of Two Institutes
Soomin Ahn, Eun Ju Cho, Soo-Hyang Jeong, Heeyoung Kim

PE-015 Failing Transplanted Liver from an Unrecognised, Recently Discovered Autoimmunity Following HCV Eradication, What Options Do We Have?
Khalil Abdul Badee SDEDOUI, Ruben A. ZIMAT

Cell Biology / Molecular Biology

PE-016 Role of Momordica Charantia Fruit Extract against Hepatic Fibrosis Induced by Carbon Tetrachloride in Rats
Pardeep Kumar, SB Sharma

PE-017 Human Fetal Liver Cells as a Bridge to the Liver Transplantation in Patients Waiting for Donors
Aiden Zulkhairam, Senk Zhankov

PE-018 Beryllium Induced Alterations in Liver Biochemistry and Histopathology: Reversal by Therapy of Aloe Vera with Piperine and Curcumin
Narottam Das Agrawal, Satendra Kumar Nirala

PE-019 Histogenesis of Human Foetal Liver
Rajev Mukhi, BP Pawan, BK Tanuja

PE-020 High Maternal Linoleic Acid Alters Maternal Hepatic Cytokines and Circulating Lipid Profile in Rodent Model
Ninan Shrestha, James SM Cuffe, Olivia J Holland, Andrew Bulmer, Anthony V Perkins, Andrew J McNich, Deanne H HRYCIUS, Deanne Skelly

PE-021 Diabetes Associated Liver Toxicity
Narendra Kumar

PE-022 Effect of Gymnema Sylvestre on Liver Function Markers in Type II Diabetic Subjects
Sarit Kumar Subraman, Sunil Mahajan, Umakumarani RAKHISAMY, Rohit Sharma, GKS Prasad

PE-023 Frequent Promoter Methylation and Gene Silencing of PTEN in Periampullary Carcinoma in Indian Population
Aasif Ali, Abhay Kumar Sharma, Shraddha Soni, Sundeep Singh Saluja

PE-024 Optimal Time and Condition of Hypoxic Preconditioning to Maximize Mesenchymal Stem Cell Function
Wasif Khalid Saed, Dae Won Jun

PE-025 TRP2, a Prodrug of BMP7 Suppresses Hepatic Fibrosis in Mice Induced by the Treatment with Carbon Tetrachloride
Kyungjo Cho, Nam Hee Kim, Hyeyung Park, Hyuk Moon, Hyun Sik Kim, Jong In Youk, Kwang Hyub Han, Sang Heon Ahn, Simon W R, Seung Up Kim

PE-026 Development of Doxorubicin-Incorporated Phenylboronic Acid Nanoparticle and Evaluation of Anti-Cancer Effect in Hepatocellular Carcinoma
Byung-Yoon Kang, Sung Min Kim, Wonhee Hur, Won Jong Kim, Seung Kew Yoon

PE-027 The Degree of HCC Differentiation Determines the Drug Diffusion in MCTS
Kyungjo Cho, Hyuk Moon, Seonjeong Shin, Simon W R, Jun Yong Park, So Young Kim, Kwang Hyub Han

PE-028 Knockdown of ATG7 Suppresses Tumorogenesis in HCC Mouse Models Induced by HRASG12V and shp53
Beom Kyung Kim, Soonyeong Shin, Hyuk Moon, Kyungjoo Cho, Seung Up Kim, Dae Young Kim, Simon W R, Kwang Hyub Han

Drug and Toxic Injury

PE-029 Effects of Anti-Tubercular Treatment on Liver in Newly Diagnosed Pulmonary Tuberculosis Patient on Intensive Phase of Treatment
Aashithesh Shresta, Saroj Pahukel, Prashithya Ari

PE-030 Prevalence and Clinical Characteristics of Antibiotics Associated Drug Induced Liver Injury: From a Single Center Experience
Jin Hea Park, Dae Won Jun, Dae Hyeun Lim, Won Woo Seo, Ji Hyun Ieo, Na Ryung Choi, Ji Nam Yoon, Kang Nyeong Lee, Hang Lak Lee, Oh Young Lee, Byung Chul Yoon, and Ho Soon Choi

PE-031 High Levels of Procalcitonin in the Early Phase after Pediatric Liver Transplantation Indicate Poor Postoperative Outcome
Samir Boakye, Nurunnabi Kydri

PE-032 Cardiovascular Risk Factors after Conversion from Cyclosporine to Tacrolimus in Children after Liver Transplantation
Ahmed Dossanow, Lassal Dossanow

PE-033 A Case of Toxic Hepatitis Induced by Noni Powder
In Ki Kim, Byung Seok Lee, Seok Hyun Kim, Eunm Soo Lee, Jang Seok Jo, Hyuk Soo Eun, Woo Sun Roi, Hie Sung Lee, Min Young Shin, Sung Han Kang, Sang Ok Jung, Min Ki Cho, Dong Yeon Kim

Genetic

PE-034 Study on Validity of Biomarkers DKK1 and HBx-LINE1 in Diagnosis and Posttreatment Monitoring of Hepatocellular Carcinoma
Hai Trung LE, Huan Quoc PHAN, Thinh Tien NGUYEN, Son Thanh LE, Thanh Van LE, Trung Tat NGO, Tien Duc DAO, Nhu Trung LE, Giang Phuong DAO, Quang Van VU, Binh Thanh MAI, Lam Nguyen Dai NGUYEN et al
<table>
<thead>
<tr>
<th>Paper ID</th>
<th>Title</th>
<th>Authors</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV, Basic</td>
<td>Ciclopirox Inhibits Hepatitis B Virus Secretion by Blocking Capsid Assembly</td>
<td>Jung-Ah Kang, Sangwan Kim, Myri Park, Hyun-Jin Park, Jeong-Hyun Kim, Sangheeek Park, Jeong-Ryu Mu, Yong-Chul Kim, Yoon Jun Kim, M Soo Jin, Sung-Gyu Park, Yoo Cho</td>
<td>411</td>
</tr>
<tr>
<td>HBV, Basic</td>
<td>cccDNA-Induced Hepatocarcinogenesis Is Regulated by HBx-Stimulated Interaction between MS2 and cccDNA</td>
<td>Xue-Li Jin, Suk-kyun Hong, Hwa-jung Kim, Sun-Kyung Lee, Nam-Joon Je, Kwang-Won Lee, and Kyung-Suk Soh</td>
<td>412</td>
</tr>
<tr>
<td>HBV, Basic</td>
<td>The Effect of Living Donor Liver Transplantation on the Treatment of Severe Hepatitis</td>
<td>Daulet Alm, Baktchan Darzigenov</td>
<td>413</td>
</tr>
<tr>
<td>HBV, Basic</td>
<td>Costs of Viral Hepatitis B in the Republic of Korea, 2002–2015</td>
<td>Dahye Bak, Byung-Hoon Kim, Jin-Kyoung Oh, Kyung-Ah Kim, Moran Ki</td>
<td>414</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Knowledge and Practice of Hepatitis B and C among Medical and Health Science Students in Nepal</td>
<td>Mani Neupane, Birnala Sharma, Bishnu Raj Tiwari</td>
<td>414</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Prevalence of Hepatitis Delta Virus Infection in Patients with Chronic Hepatitis B in Eastern Province Mongolia</td>
<td>Bayrums Anayeva, Myham Buyla, Shetabyer Nerayiya, Borkhursen Deren</td>
<td>415</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Cases of the Influence of Mare's Milk on the Course of Viral Hepatitis B + D</td>
<td>Galburt Darbyenov, Efekt Eghrapukov</td>
<td>415</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>A Large-Scale, Multi-Center Study of Entecavir vs. Tenofovir on Long-Term Prognosis for Treatment-Naive Chronic Hepatitis B in the Republic of Korea</td>
<td>Seung Up Kim, Yeon Soon Seo, Han Ah Lee, Mi Na Kim, Yu Rim Lee, Hye Won Lee, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang Hyub Han, Seong Gyu Hwang, Kyung Sung Rim, Soon Ho Um, Won Young Seo, Young Oh Kweon, Bae Kyung Kim, and Soo Yong Park</td>
<td>415</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Establishment of a Korean Chronic Hepatitis B Cohort Study</td>
<td>Mi Young Jeon, Jae Seop Lim, Jeong Seung Lee, Hye Won Lee, Sang Gyu Lee, Eun Young Cho, Young Mi Hong, Yeon Seok Seo, Ki Tae Moon, Bae Kyung Kim, Jun Yang Park, and Sang Hoon Ahn</td>
<td>416</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Projection of Health Outcomes over 5-Year and 10-Year Using Tenofovir Alafenamide for the Management of Chronic Hepatitis B in China</td>
<td>Ying Han, Bin Wu, Ming Hu, Fengqi Hou, Hua Yang, Lei Wang</td>
<td>417</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Lower Risk of Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients with Immune Tolerant Phase Than Those with Antiviral Therapy</td>
<td>Mi Young Jeon, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang Hyub Han, Bae Kyung Kim, and Seung Up Kim</td>
<td>417</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Real-Life Indication and Efficacy of Tenofovir Alafenamide, Tenofovir Disoproxil Fumarate, and Entecavir for Treatment Naive Chronic Hepatitis B Patients</td>
<td>Si Ho Kim, Bok-Jae Jung, Kyoungchan Lee, Je Heon Kim, Jin-Wook Kim, Soo-Hyang Jeong, Guwang Hyun Choi, Eun San Jung</td>
<td>418</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Association between Hepatitis B Virus Infection and Agent Orange in Non-Hodgkin's Lymphoma</td>
<td>Wonyeong Park, Sung Hoon Kim, J Soo Jung, Seong Whan Lim, Tae-goon Kim</td>
<td>418</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Comparable Incidence of Hepatocellular Carcinoma in Chronic Hepatitis B Patients Treated with Entecavir or Tenofovir</td>
<td>Daeye Bak, Jung-Won Shin, Seok-Won Jung, Seung-Bum Lee, Bi Ryung Park, Min-Ji Kim, Eun Ji Park, and Jeong Miao Park</td>
<td>418</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Frequent Radiological Assessment Using Computed Tomography Deteriorates Renal Function in Patients with HBV-Related Hepatocellular Carcinoma that Is Treated with Entecavir and Tenofovir</td>
<td>Mi Young Jeon, Tae Seop Lim, Boon Kyung Kim, Jun Yong Park, Do Young Kim, Kwang Hyub Han, Sung Hoon Ahn, and Seung Up Kim</td>
<td>419</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Low Incidence of Hepatitis B Reactivation after Kidney Transplantation in Hepatitis B Surface Antigen-Negative and Core Antibody-Positive Recipients</td>
<td>Juye Kim, Se Jin Chung, Aki-Won Lee, Je Bum Park, Kwon-Sook Kang, Dong-Hyun Sin, Guo-Yun Guak, Yong-Han Pak, Moon Seok Cho, Joen Hyeok Lee, Kwang Cheol Koh, Seung Woon Park</td>
<td>420</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Estimation of Hepatocellular Carcinoma Risk after Hepatitis B Surface Antigen Serodence</td>
<td>Yeon Park, Minseok Albert Kim, Dong Hyun Kim, Jeong-Hoon Lee, Kwon-Sook Kang, Guo-Yun Guak, Yong-Han Pak, Moon Seok Cho, Joen Hyeok Lee, Kwang Cheol Koh, Seung Woon Park</td>
<td>420</td>
</tr>
<tr>
<td>HBV, Clinical</td>
<td>Real-Life Efficacy of Glecaprevir and Pibrentasvir for Genotype 2 Chronic Hepatitis C</td>
<td>Sung Jun Suh, Njong Joong Yim, Young Gii Jung, Han Ah Lee, Tae Hyung Kim, Sun Young Kim, Young-Sun Lee, Jong Jin Hyun, Yeon Suk Seo, Ji Nsoon Kim, Jang Eun Yeon, Kwan Soo Byun, Sun Ho Lim</td>
<td>421</td>
</tr>
</tbody>
</table>
Contents

PE-054 Comparison of the Effect Tenofovir and Entecavir on Renal Function in Patients with Chronic Hepatitis B ................................................................. 421
Hong Joo Kim, Won Sohn, Yong Kyun Cha, Byung K Kim

PE-055 Comparison of Efficacy between Tenofovir and Entecavir in Treatment-Naïve Chronic Hepatitis B Patients with High Viral Load: Results from SAINT Cohort ........................................................................................ 421
Ji Won Park, Kang Hyeon Lim, Sung Eun Kim, Jae Yoon Jeong, Hyun Jin An, Dae Won Jun, Joon Hyung Oh, Eileen L. Yoon, Jae Jun Shin, Sang Bong Ahn, Yong Kyun Cha, Song Woon Jeong, Young Seok Soh, DJ. Han, Sunge Kim; SAINT cohort study group

PE-056 Fractures Related to Tenofovir Treatment in Patients with Chronic Hepatitis B: A Comparative Study in the National Database ........................................... 422
In Hye Lee, Bo Hyeon Kim, Hye Young Cho, Manan K, Jeong-Wan Park

PE-057 Persistent Viremia after Entecavir Treatment and the Risk of Hepatocellular Carcinoma in Patients with HBV-Associated Cirrhosis .......................... 422
Seung Kull Shin, Oh Sang Kwon, Jeong Han Kim, Chun Uk Lee, Jae Gun Yoon, Sang Jun Soh, Young Kuk Kang, Hyung Soon Kim, Yoon Soo Kim, Ju Hyeon Kim

PE-058 External Validation of the Modified PAGE-B Score in Asian Chronic Hepatitis B Patients Receiving Antiviral Therapy ......................................................... 423
Hyef Won Lee, Seong Up Kim, Jin Yong Park, Do Young Kim, Sang Hoe Ahn, Kwang Hyub Han, and Beom Kyung Kim

PE-059 Tenofovir Disoproxil Fumarate versus Tenofovir Disoproxil for the Treatment of Patients with Chronic Hepatitis B Virus Infection .................. 423
Min Young Shin, Hee Song Lee, Sung Hoon Kang, Sang Ok Jung, Min J Cho, Woo Sun Hou, Hyuk Soo Eun, Seok Hyeun Kim, and Byung Seok Lee

PE-060 Efficacy and Safety of 3-Year Entecavir and Tenofovir Therapy in Chronic Hepatitis B Patients with Chronic Kidney Disease: A Multicenter, Retrospective Cohort Study ............................................ 424
Ji Won Park, Nyan Hoon CN, Dae Won Jun, Jae Yoon Jeong, Hyun Jin An, Eileen L. Yoon, Jae Jun Shin, Hye Young Lee, Sang Bong Ahn, Yong Kyun Cha, Song Woon Jeong, Hyung Su Kim, Sung Eun Kim; SAINT Study Group

PE-061 Real World Data of Tenofovir Alafenamide versus Tenofovir Disoproxil Fumarate for the Treatment of Patients with Chronic Hepatitis B ............ 425
Saein Kim, Hye Won Lee, Seung Up Kim, Jung Il Lee, Soo Kim, Hye Young Chang, Bum Kyung Kim, Jun Yong Park, Do Young Kim, Kwang Hyub Han, Kiwan Suk Lee, Sang Hoan Ahn

PE-062 The Effectiveness of Tenofovir and Hepatitis B Immunoglobulin in Preventing HBV Vertical Transmission for Pregnancy ............................................. 425
Khidhagmog Lkhagvadorj, Nyam Bitya

PE-063 Cumulative Incidence of Hepatocellular Carcinoma and Hepatitis B Surface Antigen Seroclearance after Nucleos(t)ide Analogue Induced Hepatitis B e Antigen Seroclearance .................................................. 426
Hyun Woon Lee, Seon Kim, Soo Kim, Hye Young Chang, Jung Il Lee, Kiwan Suk Lee

PE-064 Clinical Impact and Correlation of Serum HBV DNA and HBeAg Titer in Patients with Chronic Hepatitis B during Antiviral Therapy ................... 426
Nguyen Van Thai, Hye Won Lee, Seon Kim, Soo Kim, Hye Young Chang, Jung Il Lee, Kiwan Suk Lee

PE-065 Determination of Liver Fibrosis Stage by Fib-4 in Patients with Chronic Viral Hepatitis ................................................................. 427
D. Bastarache, R. Bayaagdul, D. Mandel Schiwit

PE-066 HCV/HBV Co-Infection: Epidemiology, Clinical Characteristics, Viral Interactions and Mortality .......................................................... 427
D. Bastarache, R. Bayagaaga, D. Mandel Schiwit

HCV, Basic

PE-067 MicroRNA-99a Restricts Hepatitis C Virus Replication by Blocking mTORC1-Mediated de novo Lipogenesis .......................................................... 427
Eun Boul Lee, PI Soo Sung, Keunming Yang, Dong Jun Park, Jung Hee Kim, GI Won Lee, Seung Kew Yoon

PE-068 Change of Incidence of Hepatitis C Virus Infection after Transfusion by Introduction of Nucleic Acid Testing: A Big Data Analysis ................ 428
Hye Young Cho, Manan K

HCV, Clinical

PE-069 Pharmacokinetics, Safety, and Efficacy of Glecaprevir/Pibrentasvir in Pediatric Patients with Genotypes 1-6 Chronic HCV Infection: Part 1 of the DORA Study ........................................................................................................... 429

PE-070 Long-Term Hepatic and Extra-Hepatic Outcomes of CHC Patients Post Sofosbuvir-Based IPN-Free Treatment (LONGHEAD Study): Interim Report ........................................................................................................... 429
Min Young Lee, Ting-Tsung Chang, Ji-Hong Kim, Ting-Tsung Chang, Chih-Chau Chen, Yoo Na-Ni, Cheng-Yuan Peng, Hung-Huan Wang, Chih-Chao Chu, I-Shyan Steen, Yu-Chun Hsu, Jeong Hea, Young-Suk Lim, Hyung Soon Yoon, Yoon-Jae Lee, Kwan Soo Byun, Won Young Tak, Yoon Jun Kim, Sang Hoe Ahn, Seung Woon Park, Soo-Hyang Jeong, Young Seok Kim, Seok-Woo Yoon, Ju-Hyeon Kim, Young-Hyun Baek

PE-071 An Open-Label, Randomized, Active Control Trial of 8 Versus 12 Weeks of Elbasvir/Grazoprevir for Treatment-Naïve Chronic Hepatitis C Genotype 1b Patients with Mild Fibrosis (ECAULITE): Impact of Baseline Viral Loads and NS5A Resistance-Associated Substitut ................................... 430
Min Young Lee, Chang-Fei Huang, Meng Lu, You Yuan, Chao-Yan Dai, Jie Fu, Xiao Yang, Wang-Long Chang

PE-072 Decreased of Alpha-Fetoprotein Level among Patients with Liver Cirrhosis That Related to HCV Treated with Combination Therapy with Ledipasvir and Sofosbuvir .............................................................................. 430
Batuw Dachtya, Bayarmas Njampa, Nyam Bitya, Oyunedger Munkhtuushin
<table>
<thead>
<tr>
<th>Session Code</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE-073</td>
<td>Changing Cascade of Care for Hepatitis C in the Era of Direct-Acting Antivirals (DAAs)</td>
<td>Jay Chitharal, Gushin Chen, Emily Bethes, Turay Ajay, Yuan Zhou, Chin Hui, Anne Spaelding, and Fasha Kanneal</td>
</tr>
<tr>
<td>PE-074</td>
<td>Ledipasvir/Sofosbuvir for 8, 12, or 24 Weeks Is Safe and Effective in Patients Undergoing Dialysis</td>
<td>Woon Jong Chung, Young Hui Hu, Peter Buggisch, Christophe Moreira, Wei Wen Su, Luigi Biancone, Robert Hyland, Sophia Lu, Svetlana Markova, Nadia Davy-Subat, Anu Chauhan, Anuj Gaggar, Jin Yoon, Cheng Yan Peng, Chen Hua Liu, Meghan Siat, Alexandra Margie</td>
</tr>
<tr>
<td>PE-075</td>
<td>Safety and Effectiveness of HARVONI® (Ledipasvir/Sofosbuvir, LDV/SOF) from the 3rd Year Post-Marketing Surveillance (PMS) Data in Korea</td>
<td>Jee Min Lee, Seok Hwan Park, Young Hoon Kim, Chang Hyung Lee, Youn Jae Lee, Yong Kyun Cho, Jeong Il Suh, Byung Hoon Han, Eun Soo Hwang, Jin Yoon, Yum Zhang</td>
</tr>
<tr>
<td>PE-077</td>
<td>Real Life Data of Dacabasvir and Asunaprevir Combination Therapy for Korean Patients Infected With HCV Genotype 1b without NS5A Resistance: Retrospective Multicenter Study</td>
<td>Jung Hee Kim, Hyung Su Kim, Myoung Juk Kang, Ki Tae Suk, Dong Joan Kim, Sang Hoon Park, Myoung Seok Lee, Jin Won Park, Sang Eun Kim, Chang Hee Park, Jae An Shin, Sang Bong Ahn, Daewon Jun, Soong Won Jeong, Young Joo Jin, Eun Young Jo, Moon Young Kim, Seung Ha Park</td>
</tr>
<tr>
<td>PE-078</td>
<td>The Efficacy and Safety of Gileadraiprev and Ribasvir Treatment for Patients with Genotype 2 Hepatitis C Virus Infection in Real-World Experience: Interim Analysis of a Single Center</td>
<td>Woon J Hk, Sang Hoon Park, Myoung Seok Lee</td>
</tr>
<tr>
<td>PE-079</td>
<td>Efficacy and Safety of Ledipasvir/Sofosbuvir for Treatment of Chronic Hepatitis C Patients</td>
<td>Doljinsuren Enkhbayar, Bayarraa Nyamaa, Bat Erdene Dashnyam, Ariam Bayar</td>
</tr>
<tr>
<td>PE-080</td>
<td>Clinical Characteristics of Foreign Chronic Hepatitis C Patients in Daegu-Chungcheongbuk Area: Multi-Institutional Study</td>
<td>Hyun Jae Lee, Min Hyo Joon, Suk Bae Kim, Kim Hyeon, Song, Seo Hwan Lee, Hong Soo Kim, Tae Hee Lee, Young Woon Kang, Seok Hyun Kim, Byung Seok Lee, Hee Bok Choi, Seok Hwan Kim</td>
</tr>
<tr>
<td>PE-081</td>
<td>LDL-Cholesterol Level Was Elevated after Direct Acting Antivirals (DAAs) Administration in Genotype 2 HCV-Infected Patients: Real World Data from a Single Center Experience</td>
<td>Joan Ho Jong, Sang Wook Lee, Kwang Yoon, Byung Hoon Han, Eun Tae Park, Jin Woock Lee</td>
</tr>
<tr>
<td>PE-082</td>
<td>Successful Treatment of Chronic Hepatitis C with a Combination of Gileadraiprev and Ribasvir in a Patient Who Failed Previous Dacabasvir and Asunaprevir Treatment: A Case Report</td>
<td>Dong Wook Lee, Seo Hyung Ryu, Youn Jae Shin, Bo Kyung Lee, Jang Young Park, Jeong Seon Moon</td>
</tr>
<tr>
<td>PE-083</td>
<td>Prevalence and Geographical Distribution of HCV among Arkhangai Provinces in Mongolia</td>
<td>M. Batcaya, E. Byambatsogt, G. Buyanbileg, B. Ampalan, and O. Bastarkhoo</td>
</tr>
<tr>
<td>PE-084</td>
<td>Study of Alteration of Iron Metabolism in Chronic Hepatitis C in Mongolia</td>
<td>Bastarkhoo O, Bold Shara, Uugansuren G, Temendorog O, and Odgerel Tsi</td>
</tr>
<tr>
<td>PE-085</td>
<td>Direct Antiviral Agent (DAA) Treatment of Chronic Hepatitis C Results by APRI and FIB-4 Score in Mongolia</td>
<td>Amgalan B, Bat Erdene Dashnyam, Bayarshar D, Ampalan B, and Bastarkhoo O</td>
</tr>
<tr>
<td>PE-086</td>
<td>SVR 12 Weeks after Therapy with Sofosbuvir/Ledipasvir Patients with HCV Genotype 1B: Real World Mongolian Experience</td>
<td>Bastarkhoo O, Oyun Eremee Mijid, Ekhbala D, Sarual B, Gundotul Ch, Gegenbatsalhi, T. Tsetsenbaatar, Badamtsuri, D. Ulmaa, G. and Amaansaa J</td>
</tr>
<tr>
<td>PE-088</td>
<td>Extended Virological Response after Sustained Virological Response in Patients with Sofosbuvir and Ribavirin Therapy</td>
<td>Sin Hyeok Kang, Seo Hwan Lee, and Hong Soo Kim</td>
</tr>
<tr>
<td>PE-089</td>
<td>Treatment Failure Rates of Direct-Acting Antiviral Agents for Chronic Hepatitis C: A Single-Center Study</td>
<td>Hee Sung Lee, Dong Hyeon Kim, Min In KI, Min Young Shin, Min Ji Chia, Sang Ok Jung, Woo Sun Ran, Hyuk Soo Eun, Jong Seok Joo, Eun Eun Seok Lee, Seok Hwan Kim, Byung Seok Lee</td>
</tr>
<tr>
<td>PE-090</td>
<td>Direct-Acting Antivirals about Diminishment of Liver Fibrosis after Chronic Hepatitis C Treatment</td>
<td>Hyun Phil Shin, Jong Y Lee</td>
</tr>
<tr>
<td>PE-091</td>
<td>Non-Invasive Test for Estimation of Liver Fibrosis</td>
<td>O. Bastarkhoo, S. Arunsa, Badamtsuri O</td>
</tr>
<tr>
<td>PE-092</td>
<td>Treatment Effectiveness of Tenofovir Disoproxil Fumarate in Chronic Hepatitis B among Mongolian Patients</td>
<td>O. Bastarkhoo, O. Otgonbayar, D. Munkh-Orshikh</td>
</tr>
<tr>
<td>PE-093</td>
<td>HCV Treatment after Curative Liver Resection or RFA in Hepatocellular Carcinoma Patients in Mongolia</td>
<td>O. Bastarkhoo, O. Tsevelmaa, J. Chinburen</td>
</tr>
<tr>
<td>PE-094</td>
<td>Comparison of Methods That Evaluate the Prognosis of Liver Cirrhosis</td>
<td>O. Bastarkhoo, B. Enkhbileed, O. Badamtsuri</td>
</tr>
</tbody>
</table>

June 20–22, 2019 | BEXCO, Busan, South Korea
Contents

Liver Cirrhosis, Portal Hypertension with Cx., Basic

PE-095 Human Adipose Derived Stem Cells Promote Liver Regeneration in Hepatic Fibrosis Model by Controlled Releasing Hepatocyte Growth Factor .............................................................. 442
  Ju Song Choi, Sangheun Lee, Ki Jun Han, Sung-Whan Kim

PE-096 Novel Self Nano Emulsifying Formulation of Furosemide: A Drug Used in Portal Hypertension .............................................................. 442
  Pankaj Kumar Yadav

PE-097 The Expression of TSLP in Liver Fibrosis: Rat bile Duct Ligation Model .............................................................. 442
  Jung Hee Kim, Ji Seon Lee, Seung Eun Kim

PE-098 Enhanced Production of Steroid Drugs Intermediate Used in Treatment of Liver Cirrhosis .............................................................. 443
  Jayesh Vaishnav, Girish Pendharkar, Vashali Moyna, Danish Anjum

Liver Cirrhosis, Portal Hypertension with Cx., Clinical

PE-099 Helicobacter Pylori Infection in Patients with Liver Cirrhosis: Prevalence with Portal Hypertensive Gastropathy .............................................................. 443
  Nyam Biziya, Bayarmarya Namas, Shindaibay Narantuya, Borkhuukhen Derdem

PE-100 Assessment of Liver Fibrosis and Cirrhosis by Fibroscan in Patients with Chronic Liver Disease .............................................................. 444
  Le Thi Huong Yen

PE-101 Intra & Extrahepatic Portosystemic Shunt Embolization Procedure in Two Patients with Recurrent Hepatic Encephalopathy .............................................................. 444
  Seung Kyo Choi, Seoong Won Nam, Hee-Kye Chon, Jang Hyun Kim, Joo Won Chung, Si Eun Kim, Seo Ram Kang, Jung Shin

PE-102 Low Serum Creatinine Level and Acute Kidney Injury Can Predict Long-Term Mortality in Cirrhotic Patients with Ascites .............................................................. 445
  Jae-Hyoung Bae, Nan Young Choi, Ji Won Park, Jae-Kyung Kim, Sung Gun Kim, Hyung-Jik Kim, Choong Koo Park, Young Rim Song, Sung-Eun Kim

PE-103 Repeated versus Single Treatment of Esophageal Variceal Ligation after Esophageal Variceal Bleeding: Multicenter Retrospective Study .............................................................. 445
  Young-Soon Cho, Jeong-Hoon Lee, Su Jong Yu, Yoon Jun Kim, Hyung-Jin Kim, Jung-Mo Yoon

PE-104 Comparison of Gross Inspection by Surgeon or Pathologist, Ultrasonography, CT, MRI, Transient Elastography, APRI and FB-4 for Prediction of Liver Cirrhosis .............................................................. 446
  Hyeon Young, Pi Soo Song, Kwon Yong Tak, Jae Jun Lee, Hye Chul Nam, Jeong Won Jang, Si Hyun Bae, Jeong Young Cho, Seung Kwee Yoon, Sang Hoon Choi

PE-105 Clinical Spectrum of Precipitating Factors of Hepatic Encephalopathy in Cirrhosis of Liver: Experience in Western Part of Nepal .............................................................. 446
  Song Pohret, Muluneh Raj Kadi

PE-106 Comparison between Sandostatin Alone and Combined with Band Ligation for Hemostasis of Acute Variceal Bleeding .............................................................. 447
  Tran Ngoc Thuy

PE-107 Relationship of Symptom-Onset-To-Hospital Arrival with Hospital Course in Patients with Variceal Bleeding .............................................................. 447
  Taek Soo Kim, Min Jong Lee, Daehoon Choi

PE-108 Platelet Count Spleen Diameter Ratio to Predict Esophageal Varices in Patients with Liver Cirrhosis, in the Eastern Province Mongolia .............................................................. 447
  Gerbynjagd Batsham, Nyam Biziya, Badam Bungaizi

PE-109 The Diameter of Esophageal Varices Evaluated by Computed Tomography May Be an Important Predictor of Early Post-Endoscopic Variceal Ligation Bleeding .............................................................. 448
  Young Il Hwang, Ki Tae Yoon, Mung Cho, Naweewong Ryu, Tae Un Kim

PE-110 Prognosis of Surgical Hemia Repair in Cirrhotic Patients with Refractory Ascites .............................................................. 448
  Sun Wiong Kim¹, Minseok Albert Kim¹, Hee Jun Jang¹, Yun Bin Lee¹, Eun Ju Choi¹, Jeong-Hoon Lee¹, Su Jong Yu¹, Jung-Moo Yoon¹, Kyu Joo Park¹, Yoon Jun Kim¹

PE-111 The Impact of Liver Cirrhosis on the Mortality in Intensive Care Unit Patients .............................................................. 449
  Chen-Chang Liao, Dr. Liang Chen

PE-112 Changing Trends in Epidemiology and Clinical Outcomes in Liver Cirrhosis in Korea: Eight Years Data in Single Center Study .............................................................. 449
  Sunmin Kim, Je Hyun Yoon, Chung-Keun Joo, Sung Bum Cho, Sung Kyo Choi, Hee Jun Kim

PE-113 Laparoscopic Management of Cholelithiasis in Patients with Chronic Liver Disease: A 10-Year Experience .............................................................. 450
  Saubab Babhup, Purneet Mahajan, Soinder P. S. Bains, Shailu Ravi, V. Lokha, N. Ramdev

PE-114 Helicobacter Pylori Infection in Cirrhotic Patients with Portal Hypertensive Gastropathy .............................................................. 451
  Pyuo Sin Aye, Yazar Tun, Naing Lin, Yan Lynn Myint, Nwe Ni

Liver Failure, Acute

PE-115 Biofabricated Silver Nanoparticles of Aqueous Extract of Bassia Longifolia L Leaves Mitigates Diethylnitrosamine Induced Hepatocellular Carcinoma in Wistar Rats: A Novel Approach for Liver Therapy .............................................................. 451
  Deepika Singh, Manvendra Singh, Pradeep Kumar

www.theliverweek.org xliii
Liver, Infectious Disease

**PE-116**
Downregulation of PGC-1 Leads to Decreased Expression of Mitochondrial Antioxidant Enzymes in the Mouse Model of Obstructive Cholestasis
Say-June Kim, Jung Hwan Park

**PE-117**
The Role of P-JNK Expression on Hepatocyte Necrosis and Autophagy in the Cholestatic Liver
Say-June Kim, Bong Jun Kook

**PE-118**
Antioxidant Action of Hypoxic Conditioned Media from Adipose-Derived Stem Cells in the Hepatic Injury of Expressing Higher Reactive Oxygen Species
Say-June Kim, Kee Hwan Kim

**PE-119**
Effect of Extracorporeal Bioartificial Liver Support System on Fulminant Hepatic Failure Rabbits
Nurathan Kiyic; Samat Issakov

**PE-120**
Immunocorrecting Action of Roncoleukin in Patients with Acute Cholangitis in Various Ways of Application
Talga Bagdymzhau, Rymakhunov M.S., Moosh N.M.

**PE-121**
Acute Liver Failure in Kazakhstan
Zhamal Kyzylbayeva, Yermakhan Asylkhanuly

**PE-122**
Acute Liver Rejection Values of Doppler US Measurements
Yermakhan Asylkhanuly, Namakhun Asylkhanuly

**PE-123**
Organs Failure Prevention for Patients with Hepatorenal Syndrome
Aidos Kyzylkhanova

**PE-124**
The Characteristics of Acute-on-Chronic Liver Failure Patients Based on Two Different Definitions: Prospective Korean Acute-on-Chronic Liver Failure Study
Do Seon Song, Hee Yoon Kim, Young Joo Ye, Dong Hyun Sihn, Eileen L. Yoon, Chang Won Kim, Young Kuk Jung, Ki Tae Suk, Sang soo Lee, Hyeon Chin Cho, Chang Hyo Eung Lee, Hee Young Kim, Seo Hun Kim, Bae Eui Jin, Hyung Joon Yim, Sung Eun Kim, Sung Won Lee, Jung Hyun Kwon, Soon Koo Bak, Byung Soon Lee, Jae Young Jang, Jeech Chi So, Hyung Soo Kim, Seung Woon Nam, Hyook Chun Kim, Young Seok Kim, Sung Gyune Kim, Hye Suk Chae, Sin Mi Yang, Jou Yoon Sohn, Jung Gil Park, Heon Ju Lee, Yoon Jun Kim, In Hee Kim, Ju Yoon Cho, Man Woo Kim, Sang young Nam, Won Kim, Dong Jun Kim, on behalf of the Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

**PE-125**
Production of Steroid Drug Precursor Used in Treatment of Chronic Liver Diseases
Ginsh Hwanghuy, Anjan Syed Danesh, Rabil Shtrikhar

---

**LIVER, INFECTIOUS DISEASE**

**PE-126**
Pattern of Liver Disease at Tertiary Level Care in Nepal: Hospital Based Retrospective Study
Satya Narayan Yadav, Sanjit Karki

**PE-127**
Possibilities of Application of Endoscopic Techniques in the Diagnosis and Treatment of Echinococcosis of the Liver
Askhat Setibekhanov, B. Kuanyshbaev, Bauhtan

**PE-128**
Atypical Liver Resections in Liver Alveococcosis
Rokaya Sorou

**PE-129**
Surgical Aspects Treatment of Liver Echinococcosis
Bauhtan Kuanishbaev, M. Abay

**PE-130**
A Case of Acute Hepatitis E Mimicking Autoimmune Hepatitis
Khidir Yoo, Young rim Kim

**PE-131**
HIV-HCV Coinfection: Prevalence and Associated Risk Factors in the Western Region of Nepal
Bhupendra Sharma, Sanjib Mani Regmi, Surendra Joswad, Krishna Gurung, Manita Khaling Rai

**PE-132**
Seroprevalence of Hepatitis C Virus and Tuberculosis Co-Infection among HIV Infected Individuals
Sabina Rana Bhuyel, Manisha Shrestha, Srijana Sapkota, Sujan Sharma, Sunil Lamot, Ushika Maharjan, Asmita Kumar Sah, and Surendra Joswad

**PE-133**
Morphology and Histopathological Study of a Liver, Having Inflamed Left and Quadrant Lobe
Proja Garg, Sanjit Ghatak

**PE-134**
The Urinary Tract Infection with Liver Cirrhosis Patient
Bor Eiderine Durzyev, Bakhtetseg Sergelen

**PE-135**
Acute Cholestatic Hepatitis Induced by Epstein-Barr Virus Infection in an Adult
Kyoung Min Sohn

**PE-136**
Laparoscopic Liver Echinococcetomy
Yerdal Umekiev, Asjet Yelemessov

**PE-137**
A Beneficial and Protective Effect of Carica Papaya Leaves Extract on Rat Peritonitis Model
Mith Kumar, RK Khanna
## Contents

**NAFLD, Basic**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>461</td>
<td>Hepatocyte Targeted shNLRP3 Nanobiologics Facilitated Local Suppression of NLRP3 Inflammasome in the Liver and Reduced Nonalcoholic Steatohepatitis</td>
<td>Jingyun Luan, Wei Chen, Dannan Xu</td>
</tr>
<tr>
<td>462</td>
<td>NAFLD Screening among Newly Diagnosed Diabetics in Dornod Province, Mongolia</td>
<td>Tsedegmaa Damdinsuren, Ryenchindorj Erkhembayar</td>
</tr>
<tr>
<td>463</td>
<td>Ameiorating Liver Fibrosis Using the Secretome Released from miR-122 Transfected Adipose-Derived Stem Cells in an Animal Model</td>
<td>Koo-Hwan Kim, So-Yeon Kim</td>
</tr>
<tr>
<td>464</td>
<td>Association of Coffee and Caffeine Consumption with Fatty Liver Disease, Nonalcoholic Steatohepatitis, and Degree of Hepatic Fibrosis</td>
<td>Darkhan KOPZHASSARULY, Bauyrzhan DARZHIGENOV</td>
</tr>
<tr>
<td>465</td>
<td>Chorionic Plate-Derived Mesenchymal Stem Cells Attenuate Hepatic Steatosis via Restoration of Mitochondrial Function</td>
<td>Yun Bin Lee, Se-Ni Jung, Jae Hee Han, Gil Jin Kim, Jang-Hoon Yoon</td>
</tr>
<tr>
<td>466</td>
<td>Oxidized Lipoproteins Induce Accumulation of Oxidized Triglycerides and Cholesteryl Ester in Lipid Droplets of Liver Cell</td>
<td>Rojent Shrestha, Zhen Chen, Nihotosh Chiba, Shu-Ping Hui</td>
</tr>
<tr>
<td>467</td>
<td>Could Cholecystectomy Facilitate or Augment Non-Alcoholic Fatty Liver Disease? Association or Causal Relationship?</td>
<td>Wasim Khalid Saeed</td>
</tr>
<tr>
<td>468</td>
<td>Hepatocyte-Targeted shNLRP3 Nanobiologics Facilitated Local Suppression of NLRP3 Inflammasome in the Liver and Reduced Nonalcoholic Steatohepatitis</td>
<td>Kyungsoo Jung, Bae Soo Kim, Min Ji Kim</td>
</tr>
<tr>
<td>469</td>
<td>CJ-14199, a Novel Ileal Bile Acid Transporter Inhibitor for Non-Alcoholic Steatohepatitis</td>
<td>Jin Wook Hong, Kyungsoo Jung, Dong-Hoon Kim, Jeong-Soo Kim, Seung-Kyu Lee</td>
</tr>
</tbody>
</table>

**NAFLD, Clinical**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>461</td>
<td>Comparison of the Efficacy of Ursodeoxycholic Acid (UDCA) versus Vitamin E plus Vitamin C in Non-Diabetic Patients with Nonalcoholic Steatohepatitis (NASH)</td>
<td>Tato Khachadze, Gocha Barabadze, Manana Khachadze, Gela Sulbadze, Koba Bumadze</td>
</tr>
</tbody>
</table>
PE-160  Study of Biochemical and Oxidative Stress Markers in the First-Degree Relatives of Persons with Type 2 Diabetes Stratified by Glucose Tolerance Test

Dhananjay Yadav, Meerambika Mishra, Seema Rana, GBKS Prasad

PE-161  Association with Low Psoas Muscle Area and Non-Alcoholic Fatty Liver Disease in Patients with Inflammatory Bowel Disease

Min Kyu Kang, Jang Gil Park, Kyung Ok Kim, Byung-Jin Jung

PE-162  Nonalcoholic Fatty Liver Disease and Sarcopenia Are Independently Associated with Cardiovascular Risk

Eugene Han, Yong-Ho Lee, Young Dae Kim, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Byung-Woo Lee, Eun Seok Kang, Bong-Soo Cha, Kwang-Hyub Han, Hyun Suk Nam, Ji Hae Ha, and Seung Up Kim

PE-163  Sarcopenia Is Independently Associated with the Degree of Liver Fibrosis in Patients with Type 2 Diabetes Mellitus

Min-Je Sung, Tae Seop Lim, Mi Young Joon, Hye Won Lee, Beom Kyung Kim, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Jun Yong Park, and Seung Up Kim

PE-164  Lean Nonalcoholic Fatty Liver Disease and Development of Diabetes Mellitus: A Cohort Study

Dong Hyun Sim, Joo Hyoung Oh, Danbee Kang, Soo-Jin Cho, Seung-Woong Park, Elene Guallar, Juhee Choi, Geum-Youn Gwak

PE-165  Routinely Available Noninvasive Tests Discriminate Advanced Fibrosis Due to NASH in the Phase 3 STELLAR Trials of the ASK1 Inhibitor Selonsertib


PE-166  Clinical Utility and Application of Noninvasive Tests in Selecting Patients with Advanced Fibrosis Due to NASH in the Phase 2 ATLAS Trial


PE-167  Atrial Fibrillation Is Associated with Advanced Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease

Min Kyu Kang, Jang Gil Park

PE-168  Prevalence of Pre-Diabetes, Diabetes, Abdominal Obesity and Hypertension among the Service Communities of Bhilai City of India

Nutan Yadav, Deepak Kumar

PE-169  Nonalcoholic Steatohepatitis Is Associated with a Higher Risk of Advanced Colorectal Neoplasm

Sang Wook Lim, Jaemin Han, Dong Hyun Lee, Sang Kyung Suh, Yong Min Jung, Byong Gwan Kim, Won Kim

PE-170  Weight Loss Significantly Reduces the Risk of Chronic Kidney Disease Development

Young Eun Chon, Seung Gyu Haung, Kyo Sang Rim, Mi Na Kim, Joo Ho Lee, Heung Jung Kim, Hyung Joon Kim, Yo Bum Choi, and Mi Jung Lee

PE-171  The Invasive and Noninvasive Assessments for Liver Fibrosis in Korean Nonalcoholic Fatty Liver Disease Patients

Se Yoon Kim, Sang Young Han, Sang Yoon Baek, Sang-Wook Lee, and Mi Sook Jeong

PE-172  The Grade of Nonalcoholic Fatty Liver Disease Is an Independent Risk Factor for Gallstone Disease

Young Kyu Kim, Kye Hee Hur

PE-173  Appropriateness of Liver Biopsy for Nonalcoholic Fatty Liver Disease during Laparoscopic Cholecystectomy for Gallstone Disease

Kwang Sik Kim, Sang-Hyub Han, Ji Hye Nahir, Do Young Kim, Seung Wook Park, Young Jun Park

PE-174  Risk Factors for Incident Nonalcoholic Fatty Liver Disease and Liver Fibrosis in Breast Cancer Survivors

Hei Young Kim, Woonsoong Lim, Byung-Ho Moon, Hye Ah Lee

PE-175  Features of the Prevalence of Risk Factors for Non-Alcoholic Fatty Liver Disease among Residents of the City of Bishkek (Kyrgyzstan)

Saqib Uzair, Bezbotschna Byzubayeva

PE-176  Serum Biomarkers to Differentiate Non-Alcoholic Steatohepatitis, Advanced Fibrosis, and Severe Steatosis from Mild Form of Non-Alcoholic Fatty Liver Disease

Ha Seok Lee, Sung Won Chang, Sehwa Kim, Min-Jin Lee, Young-Sun Son, Sang Jun Sul, G Ho Moon, Heon Seok Lee, Chang Young Jin, Jung Eun Yeri, Soon Ho Uhm, Kwan Soo Byun

PE-177  The High Occurrence of Non-Alcoholic Steatohepatitis in Patients with Moderate Fatty Liver Accompanied by Metabolic Syndrome

Dong Hoon Lee, Soo Hyung Ryu, Yun Jee Shin, Bo Kyung Lee, Young Sun Na, Baeun Kim, Ohwah An, Tae Yong Park, Jeong Seok Moon

PE-178  The Value of Controlled Attenuation Parameter in Fibrosis Prediction by Liver Stiffness in Nonalcoholic Steatohepatitis

Seon Kim, Jung J Lee, Hwa Boong Lee, Kiwan Sik Lee

PE-179  Predictors of Sarcopenia in Obese Korean Population

Min Je Sung, Hye-Won Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, and Seung Up Kim

PE-180  Putative Relationship between Changes in Body Composition and Metabolic Characteristics under Lifestyle Intervention in Patients with Nonalcoholic Fatty Liver Disease

Jung Lim, Hei Young Kim, Hye Ah Lee, Joon Yeol Nam, Tae Hun Kim, and Kwan Yoo
Liver Cancer, Clinical

PE-202 Association between the Korean National Cancer Screening Program and Liver Cancer-Related Death ................................................................. 491
Gi-Ae Kim, Jae-Jun Shim, Eunhye Kang, Byung-Nor Kim

PE-203 Cytochrome P450 4A11 Expression in Tumor Cells: A Favorable Prognostic Factor for Hepatocellular Carcinoma Patients .............................................. 492
Hyuk Soo Eun, Sang Yeon Cho, Byung Seok Lee, Sun Kim, In-Sang Song, Kwang-Hyun Chun, Cheong-Nae Oh, Min-Kyu Ye, Seok Hyun Kim, and Kyung-Hye Kim

PE-204 Profiling Cytochrome P450 Family 4 Gene Expression in Human Hepatocellular Carcinoma ........................................................................................................ 492
Hyuk Soo Eun, Sang Yeon Cho, Byung Seok Lee, In-Cuk Seong, Kyung-Hye Kim

PE-205 Quantified Hepatic Stiffness by MR Elastography Is a Marker for Early Recurrence in Patients with HCC within the Milan Criteria ........................................ 493
Hyo Jung Cha, Bo Hyun Kim, Hee Jin Kim, Jini Huh, Jai Kon Kim, Je Hee Lee, Chul Won Sun, Young-Hwan Ahn, Jinhee Jung, Jung Wook Soo, Soon Sun Kim, Wan Sung Cho, and Jae Yong Cheong

PE-206 Antiviral Treatment Status at Hepatocellular Carcinoma Development Affects Overall Survival in Chronic Hepatitis B Patients ........................................ 493
Tae-Si Kim, Dong Hyun Shin, Wonseok Kang, Gwon-Young Gwook, Yong-Han Park, Moon Seek Choi, Joon Hyok Lee, Kwang Chek Koh, and Seung Woon Park

PE-207 Hepatitis C Virus Genotype Affects the Survival of Patients with Hepatocellular Carcinoma ........................................................................................................... 493
Bo Ra Kim, Sang Soo Lee, Hee Kyung Park, Chang Bin Im, Changso Im, Il Ri Cha, Wan Soo Kim, Jae Min Lee, Hyun Jin Kim, Tae Hyo Kim, Woon Tae Jung, Ok-Jae Lee

PE-208 Factors Associated with Postprogression Survival in Advanced Hepatocellular Carcinoma Patients with Post-Sorafenib Progression Not Eligible for Regorafenib ................................................................. 494
Hee Yeon Kim, Chang Wook Kim, Sang Wook Choi, Do Seon Song, U I Chang, Jin Mo Yang, Sung Won Lee, Han Lim Lee, Nam I Han, Sun Hog Yoo, Jung Hyun Kwak, Soon Woon Nam, Pil Soo Sung, Jeong Woon Jung, Si Hyun Bae, Jong Young Choi, Seung Woon Yoon

PE-209 Diagnostic Value of Protein Induced by Vitamin K Absence in Hepatocellular Carcinoma Patients with Normal Alpha-Fetoprotein Level ..................................... 494
Cong Long Nguyen, Young-Khun Yu, Min-Deep Lu, Nghi Thanh Nguyen, Thanh Nam Nguyen, Minh Dap Vu

PE-210 Comparing Characteristics, Treatment Outcomes of Non-B Non-C Virus and Hepatitis Virus-Related Hepatocellular Carcinoma ................................................. 495
Dong Duc Nhoang

PE-211 Lenvatinib Is Independently Associated with the Reduced Risk of Progressive Disease When Compared to Sorafenib in Patients with Hepatocellular Carcinoma .......... 495
Kyung Hyun Kim, Boom Kyung Kim, Jun Yong Park, Sang Hoon Ahn, Kwang-Hyub Han, Do Young Kim, and Seung Up Kim

PE-212 Substantial Risk of Hepatocellular Carcinoma Recurrence Even after Five Years of No-Recurrence Period among Early Stage Hepatocellular Carcinoma Patients Treated with Resection or Radiofrequency Ablation ................................................................. 496
Juye Kim, Wonseok Kang, Dong-Hyun Sim, Grum-Yoon Gwook, Yong-Han Park, Moon Seek Choi, Joon Hyok Lee, Kwang Chek Koh, Seung Woon Park

PE-213 Indications for Endoscopic Screening and Prophylaxis of Esophageal Varices in Patients with Hepatocellular Carcinoma Invading Portal Vein ................................................................. 496
Juye Kim, Ki Joon Kim, Jo Hyun Shim, Insoo Cho, Dany Lee, Kang Mo Kim, Young-Suk Lim, Han Chu Lee, Young-Na Chung, Yang Sung Lee, and Dong Jin Suk

PE-214 Alpha-Fetoprotein L3 Level, Not an L3 Fraction, is a Useful Marker for the Diagnosis of Hepatocellular Carcinoma ................................................................. 496
Han Ah Lee, Hoon Gil Cho, Ta Hyung Kim, Sun Young Yim, Soon Sun Lee, Sang Jun Soh, Young Kui Jung, Ji Hee Kim, Yeon Seok Seo, Hwang Joon Yun, Jung Eun Yeon, Kwan Soo Byun, Soon Ho Lim

PE-215 Clinical Manifestations and Prognosis of Non-Cirrhotic and Cirrhotic Hepatocellular Carcinoma Patients with Chronic Hepatitis B ........................................... 497
Jung Hwan Yu, Jangseog Shin, Young-Joo, Jin-Woo Lee

PE-216 Albumin-Bilirubin Grade Can Subclassify Patients with a Child-Pugh Score of 5 Treated with Sorafenib for Hepatocellular Carcinoma ........................................... 497
Hye Yeon Kim, Chang Wook Kim, Sang Wook Choi, Do Seon Song, U I Chang, Jin Mo Yang, Sung Won Lee, Han Lim Lee, Nam I Han, Sun Hog Yoo, Jung Hyun Kwak, Soon Woon Nam, Pil Soo Sung, Jeong Woon Jung, Si Hyun Bae, Jong Young Choi, Seung Woon Yoon

PE-217 Differentiation between Hepatocellular Carcinoma and Other Hepatic Malignancies in Cirrhosis: Performance of LI-RADS 2018 ........................................... 498
Yeun-Yoon Kim, Myeong-Jin Kim, Eun Hwa Kim, Young-Joo, Jin-Woo Lee

PE-218 Epidemiological and Clinical Features of Patients with HCC in Mongolian and Russian Population .............................................................................................. 498
Bastarkhuu, Q. Tsogtshamba Ochir, Iyon Malovi, Evgeniy Savilov, Sergey Malovi, Radion Rasulov, and Viktoria Osmyreshenba, Ariunaa Kh, Sanduijav R, and Baasanjav N

PE-219 Management of Hepatocellular Carcinoma in Mongolia ..................................................................................................................................................... 498
Anzhurin Khaisbars, R. Sanduijav, Baasanjav N, and D. Bastarkhuu

PE-220 Evaluation of the American Joint Committee on Cancer (AJCC) 8th Edition Staging System for Hepatocellular Carcinoma in 1,034 Patients with Curative Resection ................................................................. 499
Sang Yun He, Suji Park, Sangkun Choi, Dong Hyun Sim, Jong Man Kim

PE-221 Application of Multimodal Image Fusion Technology in the Diagnosis and Treatment of Intrahepatic Cholangiocarcinoma ...................................................... 499
Chihua FANG

PE-222 An Astonishing Familiar Cluster of Intrahepatic Cholangiocarcinoma (ICC) in Wilson’s Disease (WD) .............................................................................................. 500
Giovanni Brandi, Alessandro Rizzi, Andrea Pallotti, Simone Abbati, Francesca Vascari, Stefania De Lorenzo, Giorgio Frega, Francesco Vascari, Annalisa Astemi, Valentina Indio, Francesco Tovoli, Matteo Cesscon
Contents

PE-223 Serologic Detection of Autoantibodies from Patients with Cholangiocarcinoma by Proteomic Approach ................................................................. 500
Mohammad Zahid MUSTAFA, Zunera TANVEER, Eric BALLOT, Jean Charles DUOIS VALLEE

PE-224 Predictive Factors and Treatment Outcome for Recurrent Intra-Hepatic Cholangiocarcinoma ................................................................. 501
Yangen CHANG, Chun-Yi TSAI, Shao-Yu WANG, Kun-Ming CHIH, Wei-Chen LEE, Ts-I-Ching CHEN, Yi-Ting JAN, Chun-Nan YEH, Te-Sen YEH

PE-225 Efficacy of Sorafenib Alone and in Combination with Rapamycin Inhibitors for Post-Liver Transplant Recurrence of Hepatocellular Carcinoma: A Single Center Experience ................................................................. 501
Ji Hoon Park, Jae Seung Lee, Je Geun Lee, Beom Kyung Kim, Seung Up Kim, Dong Jin Joo, Do Young Kim, Sang Hoon Ahn, Myoung Soo Kim, Soon Il Kim, Kwang-Hyub Han, and Jun Yong Park

PE-226 Initial Real-Life Experience of Nivolumab Treatment for Patients with Advanced or Metastatic Hepatocellular Carcinoma after Sorafenib Failure ...................... 502
Jin Won Chang, Jae Seung Lee, Beom Kyung Kim, Seung Up Kim, Do Young Kim, Sang Hoan Ahn, Kwang-Hyub Han, and Jun Yong Park

PE-227 The Risk of Hepatocellular Carcinoma (HCC) after DAA Treatment for Hepatitis C Virus (Clinical Case) ................................................................. 502
O. Bastaresh, Z. Banyaev, B. Dalguan, R. Amurana

PE-228 Hepatocellular Carcinoma in Old Age – Are There Any Benefits of Resection of Liver in Old Age? ................................................................. 502
In Se Shin, Dong Ge Kim, Sang Woon Cha, Seong Hee Kang, Sang Hoan Kim, Moon Young Kim, Soon Joo Bok

PE-229 Postoperative Infectious Complications Decrease Overall and Recurrence-Free Survival in Patients Undergoing Liver Resection for Hepatocellular Carcinoma .......... 503
Jong Ye Yu, Ziem Li Li, Qin ZHANG, Lei LIANG, Chao Li, Ming-Dai WANG, Wan Yee LEE, Yong Yi ZENG, Tao Hao ZHOU, Jun HAN, Feng SHEN, Tian YANG

PE-230 Real-Time Navigation for Laparoscopic Hepatectomy Using Image Fusion of Preoperative 3D Surgical Plan and Intraoperative Indocyanine Green Fluorescence Imaging ................................................................. 503
Chihua FANG

PE-231 Three-Dimensional Visualization Evaluation and VR Study of Giant Liver Cancer with Blood Vessels as the Axis ................................................................. 503
Chihua FANG

PE-232 Application of Three-Dimensional Visualization, VR Technology, Combined with ICG Molecular Fluorescence in Hepatocytomy under Non-Vascular Occlusion for Centrally Located Hepatocellular Carcinoma ................................................................. 503
Chihua FANG

PE-233 Is the Outcome after Hepatectomy for Hepatocholangiocarcinoma Different from That of Classic Hepatocellular Carcinoma and Mass-Forming Cholangiocarcinoma? A Case-Matched Analysis ................................................................. 504
Damiano GENTILE, Matteo DONADON, Luca Di Tomasso, Angela PALMISANO, Matteo CROW, Jacopo GALLA, Bruno BIANCOSPROI, Guido TORZILLI

PE-234 ALPPS versus Two-Stage Hepatectomy (TSH): Indications, Safety, Efficacy ........................................................................................................... 504
Andrey KAPRIN, Dmitriy SIDOROV, Mikhail LOZHKIN, Aisha ISAEVA

PE-235 ALPPS Procedure in 20 Patients with Primary and Metastatic Malignancies: Single Centre Experience ........................................................................... 505
Andrey KAPRIN, Dmitriy SIDOROV, Mikhail LOZHKIN, Aisha ISAEVA

PE-236 Surgical Tactics for Colorectal Cancer with Synchronous Liver Metastases ........................................................................................................ 505
Muzaffar Eralan, Mamanshev Nural, Bezbegov Bakhadyr, Suvor Edzi, Manzhankulov Rauan

PE-237 Immediate Results of Surgical Treatment Hepatocellular Carcinoma ............................................................................................................. 506
Mamanshev Nural, Bezbegov Bakhadyr, Muzaffar Eralan, Suvor Edzi, Enekvulov Chynzg, Muzaffar Eralan

PE-238 The Current Status of Selecting Treatment Modalities for Naive Hepatocellular Carcinoma Patients over 70 Years Old: Single-Center Experience .................. 506
Kjong-Sik KIM, Je Suk HYUN, Seoung Yoon RHO

PE-239 A Current Status of Therapeutic Choice and Feasibility for Hepatocellular Carcinoma Patients over 70 Years Old ........................................................................ 506
Seoung Yoon RHO, Kjong-Sik KIM, Do Young Kim, Hyun Woong Lee

PE-240 Survival According to Recurrence Patterns after Resection for Transplantable Hepatocellular Carcinoma in HBV Endemic Area: Appraisal of Liver Transplantation Strategy ........................................................................ 507
Sun Young Kim, Chung Gyo Seo, Hoo In Lee, Tae Hyung Kim, Young Sun Lee, Sang Jun Soh, Na Heon NAM, Heon Seok Seo, Ji Hoon Kim, Hyung Joon Kim, Dong Sik Kim, Soon Il Kim

PE-241 The Meaning of Enhanced Liver Fibrosis (ELF) Score as a Predictive Factor for HCC Patient after Liver Resection ......................................................... 508
Abshandeer Mare Husein M, Dai Hoon Han, Gi Hong Choi, Jin Sub Choi

PE-242 Long-Term Post-Resection Prognosis of Primary Neuroendocrine Tumors of the Liver ............................................................................................... 508
Jai Jong, Shin Haeng, Seoung-Mo Hong, Ki Hun Kim, Chul-So Ahn, Deok-Bog Moon, Tae Yong Ha, Gyu-Won Song

PE-243 Development and Validation of Novel Scoring System for the Prediction of Disease Recurrence Following Resection of Colorectal Liver Metastasis ........................................................................................................ 508
Wan-Joon KIM, Tae-Wan KIM, Sang-Hee KANG, Pyoung-Jae PARK, Se-Ryul CHOJ, Sun-JI LEE, Byung-Hook MIN, Wan-Bae KIM

PE-244 Surgical Strategies of Huge Hepatocellular Carcinoma with Main Portal Vein Thrombosis: A Case Report ............................................................................. 509
Cheon Soo PARK
<table>
<thead>
<tr>
<th>PE-245</th>
<th>Outcomes after Robotic Donor Hepatectomy in 48 Consecutive Live Donors</th>
<th>509</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secoung Yoon RHO, Jae Geon LEE, Dai Hoon NAH, Dong Joo JO, Myeong Soo KIM, Seok Soon KIM, Jin Sub CHO, Gi Hong CHOY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-246</td>
<td>Synchronous Resection of Colorectal Cancer Liver Metastasis: Propensity Score Matching of Open Versus Minimally Invasive Surgery</td>
<td>509</td>
</tr>
<tr>
<td>Secoung Yoon RHO, Dai Hoon NAH, Jin Sub CHO, Gi Hong CHOY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-247</td>
<td>Treatment of Resectable Hilar Cholangiocarcinoma: A Choice of Right- or Left-Side Hepatectomy</td>
<td>510</td>
</tr>
<tr>
<td>Hye-Sung JI, Dong-Sik KIM, Yoo-Hyung KAN, Kyoung Chul YOON, Young-Dong YU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-248</td>
<td>Hypothermic Perfusion Hepatectomy for Unresectable Liver Cancer: A Single-Center Experience</td>
<td>510</td>
</tr>
<tr>
<td>Yoonhyung YOON, Sung-Gyu LEE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-249</td>
<td>Prognostic Analysis of Hepatocellular Carcinoma Greater than 5cm in Diameter after Curative Resection</td>
<td>510</td>
</tr>
<tr>
<td>Jee Do YANG, Hee Chul YU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-250</td>
<td>Preoperative Glasgow Prognostic Score (GPS) as a Predictor of Poor Prognosis in Synchronous Colorectal Cancer Liver Metastasis</td>
<td>511</td>
</tr>
<tr>
<td>Soon Ha Kwon, Sang Ho BAE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-251</td>
<td>Computed Tomograph Imaging Features and Early Response of Hepatocellular Carcinoma Treated by Transarterial Chemoembolization with Drug Eluting Beads</td>
<td>511</td>
</tr>
<tr>
<td>Dong Duc Hoang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-252</td>
<td>Clinical Outcomes after Risk-Adapted Proton Beam Therapy Using Three Dose-Fractionation Regimens for Hepatocellular Carcinoma</td>
<td>511</td>
</tr>
<tr>
<td>Tae Hyeun Kim, Jong-Won Park, Bo Hyun Kim, Hyejin Jung Kim, Sang Ho Moen, Sang Soo Kim, Sang Myung Woh, Young-Hwan Kho, Woo Jin Lee, Dae Yong Kim, Chang-Min Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-253</td>
<td>Clinical Outcomes of Stereotactic Body Radiation Therapy for Single Viable Hepatocellular Carcinoma at the Site of Incomplete Transarterial Chemoembolization</td>
<td>512</td>
</tr>
<tr>
<td>Jungtao Jung, Hye Hyeon Park, So Yeon Kim, Young-Suk Lim, Han Cho Lee, Jin Hong Park, Jong Hoon Kim, Sang Min Iyon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-254</td>
<td>Yttrium-90 Radioembolization May Have Better Efficacy in Progression-Free Survival and Disease Control Rate in Patients with Hepatocellular Carcinoma Compared with Conventional Chemoembolization: A Retrospective Cohort Study</td>
<td>512</td>
</tr>
<tr>
<td>PE-255</td>
<td>Safety of Transarterial Chemoembolization in Patients with Recurrent Hepatocellular Carcinoma after Liver Transplantation</td>
<td>513</td>
</tr>
<tr>
<td>Jia Eun Lee, Bo Hyun Kim, Seoung Hoon Kim, Joong Lee, Hyun-Bae Kim, Jong-Whi Park</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-256</td>
<td>An Earlier Follow-Up Imaging Was Not Associated with Better Overall Survival after Transarterial Chemoembolization for Intermediate- or Advanced-Stage Hepatocellular Carcinoma</td>
<td>514</td>
</tr>
<tr>
<td>Heejoon Jang, Heejoon Jang, Minsook Albert Kim, Sun Woong Kim, Cheol-Hyung Lee, Yun Bin Lee, Eun Ju Cho, Myeongsoo Lee, Soo Jong Yu, Hye-Chool Kim, Yoon Jun Kim, Jin Wook Chung, Jung-Hwan Yoon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-257</td>
<td>Survival Outcomes of TACE in Treatment-Naïve and Recurrent HCC after Curative Resection: A Propensity Score-Matched Analysis</td>
<td>515</td>
</tr>
<tr>
<td>David Sooh Kim, Tae Seup Lim, Mi Young Jeon, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Ockdo Baek, and Seung Up Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-258</td>
<td>Establishment and Validation of a Risk Prediction Model in Patients with Hepatocellular Carcinoma Treated with Trans-Arterial Radioembolization</td>
<td>515</td>
</tr>
<tr>
<td>Jae Seung Lee, Nan Ah Lee, Mi Young Jeon, Tae Seup Lim, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Soon Ho Um, Kwang-Hyub Han, Yeon Seok Seo, and Seung Up Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-259</td>
<td>Predictors of Radiological Complete Response in Patients with Intrahepatic Hepatocellular Carcinoma Treated with Transarterial Radioembolization</td>
<td>516</td>
</tr>
<tr>
<td>Yoon Ah Kim, Jae Seung Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, and Seung Up Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-260</td>
<td>Digital Subtraction Angiography Outcome during DC Bead Transarterial Chemoembolization for Hepatocellular Carcinoma</td>
<td>516</td>
</tr>
<tr>
<td>Yoon Ah Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-261</td>
<td>Curative Treatment after Transarterial Radioembolization is Associated with Better Survival Outcomes in Patients with Hepatocellular Carcinoma</td>
<td>516</td>
</tr>
<tr>
<td>Yoon Ah Kim, Nan Ah Lee, Jae Seung Lee, Mi Young Jeon, Beom Kyung Kim, Young Ki Jung, Jun Yong Park, J Hoon Kim, Yeon Seok Seo, Do Young Kim, Hyoung Joong Yim, Sang Hoon Ahn, Jong Eun Yeon, Kwan Soo Byun, Soon Ho Um, Kwang-Hyub Han, and Seung Up Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-262</td>
<td>Role and Limitation of Hepatic Arterial Infusion Chemotherapy</td>
<td>517</td>
</tr>
<tr>
<td>Beom Hui LEE, Dong-Shik LEE, Chan-Woo CHO, Sung-Soo YUN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-263</td>
<td>Laparoscopic Right Hepatectomy Is Feasible and Safe in Solitary Hepatocellular Carcinoma</td>
<td>517</td>
</tr>
<tr>
<td>Hoang Duc Nam, Juong Man Kim, Gyu-Seong Choi, Jae-Won Jih</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Biliary and Pancreatic Disease**

<table>
<thead>
<tr>
<th>PE-264</th>
<th>Predicting the Choice of Operative Treatment for Common Bile Duct Diseases Complicated by Obstructive Jaundice</th>
<th>518</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valeri Vladimirovich Boyko, Yuriy Vladimirovich Avdosyev, Anastasia Lioua Sochneva, Maria Seragira Makarevich</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Contents

PE-265 The Value of Serum Levels of Procalcitonin for Predicting the Severity of Acute Pancreatitis in Patients According to the 2012 Revised Atlanta Classification ................................................................. 518
LE THI THAO NEN, LE QUOC TUAN
PE-266 Statins Use Is Associated with Reduced Risk of Cholangiocarcinoma: A Systematic Review and Meta-Analysis ................................................................. 519
Gaurav Nepal
PE-267 Molecular Characteristics Associated with 18F-FDG Uptake in Intrahepatic Cholangiocarcinoma ................................................................. 519
Keun Soo Ahn, Kiu Jeong Kang, Yong Ho Kim, Tae Seok Kim, Kyoung Sook Won
PE-268 Risk Factors Associated with Locoregional Failure and Estimation of Survival after Curative Resection for Patients with Distal Bile Duct Cancer ................................................................. 520
K. Jae Lee, Jun Wan Kim, Jung Ho Im, Joon Seong Park, Dong Sup Yoon, Dong K Lee
PE-269 Beneficial Effects of Cassia Angustifolia (Senna Leaves) Treatment Improves Constipation, Liver Functions and Defense of Red Blood Cells in Type 2 Diabetic Patients ................................................................. 520
Sumi Rajput, Sagar Verma
PE-270 Comparison of Surgical Outcomes of Robotic and Laparoscopic Pancreaticojejunostomy after Pancreatoduodenectomy in Patient with a Soft Pancreas: Multi-Institutional Study ................................................................. 521
Sung Hoon Choi, Jie Hoon Lee, Chang Moo Kang
PE-271 Mucinous Cholangiocarcinoma with Hemobilia: A Case Report ................................................................. 521
Hanil CHOI, Jae-Woon CHOI, Dong Hee RYU
PE-272 Gallbladder Paraganglioma with Hemorrhage: A Case Report ................................................................. 521
Sanghwa SONG, Chulkyoon CHO
PE-273 Clinical Outcomes of Robotic Cholecystectomy: Single Center Early Experience ................................................................. 522
Jae Do YANG
PE-274 Differentiation of the Gallbladder Adenomyomatosis from Early-Stage Gallbladder Cancer before Surgery ................................................................. 522
Young Chan SHIN, Jisun MOON
Junghyun PARK, Jin Hyung PARK
PE-276 Laparoscopic Resection of Schwannoma in the Pancreas ................................................................. 523
Yu N LEE, Woa Young KIM
PE-277 Synchronous Ampullary Neuroendocrine Tumor and Extra-Gastrointestinal Stromal Tumor in Association with Neurofibromatosis Type 1: A Case Report ................................................................. 523
Eunkyo PARK
PE-278 Benefits and Pitfalls of Surgical Resection after Downstaging Concurrent Chemoradiation Therapy in Patients with Locally Advanced Perihilar Cholangiocarcinoma ................................................................. 523
Incheon KANG, Yi Hong CHOI
PE-279 Surgical Outcomes of Bismuth Type IV Perihilar Cholangiocarcinoma ................................................................. 524
Incheon KANG, Yi Hong CHOI
PE-280 Minimally Invasive Interventions in Patients with Mechanical Jaundice ................................................................. 524
Altai Metambek, B. Kuanyshbayev
PE-281 Minimally Invasive Endoscopic Technologies in Complex Treatment of Patients with Obstructive Jaundice Syndrome ................................................................. 524
Altaybayev Aliya, Zhaliyev Babek
PE-282 The Efficacy of Single-Stage Endoscopic Treatment of Complicated Forms of Choledithiasis ................................................................. 525
Ukolin Nurbay, Altaybayev Aliya
PE-283 Rare Experience of Complication of a Spilled Gallstone after Laparoscopic Cholecystectomy: Case-Report ................................................................. 525
Eun-Kyoung Jwa, Dong-Lak Choi
PE-284 Iatrogenic Bile Duct Injury Associated with Anomalies of Isolated Right Anterior Segmental Hepatic Duct Injury Following Laparoscopic Cholecystectomy: A Rare Case Report ................................................................. 525
HyoJai Jang, Choon Soo Park
PE-285 PD-L1 Expression in Extrahepatic Biliary Tract Cancers: A Comparative Study Using 22C3, SP263 and E1L3N Anti-PD-L1 Antibodies ................................................................. 526
Soomin Ahn, Yungkyu Lee, Ji Won Kim, Yong-Chan Lee, In-Hyok Hwang, Yoo-Seok Yoon, Jae Young Cho, Ho-Seong Han, YoungRok Choi, Hae Young Kim
PE-286 BLCC ................................................................. 526
Zhanda Amymbayu, Galymzhon Adaakhan, Babek Aldin, Babek Babek
PE-287 The Value of Lymphadenectomy in Surgical Resection of Perihilar Cholangiocarcinoma ................................................................. 527
Lei LIANG, Ming-Da WANG, Hao XING, Chao LI, Jun HAN, Han ZHANG, Wan Yue LAU, Timothy M. PAVLIK, Feng SHEN, Tian YANG

www.theliverweek.org
<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who Can Benefit from Adjuvant Transcatheter Arterial Chemoembolization after Surgical Resection of Hepatocellular Carcinoma?</td>
<td>527</td>
</tr>
<tr>
<td>Exosomal miRNA-106b from Cancer-Associated Fibroblast Promotes Gemcitabine Resistance in Pancreatic Cancer</td>
<td>528</td>
</tr>
<tr>
<td>The Regulation Mechanism of HEATR1 on the Chemosensitivity of Gemcitabine in Pancreatic Cancer</td>
<td>528</td>
</tr>
<tr>
<td>Metformin Inhibited Pancreatic Cancer Growth by Upregulating miR-143/145 Cluster and Suppressing MAPK Signaling Pathway</td>
<td>528</td>
</tr>
<tr>
<td>Acute Pancreatitis Induced by Etoposide-Lobaplatin Combination Chemotherapy Used for the Treatment of Lung Cancer</td>
<td>529</td>
</tr>
<tr>
<td>Exosomes and Pancreatic Diseases: Status, Challenges, and Hopes</td>
<td>529</td>
</tr>
<tr>
<td>Immunogenicity of Neoplastic Cells in PDA (Review)</td>
<td>529</td>
</tr>
<tr>
<td>Pancreatic Stellate Cells Promote Epithelial-Mesenchymal Transition of Cancer Cells by Notch-3 Promoter Demethylation</td>
<td>530</td>
</tr>
<tr>
<td>Smad4 Inhibits Cell Migration via Suppression of KPNA4 and MMP26 in Human Pancreatic Cancer Cells</td>
<td>530</td>
</tr>
<tr>
<td>General Surgery</td>
<td>530</td>
</tr>
<tr>
<td>Lipopolysaccharide Increase PD-L1 Expression in Pancreatic Tumor via TLR4/MyD88/NF-κB Pathway</td>
<td>531</td>
</tr>
<tr>
<td>Circulating Tumor Cells with Epithelial-Mesenchymal Transition Features Predict Metastatic Outcome in Pancreatic Cancer</td>
<td>531</td>
</tr>
<tr>
<td>Serum Lipid Levels and the Risk of Gallbladder Stones: A Population-Based Study in China</td>
<td>531</td>
</tr>
<tr>
<td>Any Time Laparoscopic Cholecystectomy in Moderate to Severe Acute Cholecystitis without Septic Shock: A Prospective Cohort Study</td>
<td>532</td>
</tr>
<tr>
<td>Post Operative Antibiotics Are Unnecessary Even in Moderate to Severe Cholecystitis According to Tokyo Guidelines: A Prospective Cohort Study</td>
<td>532</td>
</tr>
<tr>
<td>Preprocurement Pancreas Allocation Suitability Score Does Not Correlate with Long-Term Pancreas Graft Survival</td>
<td>532</td>
</tr>
<tr>
<td>MicrovesSEL Density and Impact of Angiogenesis on Survival of Resected Pancreatic Cancer Patients: A Systematic Review and Meta-Analysis</td>
<td>533</td>
</tr>
<tr>
<td>Potential Value of Serum Total IgE for Differentiation between Autoimmune Pancreatitis and Pancreatic Cancer</td>
<td>533</td>
</tr>
<tr>
<td>Conservative and Surgical Management of Pancreatic Trauma in Adult Patients</td>
<td>533</td>
</tr>
<tr>
<td>Hepaticojjunostomy (HJ): How We Do It?</td>
<td>534</td>
</tr>
<tr>
<td>Program of Transplant Organization to Coordinate the Development of Organ Donation in Kazakhstan</td>
<td>534</td>
</tr>
<tr>
<td>Frequency and Main Risk Factors of Ventral Site Hernia Development in Patients Liver Transplantation</td>
<td>534</td>
</tr>
<tr>
<td>Portal Vein Thrombosis in Patients with End-Stage Liver Disease on the Waiting List</td>
<td>535</td>
</tr>
</tbody>
</table>
Contents

PE-311 Influence of Adult Living Donor Liver Transplantation on the Waiting List in Kazakhstan ................................................................. 535
    Aigerim Mashypz, Zhankul Senk

PE-312 Pure Laparoscopic Versus Open Right Hepatectomy in Live Liver Donors: A Propensity Score Matched Analysis ........................................ 535
    Suk Kyun Hong, Kyoung-Suk Lee, Jae-Hyung Cho, Jeong-Moo Lee, Nam-Soon Y, Kwang-Woong Lee

PE-313 Survival among Pediatric Liver Transplant Recipients: Impact of Segmental Grafts .................................................................................. 536
    Yerlan Makhambetov, Samat Isakoev

PE-314 Risk Factor of Delayed Hepaticojejunostomy Site Stricture in Pylorus Preserving Pancreatoduodenectomy and Its Predicting Nomogram ................................................................................. 536
    Seong Yeon Rho, He Kyung HWANG, Woon Jung LEE, Chang Miao KANG

PE-315 A Case of Migration of Cyanoacrylate into Portal Vein after Living Donor Liver Transplantation .......................................................... 536
    Hee Yeon Kim, Chang Wook Kim, Soo Ho Lee, Tae Dong Won, Seun Lee

PE-316 Outcome of Living Donor Liver Transplantation for Secondary Biliary Cirrhosis in Adult: Single Center Experience ........................................ 537
    Young HWON, Sung-Gyu LEE

PE-317 Liver Transplantation for Patient with Emergency Indication .................................................................................................................. 537
    SH. Jukanov, A. Kulsharova

PE-318 Machine-Learning Models to Predict Tacrolimus Dosage in Liver Transplant Recipients .......................................................... 538
    Jeong-Moo LEE, Hyung-Chul CHE, Kyoung-Suk HLYN, Suk Kyun HONG, Jae-Hyung CHO, Nam-Soon Y, Kwang-Woong Lee

PE-319 De Novo Malignancy after Liver Transplantation: A Single Center Experience .................................................................................. 538
    Jeong-Moo LEE, Kwang-Woong LEE, Suk Kyun HONG, Je-Hyung CHO, Nam-Soon Y, Kyoung-Suk HWYN

PE-320 The Impact of Extra-Anatomical Hepatic Artery Reconstruction during Living Donor Liver Transplantation in Biliary Complications and Graft and Patient Survival ................................................. 539
    Jinsoo RHO, Jong Man KWIM, Gyu Seong CHO, Jae-Won KIM

PE-321 Living Donor Liver Transplantation Using Right Lobe Graft from a Donor with the Left-Sided Gallbladder Anomaly ................................................. 539
    Sung Yeon HONG, Hee-Jung HWANG, Dong-Won HWYN, Mina KIM, Xue-Shi SHEN

PE-322 The Effect of Downstaging by Local Regional Treatments for Hepatocellular Carcinoma beyond Milan Criteria before Living Donor Liver Transplantation ........................................................................................................ 539
    Byeong-Gon NA, Seong Hoong HWYN, Eung Chang LEE, Sung Jee PARK

PE-323 Effect of Internal Stent Insertion in Duct-to-Duct Biliary Reconstruction to Reduce Bile Duct Complication in Living Donor Liver Transplantation ............................................................................. 539
    Hee Jong Choi, Soo Yoon LEE, Joseph HWYN, Dong Jun HWANG, Gun Hyung NA, Tae He HONG, Young Kyu Young

PE-324 Experience of Hepatic Artery Anastomosis in Living Donor Liver Transplantation Using Surgical Loupe: In Small Volume Center ............................................................................ 540
    Kwun wooyun KIM, Sheng wei KANG

PE-325 Hepatoblastoma: From Laparoscopic Resection to Liver Transplantation ................................................................................ 540
    Nariman Isakov, Nusrat Khan Khyar

PE-326 Chronic Renal Dysfunction Following Liver Transplantation .................................................................................................................. 540

PE-327 Sirolimus and Metformin Synergistically Inhibits Colon Cancer in Vivo ................................................................................................. 541
    Nadiar Mussin, Seung Cheol OH, Kwang-Woong LEE, Min Young Park, Soon Seo, Nam-Soon Y, Nyeuyong KIM, Kyung Chul Yoon, Sung-Woo AHN, Hye-Sin KIM, Suk Kyun HONG, Dong Kyu Oh, and Kyoung-Suk HWYN

PE-328 First 4-Year Experience of Living Donor Liver Transplantation ........................................................................................................... 541
    Rymabekov M.S., Muzin N.I., Konybek Ira

PE-329 Liver Transplantation during Unresistible Liver Alveokokkoz .............................................................................................................. 541

PE-330 Renal Safety of Entecavir and Tenofovir with Hepatitis B Immunoglobulin in Liver Transplant Patients .................................................................................. 542
    Johan Lee, Deuk Gi Kim, Jin Young Lee, Seok Jeong Young, Dong Jin Bae, Myoung Soo Kim, Soon Il KIM, and Geun Lee

PE-331 Acquired Hyponatremia in Pediatric Living Donor Liver Transplantation ................................................................................ 542
    Akhmedal Dosamov, Lazzat Dosamova

PE-332 Initial Experience of Laparoscopic Right Lobectomy after Portal Vein Embolization ........................................................................ 543
    Han Dong Che, Chai Hun Kim, Dong Hwan Jung, Gi-Chul Park, Young-Jin Yoon, Shin Hwang, Chul-Soo Ahn, Deok Big Moon, Tae Yang Na, Gih-Won Sang, Sung-Gyu Lee

PE-333 Analysis of Cancer Incidence after Liver Transplantation in Korea Using Big Data .................................................................................. 543
    Han Joong KM, Yun Kyung JUNG, Dongho CHON, Byoung PARK, Junghwan YOON, Ayung Geun LEE, Neam Kjun PARK

PE-334 3D-Laparoscopic Living Donor Hepatectomy: First Experience in Kazakhstan ................................................................. 543
    K W Lee, Lyalkish Kyzhyrbaeva, M.S. Rymabekov, A.A. Kulev, I.B. Salazarev, A.A. Telemessov, Zh. AtamBoard, and N.M. Mussin

www.theliverweek.org  liii
PE-335  Transforming Growth Factor β1 in Children of Early Age with Liver Transplantation
Yermukhametzhanov, Aman Atakhozhaev

PE-336  Dynamics of Insulin-like Growth Factor-1 (IGF-1) in Children after ABO-Incompatible Liver Transplantation
Aman Atakhozhaev, Yermukhametzhanov

PE-337  Correction of Extrahepatic Portal Hypertension in Pediatric Patient after Liver Transplantation
Altat Yelibayev, Bekzada Karamat

PE-338  Portal and Arterial Flushing with HTK and Tacrolimus Can Attenuate the Incidence of Early Liver Allograft Dysfunction
Bekzada Karamat, Altat Yelibayev

PE-339  A Learning Curve for Living Donor Liver Transplantation
Aidos Biisembay, Bakhtorazov Erlan, Yerlan Bakhtorazov

PE-340  Pediatric Liver Transplantation UMC, Kazakhstan
Yermukhametzhanov, Zhanat Spatayev, Abylaikhan Sharmenov

PE-341  Cost Prediction in Liver Transplantation Using Pretransplant Donor and Recipient Characteristics
Asylkhanuly Ogpanova, Seriev Saken

PE-342  Initial Experience of Liver Transplantation
Myltykbay Rysmakhanov, Bazylbek Zhakyev

PE-343  Long-Term Outcome of the Rendezvous Technique in Patients with Severe Biliary Anastomotic Stricture That Cannot Cannulate after Liver Transplantation
Kyoung Sik Kim, Jong Min Kim, J. Soo Lee, Gyu Sung Choi, Jae-Won Jo, Suk-Koo Lee

PE-344  Prevalence of Hepatopulmonary Syndrome in Liver Transplant Candidates in the North Region of Kazakhstan
Adilshabbyzhan Sharmenov, Aymkul Ashimhanova

PE-345  Splenic Artery Steal Syndrome after Liver Transplantation
Aizhan Seitova, Abylaikhan Sharmenov

PE-346  LOREK
Zhanar Kaldie, Bazylbek Zhakyev

PE-347  Hepatic Abscess after Orthotopic Liver Transplantation
Narzhan Zhabassar, Zhanat Spatayev, Abylaikhan Sharmenov

PE-348  Liver Transplantation for Patient with Emergency Indications
Aidos Kulmaganbetov

PE-349  Immunosuppression after Liver Transplantation
S. Kulmaganbetova, M. Dołnikiewicz

PE-350  Tumor Markers at the Time of Liver Transplantation: Reliable Predictors of Hepatocellular Carcinoma Recurrence after Locoregional Treatment
Deok Gie Kim, In Sik Shin, Sang Hoon Kim, Jae Geun Lee, Myoung Seo Kim, Dong Jin Jo

PE-351  Splenic Artery Embolization Following Liver Transplantation: Single Center Experience
N. Yermukhametzhanov, Bagerzhin A.

PE-352  Pediatric Liver Transplantation in University Medical Center Astana
Yermukhametzhanov ASSYANALU, Samat ISSADOV

PE-353  LDLT Program University Medical Center Astana
Samat ISSADOV, Nurmukhametzhanov ASSYANALU

PE-354  Early-Onset and Bad Place Post Transplantation Lymphoproliferative Disorder (PTLD) after Liver Transplantation: Case Report
Sung Yub Jang, Jung Jun Lee, Sung Hoon Choi

PE-355  Laparoscopy-Assisted Hybrid versus Open Living Donor Right Hepatectomy: A Comparison of Surgical Outcomes
Myun Jin, Incheon Kang, Deok Hoon Han, Jinyoung Soo Kim, Jong Min Kim, Gi Hong Choi

PE-356  Tablet or Capsule Form Combined with Tacrolimus after Liver Transplantation: A Prospective Randomized Trial
Namjuim Gang, Jong Min Kim, Gyoo-Heung Choi, Jae-Won Jo

PE-357  Splenorenal Shunt Occlusion Associated to Portal Vein Thrombosis after Liver Transplantation: Report of Two Cases and Literature Review
Thuan Soe Wai, Lyn Min Kwan, Jin Won Choi, Jin Woik Chung
Surgery, Technical Issues

PE-358 3D-Laparoscopic Surgery in Difficult Localizations of Echinococcosis Cysts of the Liver ................................................................. 553
Kotymurzakov Gani, Rymakhankhan Mykhymbai, Musin Nadiar

PE-359 Surgery-Related DIC Predicts the Severity of Complication after Major Hepatobiliary Pancreatic Surgery .................................................. 553
Ahmet Sedekhekteto, Yuki Imazaki, Masahiro Ohi, Koki Sato, Kenichiro Umemura, Shinzaro Kazuda, Hiroaki Tahara, Kentaro Ide, Tsuyoshi Kobayashi, Hideki Ohdan

PE-360 Anterior Approach for Right Hepatectomy and Right Anterior Sectionectomy with Hanging Maneuver for Large Hepatocellular Carcinoma: A Single-Center Experience in Vietnam .................................................................................. 553
Thuang Van LE, Hieu Trung LE, Quang Van VN, et al

PE-361 An Experience of Laparoscopic Operations in the Liver Local Lesions ................................................................................................. 554
Bekzat Temmurzakov, Kuanysh Karabalaev

PE-362 Extensive Liver Resections for Alveococcosis ................................................................................................................................. 554
Surev Edic, Bebevov Bahadov, Musulayev Erdan, Umentalev Teker

PE-363 The Liver Alveococcosis Surgeries with Inferior Cava Vein and Portal Vein Invasions ................................................................. 555
Bebevov Bahadov, Surev Edic, Umentalev Teker, Marashev N.Dj

PE-364 The Liver Alveolar Echinococcosis Surgery of Children .......................................................................................................................... 555
Umentalev Teker, Bebevov Bahadov, Surev Edic, Ryspekov Bolat, Musulayev Erdan

PE-365 Developing a Preoperative Serum Metabolome-Based Recurrence-Predicting Nomogram for Patients with Resected Pancreatic Ductal Adenocarcinoma ........................................................................................................ 556

PE-366 Laparoscopic Repeat Liver Resection: Short-Term Outcomes ........................................................................................................... 556
Yang Won Nah, Jin A Kwun, Hyung Cho Choi

PE-367 Is Laparoscopic Liver Resection for Hepatocellular Carcinoma Safe for Obese Patients? .................................................................................. 556
Youngin Yoon, Ki-Hun Kim

PE-368 Using of Wearable Recording Technology for Surgical Training Video in Living Donor Liver Transplantation ........................................ 557
Jeong-Moo Lee, Kyung-Suk Suh, Suk Ken Hong, Jae-Hyung Cho, Nam-Soon YI, Kwang-Woong Lee

PE-369 Robotic Simultaneous Resection for Colorectal Liver Metastasis: Feasibility for All Types of Liver Resection ................................................................. 557
Jonathan Navarro, Incheon Kang, Gi Hong Choi, Byung Soh Min

PE-370 Parenchymal Preserving Hepatectomy in Perihilar Cholangiocarcinoma ............................................................................................. 557
Incheon Kang, Gi Hong Choi

PE-371 Analysis of Proximal Ductal Resection Margin in Patients with Hilar Cholangiocarcinoma ................................................................. 558
Woo Young Yoon, Jae Hoon Lee, Song Cheol Kim, Dae Hui Song, Jae Hoon Lee, Woon Hyoung Lee, Jaewoo Kwon

PE-372 Radical Excision for Huge Hepatic Cystic Neoplasm by Totally Laparoscopic Liver Resection: A Case Report ................................................................. 558
Bo-Hyun Jung, Jeong-Ik Park

PE-373 Optimum Timing of Emergency Cholecystectomy for Acute Cholecystitis .......................................................................................... 558
Ksenia V., Balmukhamedov J., Abybergen N.

PE-374 The Immediate Results of Surgical Treatment of Liver Hemangiomas ............................................................................................. 559
Marshakulov Rassam, Umentalev Teker, Bebevov Bahadov, Sakmantol Tolubek

PE-375 Surgical Treatment of the Liver Alveococcosis, Complicated by the Mechanical jaundice .................................................................................. 559
Ryspekov Bolat, Surev Edic, Umentalev Teker, Bebevov Bahadov

PE-376 X-Ray Endobiliary Methods in the Treatment of Patients with Alveococcosis of the Liver, Complicated by Mechanical Jaundice ................................................................. 560
Sakmantol Tolubek, Ryspekov Bolat, Surev Edic, Umentalev Teker, Marshakulov Rusam

PE-377 Advantages of Kasai Procedure through Minimally Invasive Approach in Children with Biliary Atresia ................................................................. 560
Razumovskiy A., Razumovskii, A., Degtyareva A., Kuttymuratov Gani, Imakhanova M.

PE-378 Transplantation Technologies in Surgical Treatment of Advanced Liver Alveococcosis ........................................................................ 561
Zagajkov Vladimir Evgenievich, Kiselev Nikolai Michailovich, Belki Vladislav Aleksandrovich, Mukhazayev Shamsudin Nabiullinovich

PE-379 Surgical Treatment of Liver Alveococcosis ................................................................................................................................. 561
Aliya Myrzabayeva, B. Kuanyshbayev

PE-380 The Use of Laparoscopic Echinococctectomy in the Surgical Treatment of Echinococcosis of the Liver ................................................................. 561
Malabutina Zhann, B. Kuanyshbayev

PE-381 Surgical Management of Patients with Mirizzi Syndrome ................................................................................................................................. 562
Dyubentana BS, Imametdina M.S., Kumaranji LA, Dhabanam JR
PE-382 Management of Carcinoma Gallbladder In Patients with Portal Hypertension
Kusal Panesar, Vishal Kumar Vashisth, Sundeep Singh Sukhu, Pramod Kumar Misra

PE-383 Liver Transplantation Outcomes in UMC
Namthamkham Ayikkhanady, Zhuhan Kuzhayeva

PE-384 Finger Fracture Technique with Glissonian Pedical Approach for Liver Resection Is Comparable to All Other Techniques for Liver Resection
Bhavin Vasavada, Hardik Patel

PE-385 Microwave Assisted Liver Resection: Clinical Feasibility Study and Preliminary Results
Adity Biswas, Santanu Saikia

PE-386 Pure Laparoscopic Left Hepatectomy Using Arantius’ Ligament Approach Combined Glissonean Pedicle Approach
Luu LE VAN, Thanh LE VAN, Quang VU VAN, Linh HO VAN, Hiem LE TRUNG, Luc DAO TAN

PE-387 Cystobiliary Communication in Hydatid Disease: A Recalcitrant Problem
Jenny Sohn, Christos Apostolou, Amitabh Das, Neel Merrett, Khemraj Rajkumar

PE-388 Early Experience of Single Port Robotic Cholecystectomy Using Da Vinci Xi System
Seung-Hwan Lee, Sun-Hyung Joo

PE-389 ‘Falciformoplasty’ as an Alternative to Omentoplasty for Deep Hydatic Cysts
Jenny Sohn, Christos Apostolou, Amitabh Das, Neel Merrett, Khemraj Rajkumar

Others

PE-390 Robotic Reduced-Port Splenectomy Using Single-Site Platform: 8 Cases of Single Surgeon Experience
Kyungyon Han, Jeo Hoon Lee

PE-391 Liver Cancer and its Risk Factors-Related Researches in North Korea
Eun-young Lee, Moran Ki

PE-392 Feasibility of Continuous Venous Infusion in a Porcine Hepatectomy Model
Jin-I Seok, Kyung Chul Yoon, Hye-Sung Jo, Young In Yoon, Yoon Young Cho, Dong-Sik Kim

PE-393 Mortality after Hepato-Biliary and Pancreatic Surgery (HBPS) in Queensland, Australia
Tristan Anderson, John North, Praga Pillay

PE-394 A Case of Accessory Cystic Duct with Double Cystic Artery
Dhijy Saeuru

PE-395 Case Report Cardiovascular and Acute Kidney Disease Caused by Cardiopulmonary Resuscitation in Blood Sugar
Hari Prasad Dulal

PE-396 Metformine and Insuline Resistance Is Associated with Hirsutism in Unselected Reproductive-Age Nepali Women
Yuporn Tugsila, Hari Prasad Dulal

PE-397 Effect of Millets Flours, Brown Rice, Corn Flours Consumption on Blood Sugar Levels, Lipid Profile and Anthropometric Indices among Selected Politicians and Known to Know Employees in Nepal
Rathnasamy Adikkan, Hari Prasad Dulal

PE-398 A Descriptive Study of Clinical Trials Being Conducted in India Related to the Liver Diseases
Jay Kumar, Pankaj Bhardwaj, Jagdish Goyal

PE-399 Accessory Liver Fissures: A Case Report and Its Clinical Significance
Arun Choudhary, Saraji Ghatak

PE-400 Liver Diseases in Myanmar
Aung Khing Bo, Khine Yanmye Aye, Khine Nwe Thant, Soe Thida Maung, S Thu Sein Win, Khin Maung Win

PE-401 Complementary and Alternative Medicine (CM) Deterioration of Chronic Kidney Patients in Nepal
Ganga Dulal, Hari Prasad Dulal

PE-402 Lipidogram in Patients with Type2 Diabetes Mellitus Infected with Hepatitis B and C Viruses
Yuporn Tugsila, Hari Prasad Dulal

PE-403 A Case of Hepatitis A Associated with Subchorionic Hematoma during Pregnancy
Byung Seok Lee, Seok Hyun Kim, Eunm Seok Lee, Jong Seok Jos, Hye Sun Eun, Wbo Sun Rou, Hiee Sang Lee, Mhi Young Shin, Sung Hun Kang, Sang Ok Jung, Min A Cho, Ji Xi Min, Dong Yeon Kim

PE-404 Prognosis and Risk Factors of Acute Viral Hepatitis D in Mongolia
Batuuil, B., Munk-Øskiihh Dashzhul, Swangpaa. G., Gansainhan. B., Aatsubmeg. J. and Batsetkhutsu. O.
<table>
<thead>
<tr>
<th>Location</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>
| PE-405   | Analysis of Chemical Composition of a Single Cellular Lipid Droplet in
Liver Cells                                                      | Ryohei Tamada, Rojeet Shrestha, Hitoshi Chiba, Shu-Ping Hui             |
| PE-406   | Effects of Chronic Kidney Disease on Liver Enzymes Activity during Pre
and Post Hemodialysis                                               | Sanjay Kumar Jha, Naval Kishor Yadav, Upma Jha, Daya Ram Pokhare, Pramod
Shankar Shah              |
| PE-407   | Lymphoid Hyperplasia of the Liver Mimicking Hepatocellular Carcinoma:
A Case Report                                                        | Woo Young Kim, Yu Na Lee                                                |
| PE-408   | Liver Enzymes Activity in Patients with Chronic Kidney Disease on
Hemodialysis                                                         | Naval Kishor Yadav, Daya Ram Pokhare, Shrinkhala Chhetri, Manoj Sigdel   |
| PE-409   | Diagnostic Performance of Serum Asialo-α1-Acid Glycoprotein for Advanced
Liver Fibrosis or Cirrhosis in Patients with Chronic
Hepatitis B or Nonalcoholic Fatty Liver Disease                       | Seung Up Kim, Mi Young Jeon, Moon Hyun Kim, and Tae Seop Lim            |
| PE-410   | SGOT, SGPT and Alkaline Phosphatase among Suspected Liver Patients
Attending Pyuthan District Hospital, Pyuthan, Nepal                   | Ganga Sagar Bhattarai, Man Neupane Bishnu Raj Tiwari                   |
| PE-411   | Conservative Management of Traumatic Acute Intramural Hematoma of
Duodenal 2nd and 3rd Portion: A Case Report and
Review of Literature                                                  | Jin Ho Lee                                                             |
| PE-412   | Epidemiology of Wilson's Disease in South Korea: A Population-Based
Study Using the National Health Insurance Database                    | Jong Won Choi, Minjin Kang, Chun Kyon Lee                                |
DAY 1: Thursday, June 20, 2019 (10:50-12:30)
ROOM D [2F] 205

Basic Forum 1

Hepatitis Virus (*K)

Chairs:
Soon Bong Hwang (Chonbuk National Univ.)
Jin-Wook Kim (Seoul National Univ.)
Molecular Basis for Cure of Hepatitis B Virus Infection

Kyun-Hwan Kim
Department of Pharmacology, Konkuk University School of Medicine, Seoul, Korea

More than 240 million people are chronically infected with hepatitis B virus (HBV), with some 600,000 deaths per year attributed to the virus. Chronic HBV infection is associated with significant morbidity and mortality, fibrosis, cirrhosis, end-stage liver diseases and primary hepatocellular carcinoma (HCC). However, the current antiviral drugs can efficiently control but not eliminate HBV in the carriers at risk to develop liver diseases and cancer. HBV patients often require lifelong therapies and cure is still a challenging goal because HBV establishes a stable nuclear persistence form, the so-called HBV cccDNA, in infected hepatocytes. Eliminating HBV cccDNA is a critical issue if we want to cure HBV infection.

To achieve functional or complete cure of HBV, ICE-HBV (The International Coalition to Eliminate HBV) forum was created in 2016. ICE-HBV tries to accelerate HBV cure research by proposing two strategies, namely curing of HBV infection without killing infected cells and inducing immune control to safely eliminate infected cells. These approaches will be introduced in this presentation.

Recent advances in basic HBV sciences have heralded a new horizon of innovative therapeutic approaches to the possibility of a functional cure of chronic HBV infection. These approaches include inhibitors of viral entry, cccDNA modulators, interfering RNA targeting viral RNAs, novel polymerase or ribonuclease H inhibitors, core protein allosteric modulators and capsid assembly modulators (capsid inhibitors), drugs interfering with HBx function, drugs targeting viral and HBsAg egress, or agents restoring the host immunity against HBV.

In this talk, I review the current state of science in HBV therapy and highlight new therapeutic strategies spurred by recent scientific advances in HBV field. Especially, I will focus on the action mechanisms of those approaches in detail and introduce the limitations of current strategies.

Keywords: Hepatitis B virus (HBV), Covalently closed circular DNA (cccDNA), HBV cure, Capsid inhibitor, HBsAg inhibitor
International Coalition to Eliminate the Hepatitis B Virus (ICE-HBV)

**ICE-HBV**

- Associated working groups
  - Academia (basic and clinical sciences)
  - Industry
  - Drug agencies (FDA, EMA)
  - International scientific societies (AASLD, ALEH, APASL, EASL, others)
  - Funding research agencies (ANRS, DZIF, others)
  - Nonprofit organizations (Hepatitis B foundation, others)
  - WHO
  - HBV-affected community

**HBV CURE STRATEGIES**

- Antivirals
- Therapeutic Vaccines
- Gene Therapy
- Immune-based Therapies

**Overview of Current HBV Drug Development**

- Nucleos(t)ide Analogues
- RT Inhibitor
- All current Drugs

- Capid Inhibitor

- Reverse Transcription

- No cccDNA Inhibitor

- siRNAs, Antisense work here

- Others
  - Therapeutic Vaccines
  - Immune modifier
### Table. Capsid Inhibitors in Development (updated May 2019)

<table>
<thead>
<tr>
<th>Capsid Inhibitors: Interferes with the viral DNA protein shield</th>
<th>HEC Pharma, PR China</th>
<th>pharm.hec.cn/en</th>
<th>Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphothiadin (GLS4)</td>
<td>Capsid inhibitor</td>
<td>Janssen, Scotland</td>
<td>janssen.com</td>
</tr>
<tr>
<td>JNJ 56136379</td>
<td>Capsid inhibitor</td>
<td>Assembly Biosciences, USA</td>
<td>assemblybio.com</td>
</tr>
<tr>
<td>ABI-H0731</td>
<td>Capsid inhibitor</td>
<td>Arbutus Biopharma, USA</td>
<td>arbutusbio.com</td>
</tr>
<tr>
<td>AB-423</td>
<td>Capsid inhibitor</td>
<td>Arbutus Biopharma, USA</td>
<td>arbutusbio.com</td>
</tr>
<tr>
<td>AB-506</td>
<td>Capsid inhibitor</td>
<td>Assembly Biosciences, USA</td>
<td>assemblybio.com</td>
</tr>
<tr>
<td>ABI-H2158</td>
<td>Capsid inhibitor</td>
<td>Roche, Switzerland</td>
<td>roche.com</td>
</tr>
<tr>
<td>RG7907</td>
<td>Capsid inhibitor</td>
<td>Qilu, China</td>
<td>qilu-pharma.com</td>
</tr>
<tr>
<td>QL-007</td>
<td>Capsid inhibitor</td>
<td>Emory University</td>
<td>emory.edu</td>
</tr>
<tr>
<td>GLP-26</td>
<td>Capsid inhibitor</td>
<td>Enanta Pharmaceuticals, USA</td>
<td>enanta.com</td>
</tr>
<tr>
<td>EP-027367</td>
<td>Capsid inhibitor</td>
<td>Qilu, China</td>
<td>qilu-pharma.com</td>
</tr>
<tr>
<td>QL-0A6a</td>
<td>Capsid inhibitor</td>
<td>ZhiMeng Biopharma, China</td>
<td>core-biopharma.com</td>
</tr>
<tr>
<td>CB-HBV-001</td>
<td>Capsid inhibitor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Drug Development for Hepatitis B Virus Treatment

Sung-Gyoo Park
School of Life Sciences, Gwangju Institute of Science and Technology, Gwangju, Korea

Hepatitis B virus (HBV) is a double-stranded DNA virus and Hepadnaviridae virus. Chronic HBV infection is a major global cause of hepatocellular carcinoma (HCC). Chronic carriers increase liver cancer risk by over 100 times. HBV can be treated with nucleosides (nAs) that inhibit HBV polymerases such as tenofovir (TDF) and entecavir (ETV). Both are potent and have a high genetic barrier to drug resistance. However, HBV can not be cured due to the excellent stability of viral cccDNA intermediates that are not directly targeted by NA. Combination therapy with NA and peginterferon α2a (pegIFNα2a) can improve treatment effectiveness. These combination therapies can cause synergy because they induce antiviral and immunomodulatory activities. In fact, the combination of TDF and pegIFNα2a results in a better hepatitis B surface antigen (HBsAg) loss than monotherapy. However, the combined ratio is still only 9.1%. Also, many patients can not tolerate pegIFNα2a. Therefore, new treatments are needed for patients with chronic HBV infection. In particular, a cure that directly exterminates cccDNA in the liver and continuously treats HBV infection. This goal has recently been greatly enhanced by significant advances in understanding the HBV life cycle, including how the virus enters the host cell, how the cccDNA is formed, how the HBV capsid is assembled, and so on. Insights into these mechanisms have led to the development of many new drugs for investigating HBV, including current research.


Identification and Validation of Druggable Targets in the Hepatitis C Virus Life Cycle

Soon Bong Hwang

Laboratory of RNA Viral Diseases, Korea Zoonosis Research Institute, Chonbuk National University, Iksan, Korea

Hepatitis C virus (HCV) is highly dependent on cellular machineries in all steps of viral life cycle for its own propagation. Blocking any step of the virus life cycle results in an efficient blockade of viral production and thus could be a potential target for viral therapy. To develop drugs with broad-spectrum antiviral activities using host factors as putative druggable targets, we employed various high-throughput screening strategies, including mass spectrometry-based immunoprecipitation proteomics, tandem affinity purification, siRNA library screening, protein microarray screening, and transcriptome sequencing methods. Using these technologies, we have identified highly promising candidates of HTAs against HCV. Among these, tylophorine, the natural plant product, efficiently abrogated HCV replication. Moreover, tylophorine intermediates, 5-Oxo-1-[(2,3,6,7-tetramethoxy-9-phenanthrenyl) methyl]-L-proline (O859585) displayed an anti-HCV activity at the attachment step of the HCV life cycle by neutralizing free viral particles. Of note, co-treatment of O859585 with either interferon alpha (IFNα) or sofosbuvir exerted an additive antiviral activity in HCV-infected cells. Most importantly, O859585 in combination with IFNα and sofosbuvir exhibited synergistic effects on anti-HCV activity in primary human hepatocytes. These data suggest that O859585 may be a novel antiviral agent for HCV therapy. We hope that these newly identified host-targeted antivirals (HTAs) might be novel and potent therapeutic agents for patients who have failed prior direct-acting antiviral-based therapy. Moreover, we can apply these HTAs as therapeutic candidates for combination therapy.

Keywords: HCV, High-throughput screening, Druggable targets, Direct-acting antivirals, Host-targeted antivirals
Hepatitis C Virus Vaccine Development

Eui-Cheol Shin
Laboratory of Immunology and Infectious Diseases, Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea

Prophylactic hepatitis C virus (HCV) vaccine candidates have been developed to elicit HCV-specific memory T cells and/or broadly neutralizing antibodies. In principle, only neutralizing antibodies can protect hosts from infection itself. However, virus-specific memory T cells can prevent the evolution of the infection to chronic persistent infection.

Evidence that emphasizes the crucial role of T cell responses in protective immunity to HCV infection and reinfection has accumulated from studies in patients and chimpanzees. In particular, HCV-specific memory T cells protect HCV-rechallenged chimpanzees and naturally reinfected patients, as shown by lower levels of the virus and a shorter duration of viraemia, which supports the rationale of developing T cell-based vaccines.

The key immunological factors for successful vaccine-induced protective immunity are the early proliferation of polyfunctional CD8+ T cells upon HCV infection and the high levels of expression of the memory precursor marker CD127. In a recent Phase I trial in healthy human volunteers, a simian adenoviral vector expressing HCV nonstructural proteins primed HCV-specific CD4+ and CD8+ T cells, and a boost immunization with MVA expressing the same HCV proteins elicited sustained memory and effector T cell responses with enhanced functionality and proliferative capacity. This vaccine is currently proceeding to a Phase II trial.

In this lecture, strategies to develop prophylactic HCV vaccines will be discussed.
Basic Forum 2

Hepatocellular Carcinoma and Steatohepatitis (*K)

Chairs:
Sang Hoon Park (Hallym Univ.)
Yong-Han Paik (Sungkyunkwan Univ.)
Understanding of Immune Checkpoint Inhibitors in Hepatocellular Carcinoma

Su-Hyung Park
Graduate School of Medical Science and Engineering, KAIST, Korea

Immuno-oncology drugs are considered as a breakthrough in cancer treatment because of their ability to target and enable immune cells to destroy cancer cells. The immune system is the body's natural defense system, attacking dangerous cells and destroy them. Cancer cells have developed the ability to 'hide' from the immune system and thereby prevent an immune response. Immunotherapies aim to enable the immune system to fight cancer. Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment and several agents targeting programmed cell death-1 (PD-1), PD-L1, and cytotoxic T lymphocyte-associated protein-4 (CTLA-4) have been approved for many types of cancer. However, the therapeutic efficacy of ICIs substantially varies among cancer types and patients, and only a limited proportion of cancer patients benefit clinically from ICIs. To improve the therapeutic efficacy of cancer treatments involving ICI, the mechanisms of response to ICIs and the heterogeneous pattern of immune checkpoint receptor expression need to be better understood. Therefore, this talk will introduce the current knowledge of immunity in tumor microenvironment and the prominent recent advances for improving treatment responses of anti-PD-1 therapy in hepatocellular carcinoma (HCC). In addition, heterogeneity of tumor-specific exhausted CD8 T cells in HCC patients and its clinical implications will be discussed.

Keywords: T cell exhaustion, Hepatocellular carcinoma, Immune checkpoint receptor, PD-1, Tumor-infiltrating CD8 T cells
Hepatocellular carcinoma (HCC) is one of the most lethal cancers, causing 500,000 – 600,000 deaths worldwide each year. Hepatitis virus infection, alcohol abuse, obesity, or other factors that cause chronic liver injuries lead to hepatic fibrosis and cirrhosis. Cirrhotic liver creates a pathological microenvironment in which cells with a genetic or epigenetic alteration in cancer-related genes can become malignant. Various animal models have been developed for HCC that include chemically-induced models, xenograft models, and genetically engineered mouse models. Recently, a novel approach for genetically engineered HCC models has been developed using hydrodynamics-based transfection (HT). The HT method, which is coupled with Sleeping Beauty transposon system, has allowed a variety of HCC models expressing diverse oncogenes to be developed rapidly and cost-effectively. The versatility of HT models is expected to broaden our knowledge on the genetic mechanism underlying hepatocarcinogenesis in human.

Hepatocellular carcinoma (이후 간암)은 사망률이 높은 대표적인 암이다. 전 세계적으로 50-60만 명이 매년 간암으로 사망하고 있으며, 국내 남성에서 이런 간암은 전체 암 가운데 두 번째로 높은 사망률을 보여주고 있다. 지속적인 간 손상은 염증과 함께 간에 섬유화를 유발하며, 간섬유화가 더욱 진행되면 간결핵에 이르게 된다. 이러한 손상된 간 조직 환경에서 종양유전자의 활성화나 종양억제유전자의 비활성화 등이 발생하면 간암이 일어나다고 알려져 있다.

간암의 효과적인 연구를 위해서는 인간의 간암을 그대로 모방할 수 있는 동물모델이 필요하다. 간암 동물모델은 간암 발생의 유전학적인 메커니즘을 규명하고 간암 진행의 단계적 변화를 연구하는데 적극 활용될 수 있으며, 항암치료제의 효능을 예측하는 전임상 모델로서 많이 이용된다. 간암동물모델에는 간 독성물질 또는 발암 물질을 주입한 후 간암이 자연적으로 발생하도록 하는 화학적 유도 간암모델, 면역 결핍 마우스에 인간의 간암세포를 주입하여 암을 일으키는 간암 이식모델, 그리고 간암 발생과 관련된 종양유전자 및 종양억제 유전자를 조작하여 간암을 발생시키는 유전자조작 간암 모델 등이 있다. 간암 이식모델의 경우 항암 후보물질에 대해 인간의 간암세포가 어떻게 반응하는지 생체상에서 확인할 수 있어 현재 바이오 항암효능 테스트 모델로 많이 이용되고 있다. 그러나 이질적인 조직 미세환경에서 간암이 성장하므로 인간의 간암 특성과 비교해 얼마나 유사성을 가질지에 대해 많은 의구심이 든다. 또한 면역기능이 저하된 마우스에서 간암이 성장하므로 면역기반 항암치료의 효과를 연구하기에 제한이 있다. 이에 비해 유전자조작 간암모델은 인간의 간암에서 나타나는 다양한 병리학적 특성을 모방하는 간암을 발생시키며, 특히, 인간의 간암에서처럼 간성유화, 간결핵을 동반하는 간암모델도 제작할 수 있다. 하지만 유전자조작 마우스를 제작하는데 오랜 기간이 걸리고 많이 비용이 드는 점은 이 모델의 큰 한계이다.

2000년대 후반부터 간암 유전자조작 마우스모델의 새로운 제작기법으로 간암을 발생 시킨 hydrodynamic
transfection 기법은 원하는 유전자를 발현하는 플라스미드를 혈관을 통해 간세포만으로 직접 전달하는 방법으로서, 트랜스포존 시스템을 함께 사용해 넣어준 유전자를 간세포의 genome에 삽입시켜 지속적인 유전자 발현을 도모할 수 있다.1 이 방법을 사용할 경우 다양한 종양 관련 유전자 발현을 손쉽게 조작할 수 있어 현재 전 세계 많은 연구자들이 간암의 유전적 기전 연구에 적극적으로 사용하고 있다. 본 연구자의 연구그룹에서도 hydrodynamic transfection 기법을 이용해 다양한 유전자의 발현을 조작해 간세포선종 (hepatic adenoma), 분화도 높은 간세포암부터 분화도가 낮은 간세포암, 담관암과 혼합 간세포암 등 인간의 간암에서 나타나는 다양한 조직병리학적 특성을 띠는 간암을 발생시킬 수 있었다.2 또한 hydrodynamic transfection 모델 기법을 통해 다양한 종양 관련 신호경로를 유전적으로 저해하여 간암 발생을 저해할 수도 있었다. 예를 들어, hydrodynamic transfection 모델 기법으로 간세포암 발생시 유전체적 역할을 하는 TGF-beta 신호경로를 차단할 경우 간암 발생이 현격히 줄어들음을 확인할 수 있었다.3

References
Hepatic mGluR5 Signaling in Endocannabinoid-Mediated Alcoholic Steatosis

Won-il Jeong

Graduate School of Medical Science and Engineering, KAIST, Daejeon, Korea

A key mechanism underlying alcoholic fatty liver is an endocannabinoid-induced, CB1R-mediated increase in de novo lipogenesis in hepatocytes. We have earlier demonstrated that chronic alcohol treatment upregulates the hepatic levels of the endocannabinoid 2-arachidonoylglycerol (2-AG) and its biosynthetic enzyme DAGLß in hepatic stellate cells (HSCs), and the released 2-AG acts on neighboring hepatocytes to induce CB1R-mediated de novo lipogenesis, but the metabolic trigger to induce 2-AG production in HSCs remained unknown.

Here, we provide multiple lines of evidence for a bidirectional paracrine loop between hepatocytes and HSCs, where alcohol-induced oxidative stress and the resulting cysteine deficiency and glutathione (GSH) depletion triggers a compensatory upregulation of the cysteine/glutamate antiporter xCT in hepatocytes, resulting in increased glutamate secretion. Glutamate then activates the metabotropic glutamate receptor mGluR5 on neighboring HSCs to induce DAGLß expression and 2-AG production, and the released 2-AG activates CB1R on hepatocytes to induce de novo lipogenesis. This bidirectional hepatocyte-HSC-hepatocytes loop represents a unique mechanism of alcoholic fatty liver and it also provides novel molecular targets for its pharmacotherapy. Indeed, we demonstrate that pharmacological blockade or genetic deletion of xCT or mGluR5 mitigates alcoholic steatosis, whereas exposure of HSCs to mGluR5 agonists promotes DAGLß expression and 2-AG production. Importantly, the key components of this bidirectional loop are similarly induced in patients with ALD. Patients with AFL have elevated circulating glutamate levels, increased expression of hepatic xCT and mGluR5, and positive correlation between mGluR5 and CB1R-mediated lipogenesis. This reinforces the translational potential of the novel therapeutic targets identified here.
In addition, as previously reported by us and others, we adopted in vivo mouse models of alcoholic liver disease (ALD), in vitro paradigms in isolated liver cells and in situ hepatic perfusion techniques to clarify the role of xCT and glutamate in mitigating alcoholic oxidative stress in hepatocytes and in dissecting the mechanism of mGluR5-mediated production of 2-AG in HSCs. Chronic consumption of 40 g or more of pure alcohol per day increases the risk of end-stage liver disease and the associated social burden. Alcohol-induced ROS generation is primarily mediated via the induction of cytochrome P450 2E1 (CYP2E1), which also modulates the expression of a large repertoire of genes linked to anti-oxidative response and lipid metabolism in the context of alcoholic fatty liver. Ethanol-fed mice and ALD patients have reduced hepatic GSH levels along with hyper-homocysteinemia. This leads to abnormal hepatic accumulation and elevated serum levels of homocysteine associated with decreased concentrations of cysteine and GSH, suggesting disturbed methionine cycle and transsulfuration pathway in the liver. Our findings point to a compensatory mechanism triggered by the depletion of GSH and cysteine which involves an ethanol-induced robust induction of Slc7a11 (encoding xCT) and Nfe2l2 (encoding Nrf2) in hepatocytes. Interestingly, xCT and CYP2E1 are co-localized in perivenous hepatocytes in both mice and humans, suggesting a strong relationship between CYP2E1-mediated oxidative stress and xCT induction. In this context, glutamate excretion may occur predominantly around central veins, providing a plausible explanation for the preferential accumulation of fat at the perivenous zone of hepatic lobules.

In conclusion, alcohol-induced upregulation of xCT results in increased excretion of hepatic glutamate, which triggers mGluR5-mediated 2-AG production in HSCs, a pathway that could be targeted for the treatment of alcoholic fatty liver disease.
Heterotrimeric G proteins converge with activated GPCRs to modulate cell-signaling pathways. Here, we report that muscle-specific ablation of Gα13 in mice promotes reprogramming of myofibers to the oxidative type, with resultant increases in systemic mitochondrial activity. Mechanistically, Gα13 and its effector RhoA suppressed NFATc1, a key regulator of myofiber conversion, by increasing Rock2-mediated phosphorylation at Ser243. Ser243 phosphorylation of NFATc1 was reduced after exercise, but was higher in obese animals. Consequently, Gα13 ablation in muscles enhanced whole-body energy metabolism, thus affording protection from diet-induced obesity and hepatic steatosis. In the absence of Gα13, Gα12 plays a role in mitochondrial regulation. Mechanistically, Gα12 stabilized SIRT1 protein through induction of USP22 via HIF-1α. Consistently, Gna12-KO mice fed a high-fat diet displayed greater susceptibility to diet-induced liver steatosis and obesity due to decrease in energy expenditure. Thus, Gα12 regulates SIRT1-dependent mitochondrial respiration through HIF-1α-dependent USP22 induction, which systemically contributes to the regulation of mitochondrial energy expenditure.
으로 한 신호 전달계가 핵심적이다. Gα protein은 4개의 주요 패밀리(Gs, Gq, Gi, G12 family)로 구분되며, 전형세포의 경우 진화적으로 발달한 많은 GPCR (약 800)의 리간드 자극을 인식, 증폭, 제어하는 신호변환(transducer)의 역할을 수행한다. 따라서 표면수용체의 자극은 이들 transducer의 양이 많고 적음에 따라 다른 강도로 세포 내 신호를 전달한다. 즉 Gα protein은 세포 표면의 다양한 GPCR 자극을 통합하고 신호를 수집/제어하는 중심 분자로 작용한다. 현재까지 연구지 대사에서 G단백질의 역할은 간 또는 췌장 베타세포에서 Gs 및 Gi의 인슐린 신호와 당 대사조절 기능에 관해 보고된 바가 있다. 그러나 여러 G단백질 중 G12 family의 G12/G13에 의한 대사조절 연구는 미진하였다.

그림 1. G12/G13 조절계에 의한 에너지 대사의 신호 회로

본 연구실에서는 분자생물학, 동물 및 세포 모델을 활용하여 골격근 조직에서 Gα13의 기능을 연구하여 골격근 특이적으로 Gα13 유전자를 제거할 때 근섬유의 유형이 변환되는 사실을 발견하였다. 골격근유형은 비산화형과 산화형으로 구분하는데, 산화형 근섬유는 미토콘드리아 호흡을 왕성히 수행하면서 지방산 산화를 촉진하고 산소 소비를 증가시킨다. 동물 및 세포 모델에서 Gα13 유전자를 제거했을 때는 근섬유가 비산화형에서 산화형으로 전환되어 미토콘드리아 호흡이 증가하였다. 골격근은 생체의 40-50%가량을 차지하므로 이러한 변화는 전신 에너지 대사를 증진하여 혈당의 개선, 근육조직의 당과 지방조직과의 이용을 증진하였다. 간조직에서는 고지방식이 높은 단백질 증가를 보였으며, 이로 인하여 간부의 정상회복, 조직병리학적 개선도 관찰할 수 있었다. 운동으로 인한 근육활성화는 Gα13 발현을 감소시켰으며, 고지방식이 높은 단백질 증가는 Gα13 발현을 증가시켰다. 이는 당뇨환자들의 근육에서 관찰된 G13 감소는 NRF1 활성을 증가시켰으며, 산화형 근섬유의 전환을 촉진하였다. Gα13는 RhoA-ROCK2를 매개한 NRF1의 Ser243 인자산화를 증가시키며, 운동 자극은 이 과정을 억제함으로써 NRF1의 핵내 유입과 전사활성을 촉진하여 미토콘드리아 생성성, 산소흡증, 지방산 산화 및 유산소호흡과 관련한 유전자군을 유도한다. 그리고 대사형 근섬유의 전환을 촉진하였다. 따라서 단백질 단백질의 Gα13를 제거하거나, 골격근에 Gα13 발현을 감소시킬 때는 Gα12 발현이 역으로 증가하는 것이었다. 본 연구실은 추가적으로 Gα13의 역할을 연구하였다. Gα12는 간을 비롯한 거의 모든 조직에서 풍부한 발현되는 신호 전달계의 주요 구성원으로, GPCR를 자극하는 리간드를 단일로 특정하는 것이 아니라 철저히 세포 표면의 GPCR과의 상호작용을 통해 신호를 전달한다. GPCR을 자극하는 리간드를 단일로 특정하는 것과 달리, Gα12는 여러 GPCR과의 상호작용을 통해 신호를 전달한다. GPCR-Gα12회로를 자극하는 직접적인 연관성은 아직 명확하지 않으나 GPCR의 상호작용을 통해 신호를 전달하며, Gα12는 adenosine 수용체 4형과 연관되어 있다. adenosine 수용체 4형은 adenosine의 활성 증가를 촉진하는 역할을 한다. Gα12발현이 높은 경우 수용체 4형의 adenosine 수용체 4형은 adenosine의 활성 증가를 촉진하며, adenosine 수용체 4형의 adenosine 수용체 4형은 adenosine의 활성 증가를 촉진한다.
체 신호를 증폭하고 이는 SIRT1, PGC1α, PPARα 등 core complex 분자를 활성화 시킴으로써 미토콘드리아 생성성을 자극하였다. 즉 Ga12의 증가 발현은 ATP 생산의 적응 반응을 유도하는 것으로 해석한다. 고지방식이동 에너지원의 과잉 섭취는 반대로 Ga12 발현을 감소시키고, 미토콘드리아 생성성과 산소 호흡을 감소시켜 연료 소비량 줄이는 약순환의 고리에 관여한다. 따라서 NAFLD환자 간조직을 분석하였을 때 정상 또는 단순 지방간과 비교할 때 NASH환자에서는 Ga12발현이 억제되었다. 본 연구의 결과는 지방간, 지방간염은 물론 대사질환의 병리기전을 이해하는 새로운 회로 발견의 의미는 물론 NAFLD치료를 위한 후보 약물의 기전과 개발 성공 가능성을 평가할 때 함께 고려해야 하며, 나아가 신약 도출의 새로운 전략에도 활용할 수 있을 것으로 기대한다.

References:


Symposium 1

Non-Alcoholic Fatty Liver Disease and Alcohol-Related Liver Disease

Chairs:
Dong Joon Kim (Hallym Univ.)
Yong Kyun Cho (Sungkyunkwan Univ.)
Fecal Microbiota Transplant in Alcoholic Hepatitis

SM Shasthry
Institute of Liver and Biliary Sciences, India

The current standard of care for severe alcoholic hepatitis (SAH) has several limitations. Only about a third of patients with SAH are deemed to be eligible for steroid therapy (the standard of care). Additionally, steroids have their own limitations – a. their effect on long term (beyond 28 day) survival is doubtful b. over a third of patients do not respond to steroids (as determined by Lille score) c. large chunk of patients who are ineligible to steroids at baseline do not have any definitive options as standard of care. So, we have a large gap between the quantum of problem and the available treatment options.

Gut-derived microbial LPS, a component of the outer wall of gram-negative bacteria, has been known to have a central role in the pathogenesis of ALD. Alcohol has been known to cause dysbiosis and as well disrupt the gut barrier function, consequently, promoting the translocation of microbial LPS from the lumen of the intestines to the portal vein, where it travels to the liver. In the Kupffer cell, LPS binds to CD14, which combines with toll-like receptor 4, ultimately activating multiple pro-inflammatory cytokine genes. Therefore, probiotics, prebiotics, antibiotics, or transplantation of gut-microbiota may be proposed as possible treatment avenues for AH, by attenuation of the increase in LPS or normalizing the healthy gut flora.

Recently, fecal microbiota transplantation (FMT) has been successfully used in the treatment of life-threatening infections with Clostridium difficile. Gut bacteria being actively involved in the pathogenesis of alcoholic hepatitis, FMT might have a potential role in the management of alcoholic hepatitis. Results from the mice study have proven beyond doubt regarding the utility of transfer of fecal microbiome from alcohol resistant mice into the alcohol sensitive mice in preventing the liver injury from alcohol. Pilot studies from our institute (ILBS) have confirmed the benefits of FMT from healthy donor to the severe alcoholic hepatitis patients (who were ineligible to the SMT) with improved short term and as well as long term survival. Further studies addressing the head to head comparison of steroid vs FMT are ongoing. These data from the preliminary clinical trials at our center have heightened our hopes on the utility of FMT in managing this very difficult to manage group of patients with severe alcoholic hepatitis. FMT and/or gut microbial modulation might change the way SAH patients are managed and might increase the hopes of this particularly difficult to treat and sick group of severe alcoholic hepatitis.
Nonalcoholic fatty liver disease (NAFLD) is defined as the presence of hepatic fat accumulation either by histology or by imaging after the exclusion of other causes of hepatic steatosis such as viral hepatitis, significant alcohol consumption, a medication known to produce hepatic steatosis or the different causes of liver disease. NAFLD encompasses a broad spectrum ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), advanced fibrosis, and eventually end-stage liver disease including cirrhosis and hepatocellular carcinoma. The increasing incidence of type II diabetes and obesity is leading to an increased prevalence of NAFLD, with an estimated prevalence of 20-30% in the world. The increasing prevalence of NAFLD is particularly worrying because subjects with NAFLD appear to have higher mortality from non-liver related as well as liver-related death compared to the general population. A recent large population study which consisted of 11,154 subjects in the National Health and Nutritional Examination Survey III shows that simple steatosis was not associated with higher mortality risk after a median follow-up of 15 years. Further analysis shows that NAFLD patients without advanced fibrosis do not have a higher mortality risk and mortality increases as fibrosis advances. These increases in mortality were almost entirely from cardiovascular causes. To sum up these results, cardiovascular disease is the most common cause of mortality in NAFLD and NASH.

Because of well-known association with metabolic comorbidities, NAFLD is commonly associated with obesity, type II diabetes, dyslipidemia, and metabolic syndrome. NAFLD and its comorbid conditions extend well beyond the liver. It is a multisystem and systemic clinical disease entity or syndrome with extrahepatic manifestations. These findings have emerging concerns that NAFLD may be a new, and an added risk factor for extra-hepatic diseases such as cardiovascular disease, chronic kidney disease, thyroid dysfunction, sleep disorder, psoriasis, type 2 diabetes mellitus, and polycystic ovarian disease. Indeed, the most common causes of mortality in subjects with NAFLD are cardiovascular disease, followed by malignancy, and liver-related complications at a distant third.
Update on the Management of Non-Alcoholic Fatty Liver Disease

Vincent Wong
The Chinese University of Hong Kong, Hong Kong

Currently, lifestyle intervention, vitamin E, pioglitazone and bariatric surgery (for morbidly obese patients) are available treatments for nonalcoholic steatohepatitis (NASH). Nonetheless, they are limited by applicability, efficacy and potential side effects. As a result, the medical field is actively developing new treatments for this emerging disease. Five drugs (obeticholic acid, elafibranor, selonsertib, cenicriviroc and resmetirom) have entered phase III development, and a number of agents are being tested in phase I and II trials. These agents act via diverse mechanisms ranging from metabolic, anti-inflammatory to anti-fibrotic effects, which would likely be necessary for a complex disease like NASH. This would also mean combination therapy is probably required for optimal disease control. In the REGENERATE study, obeticholic acid demonstrated increased rate of improvement in liver fibrosis without worsening of NASH at month 18, and will likely become the first registered drug for NASH. At present, serial liver biopsies are still required to evaluate new NASH treatments. This has increased the difficulty and cost of drug development. The development of validated surrogate endpoints will be an important next step. Finally, Asians remain underrepresented in NASH trials. We need to increase our representation in this area to learn how best to manage Asian patients.
Special Lectures with Debates

Can We Discontinue Hepatitis B Virus Therapy? *Pros. vs. Cons.*

**Chairs:**
- Jordan Feld (Univ. of Toronto, Canada)
- Henry LY Chan (The Chinese Univ. of Hong Kong, Hong Kong)
Nucleoside Analogue (NUC) Treatment Can Be Discontinued

Chun-Jen Liu
Department of Internal Medicine, Graduate Institute of Clinical Medicine and Hepatitis Research Center; National Taiwan University College of Medicine and Hospital, Taiwan

Treatment indication and stopping rules are different between patients with hepatitis B e antigen (HBeAg)-positive chronic hepatitis B (CHB) versus patients with HBeAg-negative CHB. Unlike patients with HBeAg-positive CHB, there are no clearly defined treatment endpoints (stopping rule) for those with HBeAg-negative CHB. Current treatment guidelines recommend long-term oral nucleos(t)ide analogue (NUC) therapy until immunological control is established, which is characterized by HBsAg seroclearance. Usually, premature withdrawal of NUC leads to virologic and even clinical relapse in more than half of the patients. Our recent data demonstrated that of 100 patients discontinuing 3-year entecavir (ETV) or tenofovir (TDF) therapy, patients discontinuing TDF exhibited significantly higher rates of virologic relapse (52.9% vs 6.1%; \( P < .001 \)) and clinical relapse (15.2% vs. 1.5%, \( P=.007 \)) at 3 months than those discontinuing ETV, but relapse rates at 12 months were comparable. The HBV DNA 1 month after NUC treatment cessation was an early predictor of subsequent relapse. Interestingly, recent data further suggest that exposure of viral antigens to host immune system post-withdrawal may trigger immune control which in some patients fortunately results in HBsAg loss. This favorable event occurs in around 20% of the patients nearly 3 years after stopping NUC. The rate of HBsAg loss was found to be even higher in those who did not receive NUC therapy after developing clinical relapse than in those who started NUC therapy for hepatitis activity. Thus, we believe that NUC treatment may be stopped in a proportion of patients after receiving NUC therapy. Notably post-treatment safety monitoring should be established, and retreatment should be initiated as clinical indicated. Further large studies are needed to validate the value of stopping NUC and to identify the biomarkers that can accurately predict the patients who benefit from finite therapy.
Special Lectures with Debates

Can We Discontinue Hepatitis B Virus Therapy? Pros. vs. Cons.

NUC Treatment Should Be Continued

Young-Suk Lim

Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

The ultimate goal of treating CHB is the prevention of cirrhosis, HCC and immature death in a long-term. However, these clinical outcomes need decades to be evaluated. And thus, intermediate surrogate endpoints, including biochemical, virologic, serologic, and histologic markers, are commonly used to determine treatment response and when treatment can be stopped.

With the availability of highly potent antiviral drugs, entecavir and tenofovir, the virologic response can be achieved in almost all patients as many real world studies have shown. With these drugs, the risk of resistance and safety concern is minimal during long-term treatment. Even in the patients with preexisting multiple drug resistant HBV, the use of tenofovir could induce virologic response in almost all patients, as our two clinical trials have shown.2-5

A systematic review also showed that long-term treatment with antiviral agents can improve clinical outcomes, in terms of hepatic decompensation and mortality as consistently demonstrated by randomized controlled trials and observational studies. Nonetheless, the risk of HCC persists even with long term treatment.6

Thus, the clinical benefits of current long-term nucleos(t)ide analogue (NA) is as follows:

• Marked decrease in mortality by hepatic decompensation
• Modest decrease in HCC risk
• Stabilizing hepatic function and improved quality of life
• Less need for frequent monitoring

After achieving HBsAg seroclearance during nucleos(t)ide analogue (NA) therapy, the long-term outcome of patients was very favorable with significantly lower mortality and HCC incidence compared to those without HBsAg seroclearance.7 The problem is that the rate of HBsAg seroclearance was too low. In our Korean cohort of patients, it was only 0.3% per year. In a modeling study for patients receiving NA therapy, the decline in HBsAg titer was very slow, and the median time needed to clear HBsAg was calculated to be 52 years.8

Thus, two most important unmet clinical needs with current long-term nucleos(t)ide analogue (NA) is as follows:

• Very low rate of HBsAg seroclearance
• Persistent risk of HCC

The idea of NA discontinuation is focusing on the potential improvement in HBsAg seroclearance rate. However, the clinical benefit of NA discontinuation is unclear. The outcomes of patients after NA discontinuation in many studies may be summarized as follows:

• Statistically higher rate of HBsAg seroclearance:
  • 39.4% (Caucasian cohort, HBV GT D 100%) during up to 6 years of follow-up9
  • 19% (Caucasian trial, HBV GT D 85%) during up to 3 years of follow-up10
  • 13% (Taiwan cohort, HBV GT B 80%) during up to 6 years of follow-up11
  • 2% (Systematic review of 25 studies including 1716 patients)12
The Liver Week 2019

- Virologic relapse (HBV DNA >2000 IU/mL) >75%12-14
- Clinical relapse (VR + ALT >x2 ULN) >60%12-14
- No reduction in HCC risk11,15
- Decompensation or death: about 4%11,14
- Unable to discriminate beneficial flares from severe potentially risky flares
- Necessity of very frequent monitoring q 2-4 weeks10

In conclusion, we have to consider following points when stop NA in CHB Patients:
- Statistically enhanced chance of HBsAg seroclearance
- Clinically unsatisfactory HBsAg seroclearance rate, esp. in Asian patients with HBV genotypes other than A/D
- Need to monitor very frequently and strictly
- Short-term risk: Potential risk of liver failure and death by acute liver failure
- Long-term risk: Unknown risk of HCC and cirrhosis with persistent viremia
- High rate of virological relapse and need to retreat without plateau up to 3 years after Tx D/C
- No reliable D/C criteria
- No reliable biomarker to predict HBsAg seroclearance
- No large-scale unbiased data
- No standard re-Tx criteria
- Unknown cost-effectiveness

Therefore, treatment discontinuation should be considered only in patients without cirrhosis or advanced fibrosis who can be followed closely with ALT and HBV DNA every 2 weeks at least during the first 6 months, and well understand the risk of acute liver failure and death.

It is important always to keep in mind that the physician’s first responsibility is “first, do no harm !”. Clinical outcomes (risk of acute liver failure and death) should not be jeopardized to achieve intermediate surrogate endpoints (HBsAg seroclearance).

References

State-of-the-Art Lecture 1

Chair:
Dong Jin Suh (KMP Healthcare Seoul Clinic)
Although hepatitis B virus (HBV) has been discovered for more than half a century with the availability of effective hepatitis B vaccines for over 3 decades, chronic HBV infection continues to be a major global health problem. It is estimated that there still exist 257 million HBsAg-positive individuals worldwide. Several host, viral, and external factors are identified to predict the progression of liver disease to cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC) in patients with chronic HBV infection. Nowadays, HBV-related disease progression can be controlled by effective treatment but a cure for chronic hepatitis B (CHB) remains a challenge. Currently approved antiviral agents for CHB therapy include direct antiviral nucleos(t)ide analogues (NUC) and immune modulatory interferon (IFN). Long-term NUC therapy profoundly suppress HBV replication through inhibition of viral reverse transcriptase/polymerase. However, viral relapse frequently occurs after discontinuation of NA in both HBeAg-positive and –negative CHB patients, primarily because of the persistence of intranuclear HBV covalently closed circular DNA (cccDNA). In contrast, despite IFN has dual effects of direct inhibition of viral replication and indirect enhancement of host immunity against the virus, the overall viral response to a finite duration of interferon therapy is far from satisfactory. To reach the goal of eliminating HBV infection, both preventive strategies and effective treatment of HBV infection are essential. First, interruption of HBV transmission routes is the most cost-effective way to reduce the global burden of HBV infection. Combining of hepatitis B immunoglobulin (HBIg) and hepatitis B vaccine as immunoprophylaxis in newborns has been shown to remarkably reduce the rate of mother-to-child transmission (MTCT). However, the implementation of immunoprophylaxis has a failure rate of 10 to 30% in infants born to mothers with an HBV DNA level of more than 200,000 IU/mL. To overcome the gap, a short-term tenofovir therapy for highly viremic pregnant mothers has been implemented as the standard of care to prevent HBV transmission. Second, treating those who are already infected with HBV would decrease the risk of transmission to others and the development of long-term disastrous clinical outcomes. From now on, HBsAg loss with or without the gain of anti-HBs has been recognized as a “functional cure” for HBV and serves as an ideal treatment endpoint. Nevertheless, it is rare to achieve this ultimate goal by using current treatment modalities. To this end, several novel strategies to clear HBsAg have been proposed. Among them, killing of HBV-infected hepatocytes via cytotoxic T cell (CTL) induced by immunotherapy is the most promising one. Although HBV-specific CTL response is vigorous and multi-specific during acute HBV infection, it is usually weak or even undetectable during CHB stage. An ideal immune-therapeutic strategy should combine profound suppression of viral replication to prevent uninfected hepatocytes from HBV infection, which can be achieved by existing NA treatment or novel direct antiviral agents (DAA) with different modes of action, and restoration of HBV-specific CTL response to clear the infected hepatocytes, which can be partially enhanced by host targeting agents (HTA). In summary, despite effective immunoprophylaxis and anti-HBV treatment, chronic HBV infection may remain a major threat in different parts of the world for a long time. Challenges ahead for the global control of HBV infection include the suboptimal coverage of universal vaccination in developing countries, a large number of chronic carriers are undiagnosed and many patients have limited access to treatments in highly endemic areas. All these barriers need to be overcome to eradicate HBV infection. Furthermore, an effective and simple treatment strategy should be implemented to reach the goal of HBV cure by 2030.
Symposium 2

Hepatitis B Virus

Chairs:
Kwan Sik Lee (Yonsei Univ.)
Jong Eun Yeon (Korea Univ.)

DAY 2: Friday, June 21, 2019 (14:00-15:30)
Viral Factors for Hepatitis B Virus-Related Hepatocellular Carcinoma

Jeong Won Jang
Department of Internal Medicine, The Catholic University of Korea, College of Medicine, Seoul, Korea

Hepatocellular carcinoma (HCC) is the commonest primary cancer of the liver. It is actually the 5th cancer worldwide and the 3rd leading cause of death. According to the National Statistical Office, the mortality rate of liver cancer in Korean population was 20.9/100,000 in 2017, ranking second after lung cancer with the corresponding rate of 35.1/100,000 in the first place. Despite a significant reduction in the prevalence of HBV infection among the young population, liver cancer mortality and morbidity rates are showing a slight increase in this country, suggesting that this is not because the burden of liver cancer disease is decreasing, but because the whole population in Korea is aging.

As its incidence continues to rise worldwide, identification of risk factors is essential so that HCC would be diagnosed at an early stage and curative treatment could be opted. In general, HCC typically develops in patients with one or more risk factors. The single largest risk factor in the development of HCC is cirrhosis of any etiology, which is present in approximately 80% of those who have primary liver cancer. Chronic HBV infection or HCV infection with advanced fibrosis follow cirrhosis as a cause of HCC. On the other hand, nonviral cirrhosis-related factors (autoimmune diseases, metabolic diseases, etc) or environmental factors (heavy alcohol consumption, cigarette, aflatoxin, etc) can also lead to the development of HCC.

A number of viral factors contribute to HBV-related hepatocarcinogenesis. Among them, high HBV DNA levels with active inflammation have been shown to independently increase the risk of HCC in chronic HBV carriers. HBV genotypes have been associated with the risk of HCC. Genotypes A and D are most prevalent in African populations; reports indicate that infection with genotype A is associated with an increased rate of HCC. HBV genotype C predominantly infecting Asians, especially Korean patients, is associated with a higher risk of liver cancer than genotype B. A high HBsAg level (>1,000 IU/mL) was reported to be predictive of HCC development among patients with HBeAg-negative disease and low HBV DNA < 2,000 IU/mL.

A multitude of reports have revealed that molecular variants of the HBV genome and HBV onco-proteins can also play a role as a viral factor in inducing liver carcinogenesis. Basal core promotor (BCP) T1762/A1764 mutation is among the most studied variants, showing the strongest association with HCC development in both Asian and Western studies. Precore mutation (A1896 mutation) was suggested as another mutants associated with HCC in some studies. Also, pre-S deletion of HBV has been associated with the progression of liver disease as well as the development of HCC in chronic HBV carriers. Viral onco-proteins from intrahepatic cccDNA or HBV integration in infected hepatocytes have been reported to drive hepatocyte malignant transformation through the direct oncogenic potential of HBV. Several studies highlighted the considerable importance of HBs protein mutants (pre-S/S variants) as well as C-terminally truncated HBx proteins in tumorigenesis. Integration of HBV DNA into the host genome occurs at early steps of clonal tumor expansion. It contributes to HCC development through cis- and trans-effects or chromosomal instability.

Hepatic carcinogenesis is a complex process with viral, host and environmental factors contributing to chronic inflammation, cirrhosis and ultimately, HCC. Interplay between persistently high HBV viral load, viral genotypes and molecular variants, HBV integration into the host genome, and HBV onco-proteins derived from cccDNA may contribute independently or jointly to the oncogenesis of HBV-related HCC. A better understanding of the HBV viral factors, its molecular mechanisms, and the development of validated biomarkers would facilitate early diagnosis, prognostics as well as therapeutics with new targets for drug interventions in chronic HBV carriers.
Novel Biomarkers in Management of Chronic Hepatitis B

Yasuhiro Tanaka
Nagoya City University Graduate School of Medical Sciences, Japan

Hepatitis B core-related antigen (HBcrAg) is a novel serum marker that correlates with intrahepatic hepatitis B virus (HBV) virological markers such as covalently closed circular DNA (cccDNA) and reflect the chronic hepatitis B disease activity in the liver. Although liver biopsy for the quantification of intrahepatic cccDNA and intrahepatic HBV DNA remains the most accurate measurement for viral reservoir, it is limited by its invasive nature, the potential for sampling error and the lack of a standardized assay.

Recently, we apply the droplet digital PCR (ddPCR) method to cccDNA quantification. The cccDNA content was correlated more closely with HBcrAg ($R^2=0.862$) than HBsAg ($R^2=0.652$). Importantly, cccDNA content/assay did not change during liver repopulation despite that cccDNA content/hepatocyte was reduced as the number of human hepatocytes increased (unpublished data), suggesting that cccDNA is extremely stable and its elimination may require cell death.

HBcrAg was measured in serum using the Chemiluminescent Enzyme Immunoassay (CLEIA) system for fully automated Lumipulse CLEIA analyzer. As for clinical practice of HBcrAg assay; 1) This marker is helpful in predicting spontaneous or treatment-induced HBeAg seroconversion, sustained response to nucleos(t)ide analogue (NA). Recently, core assembly modulators (CAMs) are developing, and the HBcrAg might be useful for monitoring during treatment among even HBeAg-negative patients. As the introduction of higher sensitive HBcrAg assay was desired, we show here fundamental and clinical information about the newly-developed assay. 2) The HBcrAg level at NA cessation point would be a predictor of non-relapse after cessation of NA therapy (Shinkai N, Tanaka Y, et al. 2007). Based on HBV guideline from the Japan Society of Hepatology, the combination of HBsAg and HBcrAg levels were scored into three groups; the percentage of prediction success was 80–90% in the low-risk group, approximately 50% in the medium-risk group and 10–20% in the high-risk group (Tanaka E, et al. Hepatol Res 2014). 3) HBcrAg is an excellent predictor of hepatocellular carcinoma (HCC) development in chronic hepatitis B patients without NA therapy. HBcrAg was superior to HBV DNA in terms of predictive power for HCC development by time-dependent receiver operating characteristic analysis (Tada T. et al. 2016). HBcrAg is also a predictor of the post-treatment recurrence of HCC during antiviral therapy. Serum HBcrAg and intrahepatic cccDNA suppression by NAs may be important to prevent HCC recurrence (Hosaka T et al. 2010). In conclusion, serum HBcrAg is a convenient and useful marker as a potential surrogate marker of cccDNA in the clinical practice. The higher sensitive HBcrAg could be applied to clinical trials including CAMs.

Introduction

Chronic hepatitis B (CHB) affects approximately 240 million persons worldwide, with an estimated 15%-40% progressing to cirrhosis, decompensation and/or hepatocellular carcinoma (HCC). Currently, hepatitis B virus (HBV) cannot be completely eradicated due to the presence of covalently closed circular DNA (cccDNA) in the nuclei of infected hepatocytes. Therefore, the present goal of monitoring is to ensure a high degree of virological suppression, ideally with hepatitis B surface antigen (HBsAg) seroclearance, leading to biochemical remission,
histological improvement and reduction of the risk of complications.\textsuperscript{6,7} Although liver biopsy for the quantification of intrahepatic cccDNA and intrahepatic HBV DNA remains the most accurate measurement for viral reservoir, it is limited by its invasive nature, the potential for sampling error and the lack of a standardised assay. Non-invasive serological markers can be used as surrogate markers of intrahepatic viral replicative activity. Established serological markers include serum HBV DNA levels and serum HBsAg titres, both of which have been shown to predict the risk of cirrhosis and HCC.\textsuperscript{8–11} However, as cirrhosis and HCC can still occur in many patients despite undetectable HBV DNA\textsuperscript{12} and HBsAg seroclearance,\textsuperscript{13,14} any promising markers with predictive value in these scenarios are very much welcome. Moreover, given that almost all patients treated with anti-viral therapy have undetectable HBV DNA, more accurate biomarkers for risk stratification are needed. Recently, linearised HBsAg (HQ-HBsAg) assay achieving an even lower limit of detection for HBsAg\textsuperscript{15} has been shown to correlate with serum HBV DNA and HBsAg levels, which makes it a potential marker for stratifying patients with HBsAg seroclearance.\textsuperscript{16} Another new marker, the hepatitis B core-related antigen (HBcrAg), has also been advocated as a serum marker for disease monitoring and prognostication of CHB. In this review, the clinical application of HBcrAg in CHB patients based on its virological features, the distinctive profiles in different disease stages and the profile under anti-viral treatment will be discussed.
Current Treatment Strategy: Towards Hepatitis B Virus Cure

Seng Gee Lim
National University of Singapore, Singapore
Future Treatment Strategy: Towards Hepatitis B Virus Cure

Henry LY Chan

Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Understanding of the intrahepatic hepatitis B virus (HBV) replication and trafficking has enabled the development of many new direct anti-viral agents. Many new treatment targets have been identified in recent years targeting to improve the chance of functional cure with a finite duration of therapy. Early clinical data has been promising. Myrcludex B is a myristoylated peptide encompassing amino acids 2-48 of the HBV pre-S1 region, which can specifically interact and block the HBV receptor, sodium taurocholate co-transporting polypeptide, on hepatocytes. RNA interference with siRNA is another strategy; it can block the mRNA and production of HBV antigens from all open-reading frames of HBV. Capsid assembly inhibitors have many potential therapeutic effects, including inhibiting of viral replication, reactivation of host innate immune response and disruption of the cccDNA maintenance.

Immune modulation is another strategy. But early data on toll-like receptor-7 agonist and therapeutic vaccine are not too promising. There is some exciting early data on the use of retinoic acid inducible protein I (RIG-I) agonist, which has a dual mode of action to directly inhibit viral replication and stimulation of type III interferon in chronic hepatitis B patients. In the long run, combination therapy of different antiviral agents is likely needed to achieve functional cure for chronic hepatitis B.
Clinical Hepatology Update

Clinical Trials of Management in Chronic Liver Diseases (*K)

Chairs:
Kwang Cheol Koh (Sungkyunkwan Univ.)
Il Han Song (Dankook Univ.)
Chronic Hepatitis B: Where Are We Now for Functional Cure?

Hyun Woong Lee

Department of Internal Medicine, Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Korea

만성 B형간염: Functional Cure를 위해 우리는 지금 어디에?

이 현웅
연세대학교 강남세브란스병원 소화기내과

Loss of HBsAg with sustained HBV DNA suppression has been termed functional cure. It also referred to as clinical or immunologic cure for chronic hepatitis B. It is the ideal goal of therapy recommended by current guidelines. It means sustained, undetectable HBV DNA and HBsAg titer with or without anti-HBs, but with the persistence of residual cccDNA, and the absence of spontaneous relapse after the cessation of treatment. However, current nucleos(t)ide analogues and pegylated interferon offers limited capability in achieving functional cure. The major cause is the lack of available drugs to eliminate cccDNA and integrated HBV DNA, and restore innate and adaptive immunities against hepatitis B virus. Current nucleos(t)ide analogues just suppress the viral load and pegylated interferon slightly enhance the immunologic response. Although it is not perfect, current potent antiviral agents with pegylated interferon combination therapy as well as selection of patients (with low viremia and low HBsAg titer) might be considered to achieve functional cure.

In the near future, antiviral agents targeting various steps of the HBV life cycle, including HBV entry (NTCP inhibitor), HBV cccDNA production and processing (cccDNA inhibitors), viral replication and viral protein expression (capsid assembly modifiers, RNA interference, Nucleic Acid Polymers, etc.) have entered preclinical or early clinical evaluation.

New combination of antiviral agents with immunomodulators might reactivate the host immune system and eliminate cccDNA and integrated HBV DNA to a complete cure of HBV infection.

1. Functional Cure의 정의

 최근 만성 C형간염이 새로운 경구용 항바이러스제의 개발로 인해 2030년 C형간염 완치 및 박멸이라는 캠페인이 시작되면서, B형간염도 완치를 위한 새로운 치료법 개발을 위한 노력이 시작되었다. B형간염의 완치란 혈액내의 HBV DNA, HBsAg의 소실과, 간조직내에 cccDNA 및 숙주 유전자에 integrated HBV DNA의 완벽한 소실을 의미한다.1,2 그러나 현재로서는 이러한 목표를 성취하기가 어려워 그 다음으로 제시된 목표가 바로 functional cure를 의미하는 혈액내의 HBV DNA, HBsAg의 소실 (anti-HBs 존재 유무와 상관없이)이다.1,2 비록 cccDNA가 존재하지만, 치료 종료 후 재발이 없으며, 간 손상이 진행하지 않고 간경변증이나 간세포암의 위험이 감소하는 것을 의미한다. 즉, 만성 B형간염의 성공적인 면역학적 조절 상태로 이는 급성 B형간염의 완치와 유사한 개념이라 하겠다. 그러나, 이러한 functional cure도 성취하기 어렵기 때문에 임상에서는 주로 혈청내 HBV DNA 음전 상태를 유지하고 간기능 검사의 정상화가 유지되는 것만으로도 좋은 치료 반응으로 평가하고 있어, 이러한 목표는 성취하기 쉽지만 임상의로서 전혀 만족스럽지 못한 목표이다.
2. 완치를 위한 도전의 어려움

B형간염의 만성화는 바이러스 요인 뿐만 아니라 숙주요인도 동반하기 때문에 접근이 어렵다. HBV 유전자는 숙주 간세포의 핵 내로 침범하여 episomal minichromosome의 형태, 이른바 cccDNA로 존재한다. HBV DNA의 일부 조각은 숙주의 유전자와 결합하여 cccDNA와 함께 바이러스 전사를 조절하면서 바이러스 복제에 유리한 세포내 환경을 만드는 것이다. 특히 cccDNA는 간세포내에 안정적으로 존재하면서, 생존기간이 길어서 새로운 virion이 들어오지 않아도 스스로 재충전이 가능하며, 다양한 HBV DNA 조각이 숙주 유전자와 결합하여 완치를 위한 도전을 어렵게 한다.33

여러 연구에서 밝혀진 대로, 바이러스 항원이 선천면역반응을 억제하고, HBV 특히 B세포의 기능을 손상시키며, 높은 농도로 유지되는 바이러스 항원이 결국에는 HBV 특이 T세포의 기능적 무력화를 유도한다고 알려져 있다. 특히 HBsAg은 episomal cccDNA와 S gene의 필수요소들이 잘 들어 있는 integrated HBV DNA 조각에 의해서 만들어지기 때문에, 숙주의 항바이러스 면역체계를 잘 유도한다면 cccDNA나 integrated HBV DNA 조각을 모두 제거하지 못하더라도 우리가 얻고자 하는 임상적인 목표인 functional cure를 성취할 수 있다. 또한 장기간 발현하는 면역세포의 기능을 강화하고 회복하게 해줄 수 있는 약제가 개발된다면 궁극적인 목표인 cccDNA나 integrated HBV DNA를 제거할 수 있다. 하지만, 현재로서 이러한 약제의 개발이 요원하여 선택된 환자들을 대상으로 기존 약제들의 병합요법에 대한 연구가 진행되고 있다.

3. 현재 약제들의 한계

경구용 약제들은 투약의 편의성과 복약 순응도가 높아 널리 사용되고 있지만, 강력한 항바이러스제로 알려져 있는 entecavir, tenofovir disoproxil fumarate, tenofovir alafenamide 조차도 cccDNA를 직접 타겟으로 개발된 약제가 아니다. 따라서, 장기간의 항바이러스제의 투약이 필요하며, 특히 HBeAg 음성 환자에서 약물을 종료하기가 어려울 것이다. 결국 전 생애기간동안 약물을 투약해야 한다는 부담감은 약제 부작용에 대한 대책과 함께 단기간 치료제에 대한 개발을 요구한다.

이에 반해서 pegylated interferon은 숙주의 면역체계를 활성화하며, 항바이러스효과를 보이는 단백질을 코딩하는 interferon stimulated genes의 생성을 유도한다. 이 기전을 통해 pegylated interferon은 HBV 전사와 억제하고 pregenomic RNA와 core particle의 파괴를 유도하며, cccDNA의 후생 유전 조절(epigenetic regulation)을 통해 바이러스 항원의 생성을 감소시킨다. 이러한 기전에 따라서 약제가 정해져 있으며, 영향력 있는ップ 격 정체 HBsAg 양의 감소와 치료 종료 후 반응의 유지를 관찰할 수 있다. 그러나 이런 효과를 보이는 환자의 비율이 적고 부작용으로 인해 임상의사의 처방 빈도가 낮다.

결국 cccDNA이나 integrated HBV DNA 조각을 제거하고, HBV에 대한 면역 관용상태를 해제하는 것이 만성 B형간염 치료를 위한 열쇠가 될 것이다. Nucleos(t)ide analogue 또는 pegylated interferon 단독으로는 간세포 내에 존재하는 cccDNA 제거에는 제한된 효과만 가지고 있어 functional cure를 획득하기도 어렵다. 그러나 두 약제의 적절히 조합할 경우에는 (De novo combination, sequential combination strategy) pegylated interferon의 장점인 선천면역을 조장하여 CD56bright NK 세포의 활성도를 유도하고 장기간의 nucleos(t)ide analogue 치료의 장단점은 HBV 특이 T세포의 활성화와 증식을 통한 적응면역의 활성화를 HBsAg 감소를 이끌어 functional cure를 획득할 수 있다.

4. Functional cure의 새로운 예측 인자

Anti-HBc 정량법이 HBeAg 음성 만성 B형간염 환자에서 functional cure의 예측인자로 이용될 수 있으며, HBV core antigen, HBeAg, 그리고 22-kDa precore 단백질을 측정하는 HBV core-related antigen (HBcrAg)이 간내 cccDNA 수치와 상관관계가 있음을 보고되었다. HBsAg 수치와 HBcrAg 수치를 이용하여 약제 중단 후 재발의 예측인자로 사용 가능성을 보고하였다. 최근에는 혈청에서 encapsidated pregenomic RNA를 측정할 수 있어 HBV RNA로 명명하고 간내 cccDNA의 전사 활동도를 반영하는 표지자로 사용될 수 있음을
보고하였다. 혈청 HBV RNA를 이용하여 항바이러스제 치료시 HBeAg 혈청 전환의 예측인자로, 항바이러스제 중단 후 HBsAg 재양전의 예측인자로 사용될 수 있다고 보고하였다.6,7 요약하면, 현재 사용되고 있는 항바이러스제 단독으로는 functional cure를 획득하기도 쉽지 않다. 최근 HBV 생활사를 단계별로 개념하며 만들어진 새로운 약제, HBV entry (NTCP inhibitor), HBV cccDNA inhibitors, capsid assembly modifiers, RNA interference, Nucleic Acid Polymers 등이 임상연구 중이다.8 미지의 미래에 새로운 약제들의 조합으로 숙주의 면역세포 능력의 회복과 바이러스 증식억제를 통해 cccDNA와 integrated HBV DNA 조각을 제거하여 궁극적인 완치까지 상상해 본다.

References
Non-Alcoholic Steatohepatitis: Key Targets and Endpoints

Byoung Kuk Jang
Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea

Non-alcoholic fatty liver disease (NAFLD) has diverse spectrum ranging from non-alcoholic fatty liver (NAFL) with only intrahepatic deposition to fatty deposits, to non-alcoholic steatohepatitis (NASH) with hepatocyte ballooning, inflammation and various stages of fibrosis, and finally cirrhosis. NAFLD is the most common cause of liver disease in western countries. In Korea, the prevalence of NAFLD diagnosed by abdominal ultrasonography is 16-33% and the prevalence is increasing.

NAFLD and NASH are chronic diseases that progress slowly, and it is very difficult to identify all-cause mortality, which are the endpoints of other common clinical studies. It is also difficult to identify liver related mortality, including complications of liver cirrhosis and the occurrence of hepatocellular carcinoma. Therefore, surrogate endpoints may be used instead for clinical studies in these chronic diseases.

According to the U.S. Food and Drug Administration (FDA), these surrogate endpoints are “reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence to predict benefit “on irreversible morbidity or mortality. Recent studies have shown that histologic features that have the greatest impact on mortality among patients with NASH were the presence of significant fibrosis. According to the natural history of NAFLD, NAFL has a low fibrogenic potential, while NASH progresses to advanced fibrosis and is known to be associated with more advanced metabolic diseases. Among the pathologic findings of NASH, inflammation and hepatocellular ballooning are known to be associated with fibrosis progression. Inflammation, hepatocellular injury is a disease activity that leads to progression of fibrosis to cirrhosis. And the degree of fibrosis means the stage of disease, which means to what extent cirrhosis has already been reached. Therefore, appropriate endpoints should be set according to which one of them is targeted. Surrogated endpoints are resolution of NASH without worsening of fibrosis or improvement in fibrosis without progression of steatohepatitis. These endpoints are based on repeated liver biopsy findings, making it difficult to perform large-scale, long-term clinical studies. In addition, if the above mentioned endpoints are reached, it is necessary to confirm whether the mortality caused by NASH is reduced. A number of new drugs are currently under clinical trials targeting these endpoints, and the results of these studies are expected to be reported in the near future.

References

Cirrhosis: Effort against Fibrosis and Portal Hypertension

Kyung-Ah Kim
Department of Internal Medicine, Inje University, Ilsan Paik Hospital, Goyang, Korea

The pathophysiology of decompensation in cirrhosis involves portal hypertension, bacterial translocation followed by systemic inflammation resulting in splanchnic arteriolar vasodilation and circulatory dysfunction. The mainstays of treatment for cirrhosis are targeted against key factors of pathogenesis of decompensation. Reducing portal hypertension by non-selective beta-blockers, targeting intestinal dysbiosis and bacterial translocation by rifaximin, improving circulatory dysfunction by long-term albumin administration and decreasing the systemic inflammation by statins have shown potential benefit to decrease cirrhosis progression. Further studies are warranted to confirm the safety and benefits of these strategies.

Keywords: Cirrhosis, Portal hypertension, Non-selective beta blocker, Statin, Albumin, Rifaximin

서 론
만성적인 간손상은 정상적인 간세포 소실 및 간섬유화를 거쳐 간경화로 귀결되며, 증상이 없는 대상성 간경화는 매년 5~7%에서 비대상성 간경화로 진행한다. 간경화 진행을 억제하는 현재 가장 효과적인 방법은 바이러스, 알코올 등 간손상의 원인을 치료하는 것이며, 아직 간섬유화 자체를 호전시키고 정상 간세포를 회복시키는 입증된 치료법은 없다. 간경화 합병증 발생의 병태 생리에 대한 이해가 깊어지면서, 이러한 병태생리의 각 단계 즉, 장내세균 전이 (bacterial translocation), 순환기능장애 (circulatory dysfunction), 전신 염증 (systemic inflammation), 문맥압강증 등을 치료함으로써 간경화 합병증과 사망을 줄이라는 다양한 시도들이 성공적으로 이루어지고 있다. 이 글에서는 간경화 및 문맥압 항진증의 합병증을 예방하고 치료하기 위한 최신 연구들에 대해 소개하고자 한다.

본 론
1. 비선택적 베타차단제
비선택적 베타 차단제 (non-selective beta-blockers, NSBB)가 내장혈류량 감소를 통하여 문맥압을 저하시킴으로써 임상적으로 의미 있는 문맥압 항진증 (clinically significant portal hypertension, CSPH)과 큰 정맥류를 동반한 간경화 환자에서 정맥류 출혈을 감소시키는 것은 잘 알려져 있으며, 현재 정맥류 출혈의 1차 및 2차 예방을 위한 표준 치료로 권고된다.1 그러나, NSBB를 정맥류가 없는 대상성 간경화 환자에게 투여하였
을 때 정맥류 발생을 예방하는 효과는 입증되지 않았고, 작은 정맥류에서 큰 정맥류로의 진행을 막는 효과도 상반된 연구 결과를 보인다.5,6 비선택적 베타차단제와 alpha1 차단제의 성질을 동시에 지닌 carvedilol이 작은 위도 정맥류의 진행을 늦출다는 연구가 최근 발표되었다.7 또한, 상반된 연구 결과를 보인다.8 브로모실 투여로 상반된 연구 결과를 보인다.9,10 그러나, 브로모실과 alpha1 차단제 복합체(sustained-release, SBR)는 동반한 비대상성 간경화 환자에서 상반된 연구 결과를 보인다.9

2. 스타틴(statins)

스타틴은 항염증 및 항섬유화 효과를 지니며 동물 실험에서 간섬유화를 억제한다.11 또한 Rho kinase와 KLF2 발현을 억제함으로써 문맥압감소를 효과적으로 억제할 수 있다.12 대부분의 후향 코호트 연구에서 스타틴 사용이 간경화 환자에서 비대상성 간경화 진행 및 사망률을 감소시키는 것으로 보고되었다.11,13 몇몇 소규모 무작위 대조군 전향 연구에서 스타틴 투여는 대상성 간경화 환자에게 안전하며, 문맥압을 효과적으로 감소시키는 것으로 보고하였다.14,15,16 158명의 정맥류 출혈을 동반한 간경화 환자를 대상으로 한 후향 연구에서 스타틴과 NSBB 동 시 투여군은 NBBB 단독 투여군에 비하여 정맥류 재출혈률의 유의한 차이는 없었으나 전체 사망률은 유의하게 낮은 것으로 보고하였다.17

3. 알부민

알부민 투여는 간경화 환자에서 대량 복수 천자로 인한 순환기능 장애를 줄이고, SBP시 발생할 수 있는 콩팥 기능 이상을 예방한다. 또한 혼합 수축제와 함께 간성중후군 치료에 사용된다.2 알부민은 주로 유효 혈장량을 증가시킴으로써 효과를 나타내지만, 항염증 및 항산화 효과도 지닌다.18 저나트륨혈증을 동반한 간경화 환자들을 대상으로 한 최근의 후향 연구에서 알부민 정맥 투여는 저나트륨혈증을 개선하고 30일 사망률을 감소시키는 것으로 보고되었다.19 그러나, 혈압이 낮은 복수를 동반한 간경화 환자에서 알부민 정맥 투여는 의미 없는 결과를 보였으나 정맥류 재출혈을 억제하는 것으로 보고되었다.20 국내에서 시행된 후향 코호트 연구에서는 알부민 정맥 투여군에서 대조군에 비해 사망률과 복수를 동반한 간경화 동반 사망률이 유의하게 높았다(77% vs. 66%, P=0.028).21

4. Rifaximin

Rifaximin은 장에서 흡수되지 않는 항생제로 간성뇌증의 2차 예방 효과가 입증되어 락툴로즈와 병행 투여가 권고되고 있다.22 Rifaximin의 SBP 예방 효과는 한 연구에서 rifaximin은 norfloxacin이나(오즈비 0.45, 95% 신뢰구간 0.19-0.76) 항생제를 투여하지 않는 것에(오즈비 0.34, 95% 신뢰구간 0.11-0.99) 비하여 SBP 발생을 효과적으로 감소시키는 것으로 나타났다.23 Rifaximin은 장내 세균인을 변화시키고 장내 세균변화가 억제하여 내독소혈증(endotoxemia) 및 혈중 염증성 사이토카인 감소시키는 것으로 보고하였다.24 그러나, 순환기능 장애 개선에 대해서는 상반된 결과를 보고하고 있다.25,26 국내에서 시행된 후향 코호트 연구에서 rifaximin과 lactulose를 병행 투여한 군이 lactulose 단독 군에 비하여 생존율이 높고, SBP, 정맥류 출혈 및 간성뇌증의 위험가 낮은 것으로 보고하였다.27 또한, 간성뇌증 예방 효과를 평가한 무작위 전향 연구를 post hoc 분석한 연구에서 rifaximin이 간경화 환영을 감소시키고 특히 MELD 점수가 12 이상인 경우 간성뇌증을 제외한 합병증도 감소시키는 경향을 보였다.28
5. 기타
반복적인 간성뇌증을 경험한 간경화 환자에서 변이식 (fecal microbial transplant, FMT)의 안정성을 평가하기 위한 1상 연구가 최근 발표되었다. 간경화 환자에서 FMT는 안전하였으며, 심장장내 미생물 다양성을 회복시키고 혈청 interleukin-6, lipopolysaccharide-binding protein 등을 감소시켰다. 간성뇌증의 재발 빈도에 차이가 없었으나 인지기능 점수가 향상되었다.29

비만한 간경화 환자에서 생활 습관 조절을 통하여 체증감량을 하면 문맥압이 의미 있게 감소한다는 연구가 발표되었다.30 이 연구에는 바이러스 간염 등 비알코올성지방간염 이외의 간경화 환자들도 포함되었으며, 체중을 10% 이상 감량한 군에서 문맥압 감소는 더욱 유의하였다. (-23.7% vs -8.2%)

결론
간손상의 원인을 제거하는 것이 간경화의 진행을 막는 현재 가장 중요하고 효과적인 치료이지만, 비대상성 간경화 발병 과정 중 여러 요인을 차단함으로써 간경화의 항병증을 줄이고 생존율을 증가시킬 수 있다. NSBB가 장내 폐혈 예방 이외에 비대상성 간경화로의 진행 예방에 효과적인 가능성이 있다. 스타틴은 문맥압을 낮추고 생존율을 항상시킨다. 장기간 일부분 투여로 생존율을 항상시킨다는 연구가 발표되었고, rifaximin이나 FMT 등 장내 미생물을 조절하는 치료에 대한 가능성이 제시되고 있다. 그러나, 이러한 치료법의 효과 및 안전성은 간경화의 진행 정도에 따라 달라질 수 있고 아직 대규모 무작위 전향 연구가 불충분하므로 향후 연구를 통한 검증이 필요하다.

References


Hepatocellular Carcinoma Treatment Showdown: Mono vs. Combination Therapy

Ju Hyun Shim

Asan Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

1. Mono-treatment options for incurable HCC

Current guidelines recommend transarterial chemoembolization (TACE) as the standard therapy for patients at an intermediate (BCLC-B) stage beyond the Milan criteria based on high levels of evidence. TACE with drug-eluting beads (DEB) has been launched with promising results and is increasingly used with less liver toxicity than and at least similar antitumor efficacy to conventional TACE. However, TACE alone is not a treatment method with curative intent, and thus cannot be generally expected to induce perfect therapeutic outcomes. On the other hand, radioembolization has been recently proposed as another modality for intermediate HCC patients, its safety issue regarding reduction in liver function remains to be figured out. Sorafenib is the first agent ever to show a survival benefit in patients with advanced HCC and has now become the standard first-line treatment for patients with BCLC-C stage HCC. Lenvatinib has recently shown to be non-inferior to sorafenib, and accordingly represents an alternative to sorafenib in the first-line setting. For the patients who intolerable or progressed on sorafenib, regorafenib and next cabozantinib exhibited a survival improvement as rescue therapy. A subset of sorafenib-failed patients with serum AFP of ≥400 ng/mL also would benefit from second-line ramucirumab. Although final results are pending, early data on immune checkpoint inhibitors have shown promising signs of therapeutic efficacy in advanced HCC patients.

2. Combination treatment options for incurable HCC

The combinations of local and systemic therapies have been eagerly studied to improve response rate and survival in patients with incurable HCC. Since ischemia and hypoxia induced by TACE would trigger the activation of proangiogenic factors, TACE combined with anti-angiogenic agents may constitute an effective strategy to achieve better outcomes. Disappointedly, a randomized phase II study testing the combination of DEB-TACE plus sorafenib versus plus placebo (SPACE trial) did not demonstrate satisfactory efficacy in terms of time to progression and overall survival in patients with intermediate-stage HCC. Additionally, a recent phase III trial failed to demonstrate a survival benefit of SIR-Spheres combined with sorafenib over sorafenib alone in inoperable patients (SORAMIC trial). As for advanced HCC, clinical benefit with sorafenib monotherapy is inadequately limited with less than 3 months of actual survival gain. Recent studies have carefully suggested TACE-based combinations with radiotherapy or sorafenib as superior tools to the standard sorafenib for fighting against advanced-stage HCC, if tumors would not have metastatic foci. Targeted therapy combined with immune checkpoint inhibitors is also an approach currently under investigation. A phase 1b trial of lenvatinib plus pembrolizumab induced possibly compelling response and progression outcomes in individuals with unresectable HCC. In 2018, the FDA has granted a breakthrough therapy for atezolizumab, an anti-PDL1 inhibitor, plus bevacizumab, a monoclonal antibody against
VEGF, as a first-line treatment for patients with advanced HCC, and a phase III trial (NCT03434379) comparing this combination versus sorafenib is currently ongoing.

3. Conclusions

The management of HCC has evolved considerably over the last decade. As the current scenario of monotherapeutic strategies still remains unsatisfactory against a myriad of refractory HCCs, future challenges would be to evaluate sequential or combination regimens and to incorporate them into clinical management as soon as possible.

References

Hepatology Associates Course (*K)

Chairs:
Byung Seok Lee (Chungnam National Univ.)
Byung-Cheol Song (Jeju National Univ.)
Treatment of Chronic Hepatitis B and C Virus

Eileen L. Yoon

Department of Internal Medicine, Inje University Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea

만성 B형간염과 만성 C형간염의 치료

윤아일린
인제대학교 상계백병원 내과학학교실

Chronic hepatitis B and C are the most important etiologies of chronic liver disease in Korea. The ultimate goals of antiviral treatment are to decrease mortality from liver disease and lengthen survival by preventing viral replication and alleviating hepatic inflammation and by preventing the progression of fibrosis, development of liver cirrhosis, and hepatocellular carcinoma. The approaches for antiviral treatment of chronic hepatitis B and C are described for the hepatology associates and they are based on the recently updated guidelines suggested by the Korean associations for the study of the liver.

Keywords: Chronic, Hepatitis, Hepatitis B virus, Hepatitis C virus, Treatment

1. 만성 B형간염

1) 서론

B형간염은 전 세계적으로 3억 5천만 명의 만성 감염자가 있고 매년 60만명 이상이 관련 질환으로 사망하는 중요한 질환이다. 우리나라에서는 1980년대에는 HBV 감염률이 8-10%의 높은 수준이었으나 신생아 예방접종 사업, 국가 예방접종 사업, 주산기 감염 예방사업이 시작되면서 HBV 감염률은 점차 감소하여 2008년 이후에는 균질한 3.0% 수준을 유지하고 있다. 그러나 우리나라 만성 간염 및 간경변증 환자의 약 70%가, 간세포암종 환자의 약 65-75%에서 HBsAg 이 검출되는 점을 고려하면, 아직도 만성 B형간염이 우리나라 국민 건강에 미치는 영향은 매우 크다. 만성 B형간염은 감염 후 면역학적 자연경과에서 다양한 소견으로 나타나기에 단 1회의 검사를 통하여 해당되는 임상 단계를 단정짓거나 항바이러스 치료 시작을 결정하는 것이 부적절한 경우가 많다 (Figure 1). 특히 다른 바이러스에 의한 중복감염, 음주력, 약물 복용력 및 HBV 감염과 간세포암증의 가족력 등에 중점을 두는 병력 청취와 신체 검사가 매우 중요하다.

2) 치료 목적과 목표

만성 B형간염의 극복적인 치료 목적은 HBV 증식을 억제하여 염증을 완화시키고 섬유화를 방지하여, 간경변증과 간세포암증의 발생을 예방함으로써 간질환에 의한 사망률을 낮추고 생존율을 향상시키는 것에 있다. 그러나 현재까지의 항바이러스 치료제는 치료에도 불구하고 백내의 cccDNA가 지속되기 때문에 HBV의 완전 퇴치를 기대하기가 어려우므로 바이러스반응을 장기간 유지하는 것이 중요하다. 이와 같이 치료 목적을 달성하기 위한 임상에서의 목표는 ALT의 정상화, 혈청 HBV DNA 불검출, HBeAg 혈청소실 및 전환, HBsAg 혈청소실
3) 치료 대상과 초기 평가

항바이러스 치료 시작을 결정하는 데에는 크게 1) 간질환의 진행 정도, 2) B형간염 바이러스의 증식 정도, 그 리고 3) 간손상의 동반 여부와 같은 요소들을 고려한다(Figure 2). 간질환의 진행 정도는 대상성 또는 비대상성 간경변증 여부를 판단하여야 하며 B형간염 바이러스의 증식 정도는 혈청 HBV DNA PCR 검사를 통하여 확인 할 수 있다. 간손상의 동반 여부는 혈청 ALT가 주로 활용되며, 그 외에도 간생검을 통해서 염증괴사 동반 여부 를 확인할 수 있다.

4) 치료 약제

2017년부터 국내에서 테노포비어 알라페나마이드 푸마르산(tenofovir alafenamide fumarate, 이하 테 노포비어AF)과 베시포비어 디피복실 말레산(besifovir dipivoxil maleate, 이하 베시포비어)이 성인에서 만 성 B형간염 치료제로 승인됨에 따라 총 8가지의 항바이러스제를 사용할 수 있다. 약제들은 크게 주사용 항바 이러스제인 페그인터페론 알파와 경구용 항바이러스제로 나눌 수 있으며 경구용 항바이러스제는 내성발현의 유전자 장벽에 따라 크게 두 부류로 나뉜다. 엔테카비어, 테노포비어DF, 테노포비어AF, 베시포비어는 유전자 장벽이 높아 HBeAg 양성 및 음성 만성 B형간염 환자의 1차 치료약제로 권고된다. 특히 엔테카비어와 테노포 비어DF는 효과와 장기간의 안전성이 검증되었으나 테노포비어AF와 베시포비어는 장기 추적 데이터가 조금 더 필요하다.
5) 경구용 항바이러스제 사용 중 치료 반응의 정의 (Table 1)

Table 1. Definition of response to nucleos(t)ide analogues therapy for chronic hepatitis B

<table>
<thead>
<tr>
<th>Category of response</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virologic response</td>
<td>Decrease in serum HBV DNA to an undetectable level on real-time PCR assay</td>
</tr>
<tr>
<td>Partial virological response</td>
<td>Decrease in serum HBV DNA of more than 2 log₁₀ IU/mL but detectable HBV DNA on real-time PCR assay after at least 12 months of therapy with high-potency NAs, or after at least 6 months of therapy with low-potency NAs in compliant patients.</td>
</tr>
<tr>
<td>Virologic breakthrough</td>
<td>Increase in serum HBV DNA of more than 1 log₁₀ IU/mL compared to the lowest value, or redetection of serum HBV DNA at levels 10-fold the lower detection limit after achieving a virological response.</td>
</tr>
<tr>
<td>Serological response (HBeAg)</td>
<td>HBeAg loss or HBeAg seroconversion</td>
</tr>
<tr>
<td>Serological response (HBsAg)</td>
<td>HBsAg loss or HBsAg seroconversion</td>
</tr>
<tr>
<td>Biochemical response</td>
<td>Normalization of ALT level</td>
</tr>
<tr>
<td>Biochemical breakthrough</td>
<td>Increase in serum ALT level after ALT normalization on antiviral therapy</td>
</tr>
<tr>
<td>Genotypic resistance</td>
<td>Detection of HBV mutations known to confer antiviral resistance during antiviral therapy</td>
</tr>
<tr>
<td>Phenotypic resistance</td>
<td>Decreased susceptibility (in vitro testing) to inhibition by antiviral drugs associated with genotypic resistance</td>
</tr>
<tr>
<td>Cross resistance</td>
<td>HBV mutation selected by one antiviral agent that also confers resistance to other antiviral agents</td>
</tr>
</tbody>
</table>

6) 경구용 항바이러스제 치료 중 모니터링

경구용 항바이러스제 치료 중에는 간기능검사 및 혈청 HBV DNA를 1-6개월 간격으로 검사하고 HBeAg/anti-HBe는 3-6개월 간격으로 검사할 수 있다. 또한 치료 중에 반응 예측과 종료 시점 결정에 도움을 줄 수 있는 HBsAg 정량검사를 고려할 수 있다. 바이러스 반응이 확인된 후에도 혈청 HBV DNA를 3-6개월 간격으로 지속적으로 측정하며 항바이러스 치료시 각각의 약물 부작용에 대한 모니터링이 필요하다.

2. 만성 C형간염

1) 서론

C형간염바이러스는 전 세계적으로 3%의 인구가 C형간염 바이러스에 감염되어 있는 것으로 추산되며 우리나라에서 만성 간질환의 15-20% 원인을 차지하여 급, 만성간염, 간경변증 및 간세포암증의 주요 원인 중 하나이다. 최근 수년간 C형간염의 치료방향은 종전에 사용하던 주사제인 인터페론 없이 경구 투여약제인 직접작용항바이러스제 (direct acting antivirals, DAA)를 각 유전자형과 과거 치료 경험에 따라 병합 투약함으로써 부작용을 최소화하고, 치료기간이 짧지만 성공률은 90%를 상회할 정도로 매우 높아 향후 C형간염 완치라는 이상적인 목표에 한층 가까이 접근할 수 있을지 기대된다. 그러나 C형간염 바이러스는 오염된 혈액 또는 혈액제제의 수혈이나 장기이식, 주사용 약물남용, 불안전한 주사나 의료시험, 오염된 주사기나 바늘에 찔리는 경우, 감염자와의 성접촉 등에 의해 비정구적으로 전염되므로 완치된 환자라도 주요 감염 경로와 예방수칙에 대해 교육해야 한다. 치료 목적, 치료 대상, 치료 약제, 치료 중 및 종료 후 모니터링에 대하여 2015년과 2017년 대한 간학회 C형간염 진료 가이드라인에 근거하여 요약하였다.

2) 치료 목적과 목표

만성 C형간염의 단기 치료 목표는 치료 종료 12주 또는 24주에 혈청 HCV RNA가 검출되지 않는 상태인 지속바이러스반응(sustained virological response, SVR)에 도달하는 것이다. 이를 통한 궁극적인 치료 목표는
HCV를 박멸하여 HCV 감염으로 인한 간경변증의 혈종증, 간세포암증, 간외 합병증의 발생 및 이로 인한 사망을 예방하는 것이다.

3) 치료 대상
치료 여부는 급성간염의 중증도, 간의 합병증, 치료 성공 확률, 심각한 부작용 발생 가능성, 동반 질환 유무, 환자의 치료 의지 등을 고려하여 개별화해야겠으나 치료 금기가 없는 모든 C형간염 환자는 치료의 대상이며 특히 F3 이상의 진행된 섬유화를 동반한 환자와 간이식 전후의 환자는 우선적으로 치료한다.

4) 치료 약제
DAA는 C형간염 바이러스의 생활사에 직접 작용하여 항바이러스 효과를 나타내며 작용 부위에 따라 HCV nonstructural protein NS 3/4A 단백분해효소억제제(protease inhibitor, PI), NS5A 억제제, NS5B 종합효소억제제 등이 있다. NS3/4A PI 는 HCV 증식에 필수적인 단백 분해과정을 차단하며 asunaprevir, grazoprevir, glecaprevir, voxilaprevir 등이 있다. NS5A 억제제는 HCV 복제 및 조립을 억제하며 daclatasvir, ledipasvir, ombitasvir, elbasvir, velpatasvir, pibrentasvir 등이 있다. NS5B 종합효소 억제제는 sofosbuvir와 dasabuvir가 있다. 현재까지 국내에서 승인된 DAA는 ledipasvir/sofosbuvir, daclatasvir, asunaprevir, ombitasvir/paritaprevir/ritonavir, dasabuvir, elbasvir/grazoprevir, glecaprevir/pibrentasvir가 있다. DAA로 치료할 때 각 약제의 특성을 이해하고 급성간염 및 부작용 등을 고려하여 적절한 약제를 선택하며 다양한 약제와 약물상호작용을 유발할 수 있으므로 반드시 치료 전에 사용하고 있는 다른 약제에 대하여 상호작용 여부를 확인해야 한다.

5) 치료 중 및 치료 종료 후 모니터링
치료 전 환자에게 치료 순응도가 SVR 도달에 중요함을 주지시키고 치료 중 약제 복용의 순응도를 정기적으로 확인하여야 하며, 치료 중 새로운 약제를 사용하게 되는 경우 약제 간 상호작용을 반드시 확인해야 한다. 치료 반응에 따른 요법을 위해 평가하는 급속 바이러스 반응(rapid virological response, RVR)은 치료 4주째 검출한계 50 IU/mL 이하의 예민한 검사법으로 혈중 HCV RNA가 검출되지 않는 상태이며, 조기 바이러스 반응(early virological response, EVR)은 치료 12주째 혈중 HCV RNA가 치료 전 기저값에 비해 2 log 이상 감소하거나 검출한계 50 IU/mL 이하의 예민한 검사법으로 검출되지 않는 상태로 정의한다. 치료 종료 12주 또는 24주째 에피데믹 검사법으로 혈중 HCV RNA가 검출되지 않는 상태를 SVR로 정의하며 최근 연구에서 치료 종료 12주째 평가한 SVR과 치료 종료 24주에 평가한 SVR의 일치율이 치료 약제와 관계없이 98%로 알려져 있다. 치료 중 소실되었던 혈중 HCV RNA가 재출현하면 바이러스 돌파현상(breakthrough), 치료 종료 후 소실되었던 혈중 HCV RNA가 재출현하면 재발(relapse)로 정의한다. 만성 C형간염에 대한 항바이러스 치료의 효과를 평가하기 위하여 치료 종료 후 12주 또는 24주에 HCV RNA 농도를 측정하여 SVR 도달 여부를 확인하여야 하며, SVR에 도달한 경우에도 치료 전에 진행된 간세포암증을 관리해야 한다. 더불어 SVR에 도달하지 못한 경우, 만성간염 및 간경변증의 일반 관리가 필요하다.

References
5. KASL Clinical Practice Guidelines for Management of Chronic Hepatitis B The Korean Association for the Study of the
Liver (KASL), Korea, 2018.


Management of Acute Variceal Bleeding

Seung Kak Shin
Department of Internal medicine, Gil Medical Center, Gachon University College of Medicine, Incheon, Korea

Acute variceal bleeding is a fatal complication in patients with liver cirrhosis. Once there is suspicion of variceal bleeding, hemodynamic stabilization should be achieved through appropriate fluid therapy and red blood cell concentrate transfusion. Vasoactive drugs should be started as early as possible, and prophylactic antibiotic treatment is also needed. If acute esophageal variceal bleeding is confirmed by endoscopy, endoscopic variceal ligation (EVL) should be performed. In case of treatment failure, balloon tamponade can be used as a temporary “bridge” until definitive treatment can be performed. Transjugular intrahepatic portosystemic shunt (TIPS) should be considered as a rescue therapy. If acute gastric variceal bleeding is confirmed by endoscopy, endoscopic variceal obturation (EVO) or EVL should be performed in gastroesophageal varices (GOV) type 1, and EVO should be performed in the fundal varices. In case of treatment failure, TIPS may be considered as a rescue therapy. Balloon-occluded retrograde transvenous obliteration (BRTO) or vascular plug-assisted retrograde transvenous obliteration (PARTO) may also be considered in patients with gastro-renal shunt.

서 론

간경변증의 대표적인 합병증 중 하나인 위·식도정맥류는 문맥압항진증으로 인한 우회혈관 발생이 주된 인자로 작용하며, 1 정맥류 확연을 위해 내시경 검사를 시행한 간경변증 환자의 52% 정도에서 정맥류가 관찰되다고 알려져 있다. 2 또한 정맥류가 동반된 간경변증 환자의 약 12%에서 1년 내 정맥류 출혈이 발생하며, 출혈의 주된 위험인자로는 큰 정맥류, 정맥류에 적색징후 동반 및 비대상성 간경변증이 있는 경우이다. 3 위·식도정맥류 출혈은 단시간에 대량 실혈을 초래하여 사망에 이를 수 있는 응급 질환으로 간경변증 환자들의 중요한 사망원인 중 하나이다. 4 따라서 정맥류가 동반된 간경변증 환자에서는 정맥류 출혈 예방을 위한 적절한 예방적 치료가 필요하며, 급성 출혈이 발생한 경우 신속한 환자의 소생 및 안정화와 함께 빠른 시간 안에 지혈이 이루어져야 한다. 본고에서는 급성 정맥류 출혈의 응급 대처 및 치료에 대해서 살펴보고자 한다.

본 론

1. 급성 위·식도정맥류 출혈의 진단

문맥압 항진증이 동반된 환자에서 상부위장관 출혈이 있는 경우 위·식도정맥류 출혈을 의심할 수 있으며, 확실한 진단은 내시경 검사로 한다. 내시경에서 정맥류로부터 활동성 출혈이 관찰되거나 정맥류 표면에 혈괴
(blood clot)나 백태(white nipple)가 붙어있는 경우 또는 위내 혈액이 관찰되나 정맥류 이외 다른 잠재적인 출혈 병소가 발견되지 않으면 급성 정맥류 출혈로 진단할 수 있다.5

2. 급성 위·식도정맥류 출혈의 일반적 치료

급성 위·식도정맥류 출혈은 집중치료를 요하는 내과적 응급질환으로서 초기 순환 및 호흡 유지가 매우 중요하다. 혈액학적 안정상태를 유지하기 위해 환자의 연령, 심혈관계 질환 유무, 활동성 출혈 여부, 혈액학적 상태를 고려하여 적절한 수액요법 및 농축 적혈구 수혈이 필요하다. 이때, 과량의 수액 투여 및 수혈은 혈액량을 상승시켜 오히려 정맥류 출혈을 조장할 수 있으므로 주의가 요구된다. 일반적으로 초기 혈소판로 150,000의 미만시에 7-9 g/dL로 유지하는 제한적 수혈이 권장된다.6 신선동결혈장 수혈 또는 제조김 응고인자 VIIa 투여를 통한 출혈조절성이의 교정 효과는 투여하지 않아 권고되지 않으며,7,8 심한 혈소판 감소증을 보이는 환자에서는 혈소판 수혈을 고려해볼 수 있으나 아직 이에 대한 임상연구는 많지 않다.

3. 급성 위·식도정맥류 출혈의 약물 치료

위장관 출혈이 있는 간경변 환자에서는 세균 감염의 발생 위험이 높으므로 내원 당시부터 예방적 항생제 치료가 필요하다.9 Vasopressin, terlipressin, somatostatin, octreotide와 같은 혈관수축제는 문맥압을 감소시킴으로써 급성 위·식도정맥류 출혈의 지혈 효과를 나타내므로 정맥류출혈이 의심되는 환자는 가능한 빠른 시간 내에 혈관수축제 투여가 필요하다.10 위정맥류 출혈 환자의 약물 치료에서는 혈관수축제의 효과에 대한 임상연구가 제한적이다.11-13 위정맥류 출혈 환자에서 정맥류 출혈을 일으킨 기저부는 뚜렷한 개선되지 않으므로 뚱뚱한 식도정맥류 출혈 환자에서는 고려되어야 할 수가 있다.14-16

4. 급성 위·식도정맥류 출혈의 내시경 치료 및 방사선 중재술

1) 급성 식도정맥류 출혈의 내시경 치료 및 방사선 중재술

내시경에서 급성 식도정맥류 출혈이 확인되면 내시경적 지혈술을 시행하여야 하는데, 내시경 정맥류 절찰술(endoscopic variceal ligation, EVL)이 1차 치료로 권장되며 내시경 주사 정화요법(endoscopic injection sclerotherapy, EIS)은 신장식, 사방, 무작용 발생 위험이 높아 더 이상 추천되지 않는다.17-21 내시경에서 정맥류로부터 활동성 출혈이 관찰되거나 최근 출혈 혈액적 정맥류 표면에 혈괴나 백태가 확인되면 이에 대한 EVL을 시행하여야 한다. 결찰할 부위를 후드에 정렬하여 후드에 푸른 분을 타고 하루에 조정한 후 내시경으로 충분히 흡입하여 정맥류를 후드내로 백아들인 후 “red out sign”이 나타나면 정맥류 기저부를 결찰해야 한다. 이후 비선택적 베타차단제 투여와 함께 관찰하던 식도정맥류에 대하여 정맥류가 완전히 소실될 때까지 2-8주 간격으로 반복적으로 EVL을 시행하는 것이 최적의 방법으로 도움이 된다. 무작위 배정 임상연구들에서 재출혈의 위험이 높은 생설피탈이 일부 환자에서 내시경적 지혈술에 이어 조기에 정맥류 간력내분인 간동맥(transjugular intrahepatic portosystemic shunt, TIPS)을 하였을 때 재출혈 예방 및 사망 유도율이 감소함을 보였으며,18,19 최근 급성 정맥류 출혈 환자를 대상으로 시행된 무작위 배정 임상연구에서 내시경적 지혈술만 도포의 치료적 가능성은 제시하였는데 추가적 연구가 필요하다.20

2) 급성 식도정맥류 출혈의 내시경 치료 실패 후 구조요법

약물 및 내시경 치료에도 불구하고 지혈에 실패한 급성 식도정맥류 출혈 후, TIPS의 내시경적 지혈술을 하여 실패했을 경우, 풍선 탐폰삽입(ballooon tamponade)은 TIPS 등의 치료 후 가교치료(bridging therapy)로서 시행할 수 있으며, 약 80-90%의 환자에서 지혈에 효과적이기는 하나 임상적 재출혈 발생 위험이 50%에 이르는 것으로 보고되고,21,22 식도내경, 식도플라스틱, 흉부형성 재활 등의 심각한 합병증을 유발할 수 있으므로 풍선 탐폰을 유지하는 기간이 24시간을 넘지 않도록 주의가 필요하다.23

3) 급성 정맥류 출혈의 내시경 치료 및 방사선 중재술

① GOV1 출혈의 내시경 치료

The Liver Week 2019
위식도정맥류(gastroesophageal varices, GOV)는 식도정맥류가 위의 소만을 따라 확장된 경우(GOV type 1, GOV1)와 위바닥(fundus)으로 확장된 경우(GOV type 2, GOV2)로 나뉘는데, GOV1은 좌위정맥(left gastric vein)으로부터 유입되는 혈류에 의해 형성되며 식도정맥류와 해부학적으로, 병태생리학적으로 비슷하기 때문에, GOV1에 대한 출혈은 식도정맥류출혈과 유사하게 치료할 수 있다고 알려져 있다.24,25 GOV1 출혈에서 에 대해서 EVL 또는 내시경 정맥류 폐쇄술(Endoscopic variceal obliteration, EVO) 치료 방법을 사용할 수 있는데 위정맥류는 식도정맥류에 비해 더 크고 얇고 있는 점막층이 두꺼워 층층체에 밴드형이 어려울 수 있으며 쉽게 밴드가 빠지게 되면 재출혈의 위험성이 있으므로 유의해야 한다. GOV1 출혈에서 EVO의 두 치료 중 어느 하나를 먼저 권고하기에는 아직 근거가 충분하지 않으며,11,25-28 환자 상태와 정맥류의 크기, 출혈 양상, 의료 기관의 경험과 자원 등을 고려하여 적절한 치료를 선택하도록 한다.

2) GOV2와 IGV1 출혈의 내시경 치료 및 방사선 중재술

식도정맥류가 위바닥으로 확장된 GOV2와 위바닥에 정맥류가 단독으로 형성된 1형 단독 위정맥류(isolated gastric varices type 1, IGV1)를 위바닥 정맥류(fundal varices)로 통칭하며, 위바닥 정맥류는 후방위정맥 (posterior gastric vein)과 좌위정맥(left gastric vein)에서 혈류가 주로 유입된다.29,30 위정맥류 출혈 환자에서 가장 활발하게 시행되는 내시경적 지혈 치료는 EVO이다. EVO는 cyanoacrylate와 같은 조직접착제(tissue adhesive)를 정맥류 안으로 직접 주입하여 지혈 및 정맥류 소실을 유도하는 치료법이다. 천자 부위는 정맥류 내부의 혈류의 방향을 고려하여 결정하는데 정맥류 중심의 돌출된 부위는 내부 압력이 집중되는 곳이므로 가급적 피하는 것이 좋다. 시술자는 천자할 정맥류의 크기와 내부 혈류 속도, 출혈 양상을 고려하여 접착제의 주입량을 결정한다. 대표적인 조직접착제인 2-N-butyl cyanoacrylate는 경화시간을 늦추기 위해 리피오솔(lipiodol)과 1:1 정도의 비율로 혼합하여 사용하며, 혼합액을 1~2 mL씩 반복적으로 주입하여 치료한다. 정맥류가 크고 내부의 혈류 속도가 빠르다고 판단되는 경우에는 시술자의 판단에 따라 일회투여량 2 mL 이상으로 증량하기도 한다. EVO 외에도 위바닥 정맥류 출혈에서 TIPS를 고려할 수 있으며, 위신장단락(gastro-renal shunt)이 동반된 경우에는 풍선차단역행경정맥 폐색술(balloon-occluded retrograde transvenous obliteration, BRTO) 또는 혈관마개보조 역행 경정맥 폐색술(vascular plug-assisted retrograde transvenous obliteration, PARTO) 등의 치료 방법을 고려할 수 있는데 임상적 판단에 따라 빠르고 안전하게 적용이 가능한 치료를 선택하도록 한다.

4) 급성 위정맥류 출혈의 내시경 치료 실패 후 구조요법

내시경 치료로 급성 위정맥류 출혈의 초기 지혈에 실패하는 경우 구조요법으로 TIPS를 고려할 수 있다.31,32 불응성 출혈에서 비록 소규모 연구이지만 BRTO도 TIPS와 비교하여 유사한 지혈 성적을 보였기 때문에 위신장단락이 동반된 환자에서 고려해 볼 수 있다.33, 34

요약 및 결론

급성 정맥류 출혈은 단기간에 대량 실혈을 초래하여 사망에 이르는 응급 질환으로, 급성 정맥류 출혈이 의심되는 경우 우선적으로 치료할 수 있도록 학습을 통해 학력학적 안정을 이루어야 하며, 가능한 빠른 시간 내에 혈관수축제 투여가 권장된다. 세균 감염의 발생 위험이 높으므로 예방적 항생제 치료가 함께 필요하다. 이후 내시경 검사를 통해 급성 식도정맥류 출혈이 확인되면 EVL을 시행하고, 지혈에 실패하는 경우 풍선 밴드형을 통과할 수 있으나 유지기간이 24시간을 넘지 않도록 하며, 구조요법으로서 TIPS를 우선적으로 고려해야 한다. 내시경 검사를 통해 급성 위정맥류 출혈이 확인되는 경우에는 GOV1에서는 EVO 또는 EVL을 시행하고, 위바닥정맥류에서는 EVO를 시행한다. 지혈에 실패하는 경우에는 구조요법으로 TIPS를 고려할 수 있고 위신장단락이 동반된 환자에서는 BRTO 또는 PARTO를 고려할 수 있다. 환자의 출혈 양상에 따라 적절한 치료 방법이 선택되어야 한다.
References

25. Park SW, Seo YS, Lee HA, et al. Changes in Cardiac Varices and Their Clinical Significance after Eradication of Esopha-
Liver Transplantation: When and How?

Bum-Soo Kim
Division of HBP surgery, Department of Surgery, Kyung Hee University College of Medicine, Korea

간이식: 언제 어떻게 하나?
김 범 수
경희대학교병원 외과

Liver transplantation (LT) is well-established and well-accepted therapeutic options for patients with acute and chronic liver failure and hepatocellular carcinoma. In 1963, Starzl et al. performed the first LT in a patient with biliary atresia.

In 1983, the National Institutes of Health (NIH) reported that the liver was no longer an experimental procedure and should be regarded as a therapeutic option for patients with end-stage liver disease and is worth expanding its application. In 1988, the first deceased donor LT in Korea was performed in a patient with Wilson's disease. Recently, LT has evolved rapidly the past two decades and outcomes of LT are improving due to postoperative management, operative technique development, development of immunosuppressive drugs, etc. The indications for liver transplantation has been expanded. In recent years, approximately 1300 to 1500 liver transplantation are being performed annually.

Patients are usually considered for liver transplantation if they have evidence of fulminant hepatic failure, a life-threatening systemic complication of liver disease, more commonly, cirrhosis with complications such as hepatic encephalopathy, ascites, hepatocellular carcinoma, hepatorenal syndrome, or bleeding caused by portal hypertension.

However, there has been no definite guideline when to consider and how to prepare for liver transplantation for individual patient with terminal liver disease. Therefore, we review when to consider liver transplantation and how to prepare for liver transplantation in Korea.

Keywords: Indication, Liver transplantation
씨병, Budd-Chiari증후군 등이 원인질환이며 진행하는 심한 황달, 조절되지 않는 복수, 정맥류 출혈, 조절되지 않는 간성혼수, 간에 국한된 결절할 수 없는 간세포암 등이 간이식의 적응증이 된다. 급성간부전의 경우 내과 치료가 예상할 수 없는 병의 악화로 이식센터에 진단되게 되는 것이 중요하다. 하지만 이식건의 부족과 높은 이식 후 단기 사망율을 고려하여 내과적, 외과적, 정신과적 급기심상이 있는지 이식이 적응이 되는지 신중하게 결정하여야 한다. 이식 승인을 받은 환자는 대기자 명단에서 병의 중증도에 따른 우선순위가 부여된다. 따라서 원인 간질환과 협력중에 대해 언제, 어떻게 적절한 간이식등록 및 평가를 하는지 기술하고자 한다.

국내 간이식 현황

뇌사자 간기증의 부족으로 우리나라를 포함한 대부분의 아시아 국가에서는 뇌사자 간이식을 대체해 생체간 이식이 활발하게 진행되고 있다. 2017년 KONOS 연보에 따르면 간이식 대기자는 5,295명이었으며 뇌사자 간 이식 450건, 생체간이식 1032건으로 총 1482건의 간이식이 시행되었다. 이식자의 평균 대기시간은 155일이었다. 주된 이식 적응증은 만성 B형간염에 의한 간경변, 간세포암, 간성혼수 등이었다. 이식 후 생존율은 뇌사자에서 3개월, 1년, 3년, 5년 82.7%, 78.0%, 72.5%, 69.6%였고, 생체간이식에서 3개월, 1년, 3년, 5년 94.1%, 89.7%, 83.3%, 80.6% 이었다.

적절한 간이식에 대한 시기결정

적절한 간이식에 대한 시기결정은 다음의 3가지 단계에 의존한다. 첫째 이식센터로의 전원, 둘째 이식팀에 의한 신중한 평가 후 뇌사자 등록 셋째 내과적 치료 및 이식편 우선순위 및 할당에 관한 정책이다.

예측할 수 없고 빠르게 진행되는 급성 간부전 및 중증의 간염 환자는 이식센터에 의뢰해야 하며 간석화 환자에 보통 간성혼수, 복수 간암, 간신증후군, 식도정맥류출혈 등의 합병증이 발생하며 이식센터로 의뢰된다. 뇌사자 잔기의 부족으로 수혜자의 엄격한 선별기준이 적용되는데 이러한 선별기준으로 이식하지 않았을 때보다 이식했을 때 낮은 단기 사망율을 예측할 수 있고 급기시 환자를 배제할 수 있다.

간이식의 결과는 급성 간부전의 경우 3개월, 1년, 3년, 5년 94.1%, 89.7%, 83.3%, 80.6% 이었다. 보존적 치료 혹은 간이식을 선택하는 기준은 임상의 판단이 중요하고 객관적인 지표로 King’s College 기준이 참고가 되고 있다.

급성 간부전

급성 간부전은 잠재적으로 가역적인 간손상으로 이전에 간질환의 병력이 없는 건강한 사람에게서 간기능 손상으로 최초 증상발생 후 8주이내에 급격히 간기능장애, 간성혼수가 진행하는 경우를 말한다. 원인으로는 약에 의한 것이 가장 많으며 바이러스성 간질환이나 간암의 경우도 있다. 이러한 환자의 10% 미만에서 간이식이 시행된다. 두개강 내 고혈압 및 수술 전후 관리가 어려운 경우 단기 생존율이 낮으나 최근의 생존율은 1년 79%, 5년 72%로 보고되었다. 보존적 치료 혹은 간이식을 선택하는 기준은 임상의 판단이 중요하고 객관적인 지표로 King’s College 기준이 참고가 되고 있다.

간성 뇌증이 없는 환자라도 INR이 1.5인 환자는 이식센터로 전원해야 하며 간성 뇌증이 나타나면 급성 간부전을 진단이 이루어진다. 이후 임상증상은 급격히 악화되며 응급 간이식을 위한 등록을 해야 한다. 간성 혼수 3, 4 단계에서는 수일 내에 매개질환, 심폐기능부전, 다발성 장기부전이 일어날 수 있다.

만성간질환에서의 간이식 적응증

간의 합성능력저하에 대한 정도는 CTP 점수에 잘 반영되어 있고 만성간질환 환자의 증상을 평가하는 수단으로 잘 알려져 왔다. 그러나 CTP점수는 주관적인 평가가 반영되고 간기능저하 환자의 생존율의 예측할 수 있는 신기능이 고려되지 않는 단점이 있다. 이에 혈청 빌리루빈, 크레아티닌, INR을 기반으로 하는 새로운 객관적인 예측모델을 개발하였는데 MELD score이다. 미국에서는 2002년부터 MELD점수에 따라서 수혜자 우선순위를 결정하였다.
간세포암에서의 간이식 적응증

간세포암에서 간절제술과 간이식은 근치적 치료이다. 하지만 단순히 하나의 방법으로 모든 간암환자에게 적용하기는 어려우며 잘 선택된 환자에서 간절제 및 이식은 5년 생존율 60~80%으로 최상의 결과를 얻을 수 있다.

간질환과 만성 B형간염을 동반한 모든 환자에서 일차병원에서 간암의 선발 검사를 하고 있으며 따라서 일차 의료를 담당하는 의사가 간암의 치료 방법 중 하나라는 것을 인식하여야 한다.

이탈리아 밀란(Milan) 그룹은 영상검사에서 간외 전이와 혈관침범이 없고, 단일결절인 경우 5 cm 이하, 다발성인 경우 결절이 3개 이하이면서 각 결절이 3 cm 이하인 간세포암 종환자에서 간이식 후 4년 생존율 75%, 무병 생존율 83%라는 우수한 성적을 발표하여 간세포암 종 중환자에서의 간이식 기준을 제시하였다. 밀란 척도 내에 포함되는 간세포암 종 중환자에 있어서 간이식은 가장 좋은 무병 생존율을 보장할 수 있는 매우 이상적인 치료법이다.

밀란 척도 시행 후 간암에서의 간이식은 전세계적으로 증가하였으며 아시아에서 간이식의 적응증에서 1/3을 차지하였으며 미국과 유럽에는 10~20%를 차지하고 있다. 하지만 아시아에서는 가정자의 비율이 상대적으로 낮아 이러한 간암환자들이 뇌사자 간이식을 받을 확률이 낮아 생체 간이식이 요구된다. 밀란 척도와 같이 간의 배분하는 시스템에 영향을 받지 않고 이식을 할 수 있기 때문에 많은 아시아 센터에서는 확장된 간암기준을 채택하여 사용하고 있다.

MELD 점수는 간성질환의 단기적을 예측하여 가장 위중한 환자에게 간을 제공하는 시스템이다. 하지만 종양의 이식 후 진행예측, 효과적인 이식 및 생존율을 예측하기 어렵다.

간세포암의 진행으로 인하여 대기자 명단의 탈락이 문제가 된다. 미국의 UNOS (United Network for Organ Sharing)에서는 간이식 대기 우선순위를 결정하기 위해 MELD 점수를 도입하여, 처음 등록 후 6개월이 지난 후에도 밀란 척도 범위에 있다면 MELD 점수 28점을 주고, 이식 대기 후 3개월마다 10%의 가산점을 준다. 그러나 우리나라는 국립장기이식관리센터에서 KONOS (Korean Network for Organ Sharing) 등급제를 운영하였고 간세포암종 환자에 대한 가산점이 없었다. 이러한 문제를 해결하고자 2016년 6월부터 MELD 점수를 도입하여, 간세포암종이 밀란 척도에 해당되는 경우, 대기자 MELD 점수가 0~12인 경우 4점을 추가, MELD 점수 13~20인 경우 5점을 추가, MELD 점수 21점 이상은 추가 점수를 부여하지 않도록 개정하였다. 하지만 대부분 MELD 점수가 30점 이상인 경우에 시행되기 때문에 간세포암종 환자에서 상대적으로 간을 배정 받기는 어렵다.

종양의 진행을 막으며 이식까지의 가교 치료로서 절제술, 고주파치료 경동맥색전술, 방사선치료 등이 시행될 수 있지만 효과에 대해서는 자료가 부족하다.

지방간 환자의 간이식

비알코올성 지질환은 단순 지방간에서 간경화에 이르기까지 다양한 임상증상을 나타내며 현재 서양인구에서 25~35% 아시아에서 5~15% 가 폐암을 가지고 있다.5 말기간질환환자는 이식을 고려해야 하며 이것은 영구적인 치료가 아니며 NAFLD가 이식 후 재발하는 것으로 나타났다.5 이것은 다양한 인자에 의해 영향을 받으므로 이식 전후에 체중조절 및 적절한 식이 요법과 당 및 지질 조절이 필수적이다.
자가면역성간질환

자가면역성 간질환은 자신의 간조직 내에 표현되는 항원에 대한 면역관용의 결핍으로 발생하는 질환군으로 자가면역성 간염(autoimmune hepatitis, AIH), 원발성 담즙성 간경변(primary biliary cirrhosis, PBC)과 원발성 경화성 담관염(primary sclerosing cholangitis, PSC)이 해당한다.10

자가면역성 간질환에서의 간이식은 다른 말기간질환에서와 마찬가지로 합병증을 동반한 간부전이 발생할 때 적용층이 된다. 즉 중증의 치료에 반응하지 않는 소양증 또는 중증 간성 뇌증 등이 발생시 이식을 고려한다.

담관 협착과 관련된 재발성 담관염 등도 드물게 간이식의 적용층이 된다. 경화성 담관염 환자에서 담관암의 발생은 10년간 7-9%로 보고되며 높은 재발율로 간이식의 급기이지만 미국 메이요 병원에서는 잘 선택된 환자에서 술 전 항암방사선 치료 후 간이식으로 좋은 성적을 보이고 있다.

알코올성 간질환에서의 간이식

알코올성 간질환은 유럽과 북미에서 가장 흔한 간이식의 적용층으로 전체 간이식의 20-30%를 차지하며 점차 증가 추세에 있다.11,12 전원시기 및 장기배분 등은 간경변의 일반적인 규칙에 따라 적용된다. 다른 질환과 달리 대부분의 간이식 센터에서는 6개월간의 금주를 해야만 뇌사자 등록을 하는데 첫번째 이유는 금주기간 동안 간기능이 호전되는 시간을 주며 두번째로는 이식 후 재음주는 가능성을 예방하기 위해서이다. 이식환자의 재음주율은 다양하게 19-50%로 보고되고 있다.13재음주율의 위험성을 고려하지 않은 경우 재음주자 간기능을 개선하는 것은 윤리적이 논란이 있다. 심한 알코올성 간염은 단기간의 금주가 필요하며, 금주기간 동안 간기능이 호전되어야 한다.14

결론

간이식을 준비하기 위해 임정기간이 소요되며, 간이식의 성공률은 국외과 기관에서의 성공률이 90% 이상이다. 간염, 급성간부전, 생명을 위협하는 간질환의 합병증이 있는 간질환 환자는 간이식센터에 전원되어 적절한 간이식 등록이 필요하다. 임상상황에 따라 적절한 간이식을 고려해야 하는 간질환의 합병증을 선택할 수 있다. 간이식센터에서는 환자 간 상호작용을 갖춘 간이식의 조건을 충족하는 환자를 선택하는 기준이다.

References

6. 2018 간세포암종 진료 가이드라인
간세포암종: 진단과 병기 평가

정우진
계명대학교 의과대학 소화기내과

서 론
우리나라 시민들의 가장 중요한 사망원인은 암으로, 두번째 원인인 심장질환보다도 유의하게 높게 평가된다. 2017년 자료에 의해 악성신생물에 의한 사망을 보면 전체 연령에서 간암에 의한 사망은 남성에서 2위, 여성에서는 4위의 원인으로 평가되었으나, 40~59세 사이에서는 간암으로 인한 사망률이 1위로 평가되었다. 지난 20여년간 연간 절대 간암 조사망률과 조발병률은 증가하였으나 연령표준화사망률과 연령표준화발병률은 감소 추세를 보이고 있는데, 이는 우리나라 인구집단과 간암 발생자들의 연령분포가 다르게 고령화되고 있는데 기인한 것으로 추정된다. 여전히 소폭 증가추세를 보이는 간암 조사망률과 조발병률은 극복하기 위한 수단으로 간암, 특히 간세포암종의 정확한 진단과 병기 평가는 중요하게 평가된다.

본 론
간세포암종의 고위험군으로 평가하는 만성 B형간염, 만성 C형간염, 간경변증환자에서 6개월 간격으로 간 초음파검사와 알파태아단백검사를 시행하는데, 이러한 감시검사에서 간 종괴가 확인될 경우 어떠한 성격의 병변인지 확인해야할 필요성이 대두된다.

I. 간세포암종의 진단
1) 병리학적인 진단: 병리 검사를 통한 진단
간질환의 진단을 위한 영상학적 방법의 발달로 인하여 생검을 통한 진단이 많이 감소하고 있지만, 간생검은 아직도 주요한 진단의 수단이다. 간 종괴가 확인된 경우 간암의 진단이 영상학적 방법으로 가능하다면 조직학적 진단은 필요하지 않을 수 있었지만, 영상학적 소견이 전형적이지 못할 경우 조직학적 진단이 필요할 수 있다. 대부분의 간암환자는 그 기저에 간경변증을 동반하고 있는 경우가 많아서 실제로 간생검을 시행하기 어려운 경우가 많다. 세침흡입세포검사, 세침흡입생검, 침핵생검 등의 진단 민감도는 67~93%로 다양하며, 2 cm 이하의 소간암의 경우 민감도가 더 떨어질 수 있는 점, 생검을 통한 암종의 진단이 0.6~5.1% 정도로 보고되는 점, 생검 자체의 위양성률이 33% 정도로 보고되는 점 등의 이유로 대부분의 간암 진단은 임상적 기준에 따라 비침습적으로 진단된다. 대한간암학회/국립암센터에서의 진료가이드라인에 따르면 간세포암종의 고위험군에서 1 cm 이상의 결절이 확인되고 역동적 조영증강 CT, 역동적 조영증강 MRI, 또는 간세포특이조영제를 이용한
MRI 중 하나 또는 둘 이상에서 간암에 합당한 소견이 없거나, 1 cm 미만의 간결절이 발견된 경우 간암 활동성이 억제된 환자에서 혈청 aFP가 정상범위보다 상승되고 추적검사에서 지속적으로 상승하며 상기 영상검사 중 둘 이상에서 합당한 소견을 보이는 조건에 해당되지 않거나 간암의 전형적인 소견을 보이지 않는 경우에 진단을 위해 간 생검을 고려하는 것으로 권고된다(Fig. 1).

Figure 1. KLCA/NCC diagnostic algorithm and recall policy in patients with a high risk of hepatocellular carcinoma.

2018년 AASLD의 진료가이드라인에서는 1 cm 이상의 간세포암종에서 동맥기 조영증강과 문맥기 조영강소의 전형적인 소견을 보이는 일반적인 진료가이드라인의 권고대로 진단 시 90% 이상의 민감도를 보이며, 이러한 진료가이드라인에서의 기준을 만족하지 못하거나 1 cm보다 작은 경우에는 조직검사를 고려할 수 있다고 권고한다.1

2) 영상학적 방법을 통한 진단
간세포암종의 고위험군에서 감시검사 중 발견된 1 cm 이상의 결절은 진단을 위해 역동적 조영증강 전산화단층촬영, 역동적 조영증강 자기공명영상 혹은 간세포특이조영제 조영증강 MRI를 일차 영상검사로 시행하는데, 역동적 조영증강 CT의 병변별 민감도는 76%, MRI 83%, 환자별 특이도는 CT 91%, MRI 89%였고, 간세포특이 조영제를 사용하였을 경우에는 세포외액조영제를 사용한 역동적 MRI보다 높은 민감도(85.6% vs. 77.5%)와 양성 예측도(94.2% vs. 83.6%)의 메타분석 결과를 보였다.2 3 일차 영상검사에서 전형적인 소견을 보이지 않을 경우, 단계적으로 역동적 조영증강 CT, 역동적 조영증강 MRI 혹은 간세포특이조영제 MRI, 혈관내조영제 조영증강 초음파를 통한 추가 영상검사를 시행하여 민감도를 향상시킬 수가 있다.
간세포암종의 전형적인 영상진단은 1 cm 이상의 결절이 동맥기 조영증강 CT, 역동적 조영증강 MRI 혹은 간세포특이조영제 MRI에서 동맥기 조영증강과 문맥기, 지연기 혹은 간담도기에서 조영제 씻김현상을 보일 때를 의미한다. 전향적 연구에서 역동적 조영증강 CT 또는 MRI의 동맥기 조영증강 및 문맥기 또는 지연기 조영제 씻김현상을 보이는 간암의 진단에 따라 이는 간세포암종의 진단을 한 단계 더 정확하게 만들고 있다.
김현상만을 진단 기준으로 하였을 때 민감도는 약 65-89%, 특이도는 91-100%로 보고된다. 간세포암종의 고위험군에서 감시검사 중 새로 발견된 1 cm 미만 결절은 6개월보다 짧은 간격으로 추가 초음파검사를 시행한다.4.

II. 병기 평가

간세포암종의 병기는 환자의 예후를 평가하고 적절한 치료를 결정하는데 필요할 뿐 아니라 서로 다른 치료법에 대한 연구의 결과를 비교하는데 필수적으로 현재까지 다양한 병기 분류법이 개발되어 왔고, 전술한 바와 같이 대부분의 간세포암종 환자는 기저 간기능 장애를 가지고 있기 때문에 간세포암종 환자의 예후를 평가하기 위해서는 간세포암종의 요소와 위험정이 여부 뿐 아니라 간기능의 평가가 중요할 수 있다.

간세포암종의 병기 분류중 하나인 Okuda 분류법은 간세포암종의 크기 뿐만 아니라 혈중 알부민, 벌리루빈, 복수 유무 등 환자의 기저 간기능을 병기 분류에 포함시킨 최초의 분류법으로서의 의의가 있지만, 이 분류에서의 분석에 사용된 대부분의 환자가 진행된 간세포암종 환자였기 때문에 초기 간세포암종의 경우에 사용하기에는 적절하지 않은 단점이 있다(Table 1). 이후 발표된 병기 중 환자의 간기능을 포함시킨 대표적인 것으로는 Cancer of the Liver Italian Program (CLIP) 분류, Barcelona Clinic Liver Cancer (BCLC) 분류, Japan Integrated Staging (JIS) 분류 등이 있다.

Table 1. Okuda classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor size &gt;50%</th>
<th>Ascites</th>
<th>Albumin (g/dL)</th>
<th>Bilirubin (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>II</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>III</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
</tbody>
</table>

CLIP 병기는 환자의 간기능과 종양의 크기, 알파태아단백, 문맥침범 유무로 병기를 결정한다. 합산된 점수에 의해 CLIP 0에 속하는 간세포암은 종괴의 크기에 대한 세부 분류가 없이 전체 간 부피의 50% 미만으로 정의하고 있어서 초기 간세포암종의 분류에 취약한 단점이 있어서 수술이 가능한 환자의 치료 후 예후 추정이 어려울 수 있다(Table 2).

Table 2. Cancer of the Liver Italian Program (CLIP) classification

<table>
<thead>
<tr>
<th>Variables</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh stage</td>
<td></td>
</tr>
<tr>
<td>uninnodular and extension</td>
<td>0</td>
</tr>
<tr>
<td>multinodular and extension</td>
<td>1</td>
</tr>
<tr>
<td>massive or extensive</td>
<td>2</td>
</tr>
<tr>
<td>Tumor morphology</td>
<td></td>
</tr>
<tr>
<td>≤50mm</td>
<td>A</td>
</tr>
<tr>
<td>&gt;50mm</td>
<td>B</td>
</tr>
<tr>
<td>&gt;100mm</td>
<td>C</td>
</tr>
<tr>
<td>AFP (ng/ml)</td>
<td></td>
</tr>
<tr>
<td>≤400</td>
<td>0</td>
</tr>
<tr>
<td>&gt;400</td>
<td>1</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>1</td>
</tr>
<tr>
<td>yes</td>
<td>2</td>
</tr>
</tbody>
</table>

BCLC 분류는 환자의 간기능 평가에 있어서 Child-Pugh 등급 외에 ECOG 수행능력, portal hypertension 유무 등을 추가시킨 특징이 있는데 단순히 환자의 병기만을 분류하는 것이 아니라 각각의 병기에 해당하는 치료법을 정한 치료 지침의 성격을 또한 가지고 있다(Fig. 2). BCLC 분류법은 미국간학회 간세포암 치료 가이드라인에서도 제시되어 널리 사용 중이지만, intermediate stage의 정의가 ECOG 0로 한정되어있고, 경동맥화학색전술의 적응증을 이 환자들을 대상으로 한 것은 임상 현장에서 의견의 차이가 있어 intermediate와 advanced stage의 세부 분류가 더 필요할 것으로 보여진다.

JIS 분류법은 일본 간암연구회에서 정의한 TNM stage와 Child-Pugh 등급에 따라 점수화하여 환자를 분류하는 것으로, CLIP 분류법과 비교하여 초기 간세포암 환자의 분류에 장점을 가진다(Table 3).
Figure 2. Barcelona Clinic Liver Cancer (BCLC) classification; M, metastasis classification; N, node classification; PS, performance status; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

Table 3. Japan Integrated Staging (JIS) classification

<table>
<thead>
<tr>
<th>Variables</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh grade</td>
<td>A</td>
</tr>
<tr>
<td>TNM stage by LCSGI</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>C</td>
</tr>
</tbody>
</table>

위의 분류법과 다르게 전통적으로 간세포암 자체의 병기를 분류하는 것으로 American Joint Committee on Cancer (AJCC) tumor node metastasis (TNM) 병기가 있으며, 이 분류법은 BCLC와 더불어 여러 연구에서 널리 사용되고 있는데 섬유화 정도가 포함되어 있는 특징이 있다(Table 4).

Table 4. American Joint Committee on Cancer (AJCC) TNM staging for liver tumors (8th ed., 2017)
대한간암학회/국립암센터에서의 진료가이드라인에서 간세포암종 병기는 modified UICC 병기를 기본으로 하고, BCLC 병기와 AJCC/UICC 병기를 보완적으로 사용한다(Table 5).

Table 5. Modified UICC stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IV A</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IV B</td>
<td>T1, T2, T3, T4</td>
<td>N0, N1</td>
<td>M1</td>
</tr>
</tbody>
</table>

결 론

바르게 고령화되고 있는 간암 발병자들에서 소폭 증가추세를 보이는 간암 조사망률과 조발병률을 극복하기 위한 수단으로 간세포암종 환자에서의 정확한 진단과 병기 평가는 환자의 예후를 결정하는데 매우 중요하다고 평가되므로 이를 위한 좀 더 체계화된 진단과 병기 분류법은 매우 중요하다고 평가된다.

References

4. 대한간암연구회, 국립암센터. 2018 간세포암종 진료 가이드라인.
The Liver Week
Satellite Symposium for Regeneration Medicine

Chairs:
Shuji Terai (Niigata Univ., Japan)
Soon Koo Baik (Yonsei Univ. Wonju)
Comparison of Bone Marrow-Derived Mesenchymal Stem Cells Isolated from Normal and Cirrhotic Patients

Young Woo Eom

Cell Therapy and Tissue Engineering Center, Wonju College of Medicine, Yonsei University, Wonju, Korea

Background/Aims: Mesenchymal stem cells (MSCs) have been actively studied for use as regenerative medicine for various intractable diseases including cirrhosis. In particular, autologous or allogenic MSCs isolated from bone marrow (BM) and umbilical cord have been applied in clinical trials. Nevertheless, none of the autologous MSCs of the cirrhotic patient and normal MSCs have been shown to be effective in the treatment of cirrhosis. The aim of this study is to identify the BM-derived MSCs (BMSCs) suitable for the treatment of cirrhosis by comparing the characteristics of the BMSCs isolated from the BM of liver cirrhosis patient and normal BM.

Methods: Mesenchymal stem cells from liver cirrhosis patients (BpMSCs) were obtained from Pharmicell. Normal MSCs (BcMSCs) were isolated and cultured from normal BM mononuclear cells in Lonza. Potentials of proliferation and differentiation, cell surface antigen expression, immunosuppressive activity and mitochondrial activity of BMSCs were compared and analyzed.

Results: In the early passage, the population doubling time of BpMSCs was 68 hours, 10 hours shorter than that of BcMSCs, when the BMSCs were cultured until 150 hours of population doubling time. But the number of cells finally obtained was higher in BcMSCs. Adipocyte differentiation was slightly better in BcMSCs and cell surface antigen expression (MFI) of CD90 and CD105 was higher in BcMSCs. The inhibition of active IL-1β secretion in macrophages was also higher and the activity of mitochondria was slightly higher in BcMSCs.

Conclusions: The proliferative capacity of BMSCs in the early stage of subculture was high in BpMSCs, but the differentiation potential, cell surface antigen expression, immunosuppressive activity and mitochondrial activity were higher in BcMSCs. However, there was no statistical significance. Therefore, a larger number of BMSCs need to be compared and analyzed, and there is a need to analyze the therapeutic effect in an animal model of liver cirrhosis. Therefore, it is necessary to comparatively analyze a larger number of BMSCs, and it is necessary to directly analyze the therapeutic effect in an animal model of liver cirrhosis.

Keywords: Mesenchymal stem cells, Cirrhosis, Proliferation, Differentiation, Mitochondria

References

Feasibility of Enhanced PRL-1 in Placenta-derived Mesenchymal Stem Cells by Gene Modification on a Rat Model with Hepatic Failure

Gi Jin Kim
Department of Biomedical Science, CHA University, Seongnam, Korea

Translational studies have explored the therapeutic effects of stem cells raising hopes for the treatment of numerous diseases. Liver diseases are the most common medical diagnoses worldwide and millions of people suffer from difficult-to-treat liver diseases. Currently, orthotopic liver transplantation is the only effective treatment of end-stage hepatic disease, but this procedure is associated with many problems, including the donor scarcity, operative damage, high cost, risk of immune rejection and the lifelong immunosuppressive treatments. Human placenta-derived stem cells (PDSCs) have recently been classified and have become the focus of attention in stem cell research because they are the first of the adult stem cells to appear, they have great potential for proliferation, differentiation and self-renewal, they are readily available and they are easily procured without invasive procedures. Also, PDSCs have strong immunologic privileges. Nevertheless, powerful MSCs generation through gene regulation by non-viral gene delivery system should be enhanced the therapeutic effect in degenerative medicine. In this section, we introduce enhanced PRL-1 which plays a critical role during liver regeneration in PD-MSCs (PRL-1+) using gene delivery systems, highlight the characterization of placenta stem cells and their therapeutic effects on hepatic diseases models. Also, we will discuss recent investigations that their therapeutic potential in repair of injured liver with a view to its utility in regenerative medicine.

Keywords: Hepatic cirrhosis, Liver regeneration, Phosphatase of regenerating liver-1, Placenta-derived mesenchymal stem cells
Vascularized Liver Tissue with Different Types of Endothelial Cells and Recovery Aids for Acute Liver Failure

Jaeseo Lee¹, DoYeun Park¹, Soo Hyun Kim²

¹KU-KIST Graduate School of Converging Science and Technology, Korea University, 145 Anam-ro Seongbuk-gu, Seoul, Korea; ²Biomaterials Research Center, Korea Institute of Science and Technology, 5, Hwarang-ro 14-gil, Seongbuk-gu, Seoul, Korea

Aims: Liver is one of the most highly vascularized organs, so it is inevitable to make vascularized liver tissues (VLT) for implementing the nature of liver structures, physiologies and functions. We designed VLT models to produce functional and highly vascularized liver tissues and assessed the effects of each model in vitro and in vivo.

Methods: We used simple methods that use collagen gel to induce angiogenic sprouting of endothelial cells and made VLT models with different types of endothelial cells. We assessed the morphological and functional features of each VLT model in vitro, and conducted partial hepatectomy and subcutaneous implantation to immunodeficient mice. We also observed and compared the recovery process of different VLT-implant groups.

Results: Macro-vascular endothelial cell types showed vigorous vascularization while the liver sinusoidal endothelial cell (SEC) is less effective for making vascular networks around the in vitro cultured tissues. In terms of morphological and functional advances, however, SEC cocultured VLT showed most synergic effects with hepatocytes to make in vivo like features and enhanced functionality. We designed in vivo experiments to show the possibility of VLTs to be used as bioartificial recovery aids for acute liver failure. The VLT implanted groups successfully showed much faster recovery process than the non-VLT implanted group.

Conclusion: We fabricated vascularized liver tissue models for producing functional and highly vascularized liver tissues. With these models, the liver functions were supported by the implants after the induced hepatic failure and the recovery process via regeneration of the liver was expedited.
MicroRNA Profile Analysis in Liver Fibrotic Tissue and Hepatic Differentiated Human Bone Marrow-Derived Mesenchymal Stem Cells

Jung Hoon Cha¹²

¹The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Korea
²Department of Biomedicine & Health Sciences, Graduate School, The Catholic University of Korea, Seoul, Korea

**Background:** Although the therapeutic mechanisms of bone marrow-derived mesenchymal stem cells (BM-MSC) are still unclear, BM-MSCs play key therapeutic roles in liver fibrosis. Furthermore, microRNAs (miRNAs) are regulators in hepatic differentiation and liver fibrosis. miR-101-3p, miR-26a-5p, and miR-26b-5p are upregulated during hepatic trans-differentiation, whereas these miRNAs are downregulated in a stage of liver fibrosis. The purpose of this study is to investigate three miRNAs' roles in the hepatic differentiation of human BM-MSC (hBM-MSCs) and in hepatic stellate cell (HSC) activation.

**Methods:** To detect the miRNAs of hBM-MSC into functional hepatocytes and liver fibrotic tissue, the next-generation sequencing (NGS) was performed in hBM-MSCs before and after differentiation, hepatocyte, normal liver tissue, portal fibrotic tissue, and septal fibrotic tissue. To determine the effects these miRNAs, HBM-MSC was treated with mimic or inhibitor during the hepatic differentiation. HSC LX2 was treated with TGF-β₁ (2.5 ng/mL), and with or without three miRNAs mimics or inhibitor. The role of miRNA was identified through the change of liver-specific genes, EMT markers, apoptosis genes, and fibrosis genes using the quantitative real-time PCR (qRT-PCR) and western blotting.

**Results:** As a result of NGS analysis, three miRNAs showed a significantly higher expression level in differentiated hepatocyte-like cells and hepatocyte than hBM-MSC but lower expression level in liver fibrosis than the normal liver. At the validation phase, qRT-PCR results showed that the level of three miRNAs was up-regulated during hepatic differentiation of hBM-MSCs. In contrast, three miRNAs expression was down-regulated in TGF-β₁ activated human HSC line (LX-2) and bile duct ligated (BDL) rats. Furthermore, three miRNAs were increased in BDL rats one week after transplanting BM-derived hepatocyte-like cells.

As a result of the ability of the three miRNAs to differentiate into hepatocytes, miR-101-3p and miR-26b-5p mimic promoted the hepatic differentiation of hBM-MSC. After transfection of miRNA-26b-5p and miR-101-3p, expression of hepatocyte-specific genes SOX17, ALB, HNF4α, and TAT increased on day 7. Overexpression of the three miRNA combinations resulted in more efficient induction of hBM-MSC differentiation into functionally mature hepatocytes. However, only the up-regulation of miR-101-3p inhibited activation of LX-2 by TGF-β₁. miR-101-3p caused the mesenchymal markers (SNAI1 and CDH2) and fibrosis markers (α-SMA and COL1α1) decreased in LX2. These results show that miR-101-3p have the capability to directly convert the hepatic differentiation of hBM-MSC and inhibited the TGF-β₁ mediated LX2 activation.

**Conclusions:** In this study, we identified novel miRNAs (miR-101-3p, miR-26a-5p, and miR-26b-5p) that can regulate the hepatic differentiation of hBM-MSC and the hepatic fibrosis. Our results demonstrate that miR-101-3p may be a biomarker, monitoring the response to therapeutic effect by BM-MSC in liver fibrosis.

**Keywords:** Human bone marrow-derived mesenchymal stem cells (hBM-MSCs), Hepatic differentiation, Next-generation sequencing (NGS), microRNAs (miRNAs), Fibrosis
The Liver Week Satellite Symposium for Regeneration Medicine

Proteomics Approach for Translational Research, Focusing on Liver Disease

Kyunggon Kim
Asan Medical Center, University of Ulsan, Korea

간질환 중심으로 본 중개연구에서의 단백체학의 응용
김 경 곤
울산대학교 의과대학 서울아산병원

High resolution mass-spectrometry coupled with effective protein/peptide separation technique have been applied on biology and translational area. And combination of other omics technology such as transcriptomics and genomics with proteomics have been extended the spectrum of its application to the precision medicine. This divergence phase of proteomics technology is playing an important and novel role as a name of proteo-genomics. At the same time, area of proteomics is reached to deep down of clinical unmet needs by not only instrument development but also deep understanding about the usefulness of proteomics application on translational research. Nowadays, proteomics also has been in convergence phase in clinical and translational area, especially in biomarker development and validation.

Herein, I would like to introduce some applications of proteomics on translational research. Especially, comparative proteome analysis for human primary hepatocytes (hPH) and liver tissues from donor in living donor liver transplantation could give us information for organ transplantation efficiaicy. Also, longitudinal plasma exosome proteome analysis of mesenchymal stem cell-grafted mouse which have liver fibrosis revealed that exosome proteome can be a valuable resource of translational research.

This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (Grant Number: NRF-2019M3A9B4030961 and NRF-2015K1A4A3046807).
KLTS Symposium 1

Conundrum: Transplanted Liver Pathology

Chairs:
Shin Hwang (Univ. of Ulsan)
Haeryoungh Kim (Seoul National Univ.)

DAY 2: Friday, June 21, 2019 (08:30-09:30)
Liver Allograft Pathology: Developments in Antibody-Mediated Rejection

Christopher Bellamy

University of Edinburgh, Scotland

Antibody-mediated rejection (AMR) in ABO-compatible liver allografts is increasingly recognised as an unusual sometimes severe early complication but more prevalent later complication after transplantation, with consequences for allograft dysfunction and chronic rejection.

This presentation will begin with a brief review of functional liver microanatomy relevant to the better understanding of the pathogenesis and manifestations of antibody-mediated rejection in the liver. We will outline a credible sequence of pathologic events and emphasize the common features of antibody-mediated rejection across different solid organ allografts, which facilitate understanding and interpretation of liver allograft changes. We will then will consider in detail the microscopic features in allograft biopsies that suggest the diagnosis. The emphasis will be on practical interpretation and integration of findings, including immunohistochemistry for Complement fragment C4d deposition in the microvasculature. Specifically, we will review the recent Banff 2016 Working group criteria for the pathologic diagnosis of active AMR and illustrate examples of microvascular endothelial injury, luminal microvasculitis, arteritis and C4d deposition. We will briefly consider emerging evidence for non-HLA anti-donor antibody injury. Finally, we will review the current Banff working formulation criteria for suggesting chronic AMR-related injury in liver allograft biopsies.
Is a Protocol Biopsy Needed in a Liver Recipient?

Suk Kyun Hong

Department of Surgery, Seoul National University College of Medicine, Seoul, Korea
KAHBPS-KLTS Joint Symposium

Diagnosis and Management of Combined Hepatocellular Carcinoma (HCC) and Cholangiocellular Carcinoma (CCC)

Chairs:
Hee Chul Yu (Chonbuk National Univ.)
Young Kyung You (The Catholic Univ. of Korea)

DAY 2: Friday, June 21, 2019 (11:10-12:10)
Pathological Point of View of Combined HCC and CCA: What Is the Origin and Diagnostic Criteria of Combined HCC and CCA?

Young Nyun Park
Department of Pathology and BK21 PLUS for Medical Science Yonsei University College of Medicine, Seoul, Korea

Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a malignant primary liver carcinoma (PLC) defined by the unequivocal presence of both hepatocytic and cholangiocytic differentiation within the same tumor. This tumor, although described over 100 years ago, has attracted greater attention recently because of greater frequency and clinical recognition. The classification of combined HCC-CCA has been updated in 5th ed of WHO classification of the digestive system. In cHCC-CCA, the tumor areas with hepatocytic differentiation show the architectural and cytological features of HCC and the tumor areas with cholangiocytic differentiation show those of CCA. There is no definite data at present to support inclusion of minimum cutoff criteria of each component for the diagnosis of cHCC-CCA and this diagnosis can be made regardless of the percentage of each component, provide that they are unequivocal. Small uniform tumoral cells, with high N/C ratio and scant cytoplasm, so-called ‘cancer stem cells’ can be identified in various proportions either in the transitional zone between HCC and CCA or at the periphery of HCC area. Their presence and percentage is recommended to be mentioned in the pathologic report, although it does not reflect the origin of the PLC. Hence, the use of the category of cHCC-CCA subtype with stem cell features is no longer recommended. Intermediate (hepatobiliary) cell carcinoma, a histological variant of cHCC-CCA shows morphologic features that are intermediate between hepatocytes and cholangiocytes only at the cellular level without tumor area of HCC or CCA. The designation of intermediate cell carcinoma should be reserved for PLC in which intermediate features are present in the entire tumor. Cholangiolocarcinoma (cholangiolocellular carcinoma, CLC) can be a component of cHCC-CCA when a HCC or intermediate carcinoma component is present. However, if CLC is present alone, or if CLC is mixed with a CCA, it belongs to the histopathological spectrum of CCA based on its molecular characteristics.

Keywords: Combined hepatocellular-cholangiocarcinoma, Hepatocellular carcinoma, Cholangiocarcinoma
Imaging Features of Combined HCC and CCC: What Is the Difference Compared with HCC or CCC?

Chang-Hee Lee
Department of Radiology, Korea University Guro Hospital, Korea University Medicine, Seoul, Korea

Combined Hepatocellular Cholangiocarcinoma (CHC) is an uncommon primary liver cancer, which comprises a mixture of hepatocellular carcinoma (HCC), cholangiocarcinoma (CCC), and/or hepatic progenitor/stem cell features. The 2010 WHO classification system categorized CHC into classic type and subtypes with stem cell features. The CHC predominantly occur in patients with liver cirrhosis or chronic viral hepatitis, while CHC were rarely associated with biliary disease. However, CHC can have overlapping imaging features with HCC and CCC.

The imaging features of CHC were diverse, ranging from HCC like wash in and wash out patterns to CCC like peripheral rim enhancement on the arterial phase and progressive centripetal enhancement pattern. Even though the imaging feature of CHC was confused, the knowledge of typical HCC feature or CCC feature can guide the helpful guidance of the differentiation. In this lecture, I will introduce the common imaging features of the HCC compared with CHC and CCC. These are arterial globular hyperenhancement, washout, delayed enhancing capsule, paradoxical uptake of EOB on hepatobiliary phase (HBP), intra-tumoral fat, intra-tumoral hemorrhage, T2 bright signal intensity spots, and intra-tumoral septum. The CHC favoring imaging features will be also illustrated in this lecture. These CHC/CCC features are targetoid features, which visualized as peripheral rim arterial enhancement, peripheral wash out, progressive central enhancement, targetoid diffusion restriction, target sign (EOB Cloud) on HBP / transitional phase, peritumoral bile duct dilatation, and surface retraction.

To standardize the imaging diagnosis of HCC in at risk patients, the Liver Imaging Reporting and Data System (LI-RADS) was developed in 2011 and updated in 2014, 2017, and 2018. LI-RADS 2018 was also incorporated into the AASDL guideline last year. With LI-RADS, each hepatic observation is categorized according to its likelihood of benignity and HCC (LR-1 to LR-5), as well as non-HCC malignancies (LR-M). The LR-5 category allows for a highly specific diagnosis of HCC and the LR-M category includes non-HCC malignancy and HCCs with atypical imaging features. To avoid the confusion from various terminology of imaging features, I will introduce the imaging illustrations of LR-M features, which are nearly similar to targetoid CHC features.

Liver MRI findings of CHC are diverse, reflecting the heterogeneous histologic features of these tumors, and their enhancement patterns reflect the tumor composition. The targetoid appearance (LR-M) was very sensitive imaging feature to identify the CHC from the HCC. And the presence of washout, intralesional fat, and intralesional hemorrhage help differentiate CHC from CCC.

References

Combined hepatocellular and cholangiocarcinoma (CHC) is a rare type of primary liver cancer. Allen and Lisa described the distinct pathologic characteristics of CHC in 1949, such as hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) coexisting in the same tumor or in the same liver. CHC was defined as a tumor containing unequivocal, intimately mixed elements of both HCC and ICC according to the World Health Organization (WHO) classification and the General Rules for the Clinical and Pathological Study of Primary Liver Cancer of the Liver Cancer Study Group of Japan (LCSGJ). The clinicopathologic features and outcomes after surgery of CHC have been reported previously. Many studies reported that CHC patients showed more lymph nodes or peritoneal recurrence than HCC, postoperative survival was significantly poorer in CHC patients than HCC patients, and poor but statistically similar to that of ICC patients. Therefore, clinical backgrounds of CHC patients were thought to be similar to those of HCC, but postoperative survival rate and type of recurrence were similar to those of ICC patients. April 1992 and December 2018, our department surgically treated 6 cases of CHC. In this study, we reviewed the some literatures about the surgical treatments and results of CHC, and the features of surgically treated CHC patients (n=6) in our department were retrospectively investigated and compared to those of patients with HCC (n=736) and ICC (n=143), and considered the treatment strategies of CHC from the viewpoint of surgical treatment result of ICC.
Combined hepatocellular carcinoma and cholangiocellular carcinoma (cHCC-CCC) is rare, accounting for 1.0% to 14.2% of all primary hepatic malignancies. The CCC element of cHCC-CCC may represent a partial modification of the HCC, and it has been suggested that cHCC-CCC is actually a modified form of HCC involving metaplasia of the bile duct epithelium, rather than an intermediate between HCC and CCC. Compared with typical HCC, the clinicopathologic characteristics of cHCC-CCC include more frequent multifocal lesions and reduced capsule formation compared with other tumors, as well as more frequent microvascular emboli, portal or hepatic vein invasion, and lymph node metastasis. These findings suggest that patients with cHCC-CCC have a relatively poor prognosis because all of these factors are associated with higher recurrence rates. But, analyses of data from curative surgical resections have suggested that cHCC-CCC shows a better prognosis than CCC but worse than HCC.

Differential diagnosis of HCC and cHCC-CCC is often difficult and the definite diagnosis of cHCC-CCC requires histopathologic tissue confirmation. Therefore, none had been diagnosed as cHCC-CCC before transplantation by most reports.

In cHCC-CCC patients with liver transplantation, the 5-year survival was better than liver transplantation for intrahepatic CCC but poorer than that of HCC meeting the Milan criteria. Patients with tumors measuring less than 2–5 cm have good outcomes, whereas, if they have multiple and bigger tumors, they are at higher risk of recurrence, with a consequent reduction of survival.

Retrospectively collected data in literature, although without statistical significance because of very small series, seem to suggest the use of mTOR inhibitors in those kinds of patients. Exploiting the anti-proliferative and anti-angiogenic effect of the mTOR inhibitors is the rationale that can explain why they could improve the outcome of those patients. To elucidate the effects of mTOR inhibitor, the design more studies advocating analysis of biological effects are necessary.

If summary, the role of liver transplantation for cHCC-CCC is not clear. Thus, cHCC-CCC can be prudently considered for LT indication.
KLTS Special Lecture

Chair:
Kyung-Suk Suh (Seoul National Univ.)
Donation after Circulatory Death Liver Procurement in Real Practice

Koji Hashimoto
Department of General Surgery, Digestive Disease & Surgery Institute, Cleveland Clinic, OH, USA

Donation after circulatory death (DCD) donors are an increasing source of transplant organs. In liver transplantation, the use of DCD donors has been well recognized as an alternative to donation after brain death (DBD) donors. However, liver transplantation using DCD donors is characterized by inferior graft survival compared with transplantation from DBD donors because of graft tissue damage from mandatory donor warm ischemia during organ procurement. Therefore, early experience has demonstrated high rates of primary graft dysfunction/non-function and ischemic biliary complication. Although graft survival and complication rates have improved over time, there is still room for improvement. DCD organ procurement is a fight against the clock. Conventionally, DCD organs are retrieved with the super rapid technique. Although this is still the standard technique, several modifications have been implemented to improve DCD graft quality, including choice of preservation solution, use of a thrombolytic agent, systemic heparin administration, and arterial reperfusion. More recently, ex vivo machine perfusion technology has been implemented in the field of DCD transplantation. In addition to a new update of DCD liver transplantation, Cleveland Clinic experience over 15 years will be presented.
KLTS Symposium 2

Use of Donation after Circulatory Death to Overcome the Decrease of Brain Death Donor (*K)

Chairs:
Yang Won Nah (Univ. of Ulsan)
Myoung Soo Kim (Yonsei Univ.)
Current Status and Problems of Organ Donation in Korea

Won-Hyun Cho
Korea Organ Donation Agency

한국의 장기기증 상황과 당면한 문제점
조 원 현
한국장기조직기증원

After legislation of transplant act and establishing Korea Organ Donation Agency(KODA), deceased organ donation increased continuously until we met an unexpected obstacle two years ago. The number of deceased organ donor per million population was reached up to 11.3 in 2016 but dropped down to 9.95(liver 8.69) in 2017, however, we still performed living donor organ transplantation up to 44.3 pmp(liver 19.93) in 2017. The donated organs per deceased donor were 3.35 last year.

Current problems we have are 1) decrease in family consent rate, 2) increasing old population, and 3) decreasing the main cause of brain death such as death from head trauma by traffic accident and from cerebrovascular accident. About changing cause of brain death, we don’t have much work to do but for the increasing tendency of hypoxic brain injury, we need to prepare a donation procedure from circulatory death. Increasing aged population elevate the incidence of ECD rate which ask us an experienced, good skilled management and procurement.

The rate of family consent declined by 15% from the previous year because of the negative news about donor transfer which causes public sentiment. Sometimes, donation news of social leaders increased organ donation, but lasted for one or two months. But Instead, negative news deeply affected public’s heart and lasted for more than a year.

In order to raise public awareness about effect of transplantation and donation, we made every possible effort to increase the number of registrants. Over the past two decades, more than 95% of Koreans are aware of the need for organ donation, 65% are willing to donate but only 4.1% were actual donor card registrant.

Recently we have a bit of conflict with other organization in relation to the discontinuation of end of life care. Most of these patients who wish to stop the end of life care are not eligible for organ donation, but some acute injured or rapidly processed cases may be considered for organ donation. We will prepare and apply standardized guidelines for treatment decisions in two conflicting end of life care under the view of patient’s will and respect of dead person’s life.

One of the problems we face today is the lack of medical personnel needed to manage brain death patients. The shortening of labor time that the government is enforcing is also causing serious labor shortages in medical field.

These difficult environments and medical conditions are becoming a big obstacle to the activation of organ donation. However, we are considering the implementation of DCD in a way that the western countries have applied. And we also revising the transplantation law to enforce the first person consent authorization, and end of life care.

In order to increase the number of registrants who wish to donate organs, we intend to implement active and effective campaigns and education for the public.

What Koreans are most afraid of organ donation is body damage and corruption. But the fact that our ancestors did not make pockets in the shroud and did not want to leave anything in this world after death would be a great help for our people to encourage and understand organ donation.
Current Status of Liver Allocation System

Jae Geun Lee

Department of Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Introduction: Organ shortage is the greatest challenge in liver transplantation (LT). Many patients have died during waiting for LT, although organ allocation policies have evolved to reduce mortality among those on waiting lists. In 2002, the Model for End-stage Liver Disease (MELD) score-based allocation system was implemented in the United States, and thereafter, other countries in Europe and Latin America adopted MELD systems. However, MELD systems represent different effects around the world and continue to evolve to meet various regional requirements. In Asia, novel surgical techniques for living donor liver transplantation (LDLT) have been devised to overcome organ shortages. However, the development of organ allocation systems has been relatively neglected. Although MELD systems have been reported to generally improve outcomes in the West, the adoption of such systems in Asia might have unintended consequences, because donation rates, medical environments, and disease entities differ from those of Western countries. The Child-Turcotte-Pugh (CTP) score-based allocation system has been used in Korea since 2000. In June 2016, Korea became the first Asian country to implement a MELD score-based allocation system. This study was undertaken to investigate the short-term impact of the implementation of MELD allocation system in Korea.

Methods: We used data from the Korean Network for Organ Sharing (KONOS) database, which contain comprehensive national data on waiting lists, organ donations, and transplantations. The study population included deceased donor liver transplantation (DDLT) between June 2014 and May 2018 in Korea. All patients were followed until death, drop-out on the waiting list, or 31 June 2018. In June of 2016, KONOS implemented the MELD score to prioritize liver allocation. Outcome data were collected from June 2014 to May 2016 (24 months prior to MELD implementation), and from June 2016 to May 2018 (24 months after MELD implementation).

Results: A total of 1805 patients underwent DDLT in Korea until study period, 888 during pre-MELD era, and 917 during post-MELD era. Comparing with pre-MELD era data, portion of alcoholic liver disease increased in the post-MELD era (33.1% vs. 39.8%, \( p = 0.003 \)), and rate of re-transplantation also increased (7.3% vs. 11.0%). Regional distribution rate was also higher in post-MELD era than that in pre-MELD era (25.8% vs. 39.0%, \( p < 0.001 \)). Excluding Status 1 and pediatric cases, the mean and median MELD score in post-MELD era were 36±5.4 and 40 [6-40]. In same study population, the 1-year patient survival rate was 79.8% and 76.1% in the pre- and post-MELD era. (\( p = 0.039 \)). The 3-months patient survival rates also were 85.8% and 81.3%.

Conclusion: The MELD score-based allocation system in Korea improved the fairness of DDLT allocation by providing greater organ access to the sicker patients and by reducing regional disparities. In contrast to the previous studies, the nationwide survival rate was slightly lower in post-MELD era than in pre-MELD era. MELD score-based system appears to be a good option for organ allocation, but it is not perfect thus must be improved through continuous feedback and modifications.
Institutional Issue and Limit of Donation after Cardiac Death

Dong-Sik Kim
Division of HBP Surgery & Liver Transplantation, Department of Surgery, Korea University College of Medicine, Seoul, Korea

Although shortage of organ in comparison to waiting list is a global issue, the situation in Korea has been getting worse especially for last several years. The rate of donation after brain death (DBD) reached its peak and, in fact, has been even decreasing recently. Considering the fact that median MELD score of recipients of liver graft from DBD donors is close to 40, development of new strategy to overcome current extreme shortage of organ is urgently required.

Besides issues related to organ allocation, expanding donor pool is a critical issue. Donation after cardiac death (DCD) is a well-established way of organ donation to increase donor pool in western countries. In Korea, DCD is permitted by law only in Maastricht category IV, which means cardiac arrest in or after the process of determination of brain death. In real clinical practice, however, not a small number of potential donors misses chance of donation due to rapid aggravation of vital signs even before the first or second determination of brain death.

In this presentation, critical issues related to execution of DCD practice under current law in Korea will be discussed including limitations and potential ways to improve in legal, cultural, and medical perspectives.
KASL-KLTS Joint Symposium

Hepatorenal Syndrome (HRS) (*K)

Chairs:
Jae-Won Joh (Sungkyunkwan Univ.)
Jong Young Choi (The Catholic Univ. of Korea)
HRS: Definition, Pathophysiology, and Medical Management

Yeon Seok Seo
Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Introduction

Ascites is the most common complication of liver cirrhosis and portal hypertension, with the incidence of approximately 60% within 10 years of diagnosis of cirrhosis. The appearance of ascites represents the onset of de-compensation and is associated with poor prognosis with a mortality rate of 20% per year. The development of ascites is related to the splanchnic vasodilatation followed by a decrease in effective blood volume and activation of vasoconstrictor system such as renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS), which induce renal sodium and water retention and fluid accumulation in the peritoneal cavity. With progression of the disease, these hemodynamic alterations lead to hypersecretion of anti-diuretic hormone (arginine vasopressin, AVP) and development of hyponatremia, which is considered as one of the important prognostic factors in patients with liver cirrhosis. Despite of these efforts to compensate hypovolemia, hypovolemia due to further splanchnic vasodilatation leads to decrease in the blood flow to the kidney, and eventually renal vasoconstriction, and development of renal dysfunction, including acute kidney injury (AKI) and hepatorenal syndrome (HRS), which are associated with poor prognosis in these patients.

Definition

Renal dysfunction is usually classified to AKI, chronic kidney disease (CKD), and acute on CKD according to the acuity of presentation. AKI is defined as a rise in serum creatinine (Cr) of more than 50% from baseline or an increase in Cr of at least 0.3 mg/dL in less than 48h, and CKD is defined as eGFR of less than 60 ml/min for more than 3 months. Acute on CKD is defined as the increase in serum Cr of at least 50% from baseline or the increase in Cr by at least 0.3 mg/dL in less than 48h in a cirrhotic patients with GFR below 60 ml/min for more than 3 months. There was significant changes in the definition of AKI compared to the previous conventional definition of increase in serum Cr level of more than 50% to a final value of serum Cr level >1.5 mg/dL in terms of addition of absolute increase in serum Cr of ≥0.3 mg/dL and deletion of cut-off serum Cr level of 1.5 mg/dL, because minor increases in serum Cr is clinically relevant and adversely affect survival in patients with cirrhotic ascites.

HRS is the most severe form of functional renal disorder which is not responsive to volume challenge. HRS was divided into two types based on prognosis and clinical characteristics: type 1 HRS (HRS1) is the rapid onset of renal failure that occurs in patients with rapid hepatic decompensation and type 2 HRS (HRS2) is the renal impairment that progress gradually over a relatively long period of time. HRS1 is regarded as a specific form of AKI, while HRS2 is included in CKD. The definition of HRS was also recently updated as no improvement in serum Cr after at least 2 days of diuretic withdrawal and volume expansion with albumin in patients with cirrhotic ascites and AKI. Therefore, patients could be diagnosed as and treated for HRS1 before resolution of bacterial infection and without delay until rise in serum Cr level up to 2.5 mg/dL. Considering that rapid treatment for HRS1 with va-
soconstrictors plus albumin improves treatment response and prognosis,\textsuperscript{10} this revision of the definitions for HRS1 would be helpful for these patients.

**Prevalence & Precipitating Factors**

AKI is the most common form of renal dysfunction in patients with liver cirrhosis. In patients with liver cirrhosis and renal dysfunction, 70\%, 17\%, and 13\% of the patients had AKI, acute on CKD, and CKD, respectively.\textsuperscript{11} In addition, AKI is a common complication in patients with liver cirrhotic ascites and it develops in 19\% of these patients admitted to hospital.\textsuperscript{12} Renal function can be improved with volume replacement in about 70\% of patients with AKI, while renal dysfunction does not respond to volume challenge in the remaining 30\% of these patients.\textsuperscript{12} A previous study suggested that the incidence of HRS in patients with cirrhotic ascites at 1 and 5 years are 18\% and 39\%, respectively.\textsuperscript{13}

Precipitating factors can be identified in most cases of AKI (85\%).\textsuperscript{7} Most common precipitating factors are bacterial infection, large volume paracentesis, gastrointestinal bleeding, diarrhea, and overdoses of diuretics, which are very similar with those for HRS.\textsuperscript{7} Use of vasodilators, and renal vasoconstriction due to nonsteroidal anti-inflammatory drugs (NSAIDs) or intravenous contrast agents could also precipitate the development of AKI.\textsuperscript{12} Similarly, precipitating factors can be identified in almost half of patients with HRS, and bacterial infection, gastrointestinal bleeding, and large volume paracentesis were the most common precipitating factors for HRS.\textsuperscript{14}

**Prognosis**

The development of AKI in patients with cirrhotic ascites is associated with increase in mortality and development of complications such as variceal bleeding and spontaneous bacterial peritonitis (SBP).\textsuperscript{15,16} In a recent study suggest that AKI in patients with liver cirrhosis is frequently progressive and independently associated with mortality in a stage-dependent fashion.\textsuperscript{17} Although recent studies suggested that vasoconstrictors or liver transplantation can improve survival in these patients,\textsuperscript{18} HRS still represents one of the most serious complications of liver cirrhosis.\textsuperscript{13} Median survival of patients with HRS1 is less than 2 weeks, if untreated.\textsuperscript{13} Median survival of patients with HRS2 is 6 months.\textsuperscript{19}

**Treatment**

A previous prospective observational study suggested that AKI in patients with liver cirrhosis is frequently progressive and associated with mortality in a stage-dependent fashion.\textsuperscript{17} Furthermore, HRS may be reversed with restoration of renal blood flow by vasoconstrictors plus IV albumin or liver transplantation.\textsuperscript{20,21} Therefore, the early identification and treatment of its cause are very important. At first, NSAIDs and diuretics should be discontinued and, in patients with hypovolemia due to bleeding, aggressive volume expansion and prompt treatment for hemoedema should be performed.\textsuperscript{22} If renal dysfunction does not respond to these management, patients could be treated as HRS with vasoconstrictors plus albumin.\textsuperscript{10,23,24}

Terlipressin, an analogue of vasopressin, is the firstly recommended vasoconstrictors for HRS1 treatment. Terlipressin, by stimulating vasopressin receptors in the vascular smooth muscle cells, induce splanchnic vasoconstriction, which in turn, reduce portal blood flow and portal pressure.\textsuperscript{25} In addition, albumin increases effective arterial volume and lead to increase in preload to the heart, cardiac output, and mean arterial pressure.\textsuperscript{26} Terlipressin plus albumin treatment improves renal function in 40-50\% of patients with HRS.\textsuperscript{10,23,27-30} This treatment is considered effective if serum Cr is reduced at least 25\% within 3 days after initiation of treatment and should be continued until serum Cr level reduce below 1.5 mg/dL. After withdrawal of treatment, HRS recurs in about 20\%, however,
it usually responds well to retreatment. However, survival benefit of this treatment in patients with HRS1 have not been confirmed yet.

Conclusions

AKI is a frequent complication and associated with poor prognosis in patients with liver cirrhosis, especially in patients with cirrhotic ascites. Recently, definitions for AKI and HRS were revised to facilitate prompt diagnosis and treatment in these patients, because prompt diagnosis and rapid initiation of appropriate treatment is very important, considering poor prognosis in these patients. In patients with AKI, sufficient volume replacement with intravenous albumin as well as withdrawal of potentially nephrotoxic drugs are recommended. Patients whose renal dysfunction does not respond to volume replacement could be diagnosed as HRS and treatment with vasoconstrictors and albumin should be considered.

References

Urol Nephrol 2011;43:175-84.
When to Consider Simultaneous Liver Kidney and How to Prevent Adverse Renal Outcome after Liver Transplantation

Jae Min Chun

Department of Surgery, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, Korea

간선 동시 이식의 적응증 및 간이식 후 신기능의 보호

천 재 민
경북대학교 의과대학 외과학교실, 경북대학교병원

Acute kidney injury (AKI) is common in patients with liver cirrhosis, occurring in up to 23% of patients with cirrhosis, while chronic kidney disease (CKD) is present in 1% of such patients. AKI after liver transplantation is unfortunately a frequent complication with a reported incidence of 12% to 95%, and liver transplant recipients develop CKD after transplantation at higher rates than heart and lung transplant recipients, with a 5-year cumulative incidence of 22%.1 Both pre-, post-transplant renal dysfunction have associated with morbidity and mortality after LT.

Since the adoption of MELD-based liver graft allocation in 2016, the deceased donor LT was performed in recipients with high MELD score of mean 35.9, and mean serum creatinine level was 1.95 mg/dL in Korea, which trend can translate to a higher prevalence of CKD or ESRD after LT. Therefore, effort to protect the kidney in LT recipients is more important in the MELD era.

For simultaneous liver kidney (SLK) transplantation, decision to perform SLK depends on the ability to predict recovery of renal function after LT. In LT candidates with established ESRD, criteria for SLK allocation are relatively obvious and homogeneous. Current UNOS Criteria for SLK allocation in the setting of CKD in liver patients include (i) GFR ≤ 60 ml/min for >90 days and subsequent GFR ≤ 30 ml/min or requirement for dialysis and (ii) CKD because of metabolic disease that can be corrected with a liver transplant (hyperoxaluria, atypical haemolytic uremic syndrome, familial nonneuropathic systemic amyloidosis and methylmalonic aciduria). However, in those with varying degree of AKI, it may be difficult to confirm performing SLK because renal function can recover after LTA as to duration of AKI, need for renal replacement, degree of renal dysfunction and age of the transplant recipient. UNOS Criteria for SLK allocation in the setting of AKI in liver patients include (i) duration of AKI >6 weeks with persistent GFR ≤ 25 ml/min, (ii) dialysis dependence or (iii) a combination of both. Also, criteria included “safety Net” giving additional priority to all LT alone (LTA) recipients as well as SLK recipients who experienced immediate and permanent non-function of the transplanted kidney who are on kidney waiting list after becoming dialysis-dependent or having a GFR ≤ 20 mL/min between 60 and 365 days following liver transplantation.2

The predisposing factors for renal dysfunction after LT can be classified as (i) drug toxicity, (ii) other disorders related to the severity of the patient’s condition and allograft dysfunction. Calcineurin inhibitor (CNI) –induced
nephrotoxicity contribute to short- and long-term renal deterioration. Delay and reduction of CNI exposure may lessen or protect against postoperative AKI and use of mTOR inhibitor in combination with CNI reduction is another option for protecting kidney early (0-12 month) after LT. Nephrotoxic drugs such as radiocontrast, aminoglycosides, amphotericin B and NSAIDs are also well known cause of developing AKI after surgery, and should be avoided when possible.³

In addition, control of metabolic disease such as diabetes and hypertension is essential for preventing CKD. At the initial recognition of hypertension, lifestyle modification such as adoption of a low-sodium diet, cessation of smoking, avoidance of alcohol, and loss of weight should be emphasized to the patient. Calcium channel blockers are the preferred first-line agent in patients who do not exhibit proteinuria. Meanwhile, patients with proteinuria and hypertension should take an angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers.⁴ The prevalence of diabetes ranges from 31% to 38% in post-LT patients and plasma glucose control must start immediately after the transplant procedure in order to improve long-term results. The suitable goal for transplant patients with identified diabetes is a hemoglobin A1c level of less than 7%. For patients with a short disease duration, younger age and few comorbidities aside from their liver problems, an HbA1c of < 6.5% is both feasible and desirable. For patients with advanced age, multiple comorbidities, high risk of hypoglycemia and/or limited life expectancy, an HbA1c of < 8.0% is a more realistic and potentially less iatrogenic objective.⁵

In conclusion, with advances in surgical technique, anesthetic management, and immunosuppression, major obstacles to rapid deterioration of the recipients have been in overcoming and the overall survival rates at 5 years after LDLT and DDLT currently exceeds 80%, and 68%, respectively. Therefore, protecting renal dysfunction after LT remains a critical issue that affects the long-term outcomes of LT recipient and precise decision for SLK is mandatory to obtain best survival benefit.

References
MELD Purgatory in HRS and Allocation Policy: When to Start Renal Replacement Therapy?

Shin Hwang

Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Model for End-stage liver disease (MELD) score-based liver allocation system has been adopted since June 2016 in Korea. After adoption of MELD score, the proportion of patients with MELD score >=31 occupied three-fourths of recipient. In patients with high MELD score, the impact of serum creatinine is critical to be status 2. In patients undergoing renal replacement therapy, serum creatinine level is replaced with 4 mg/dL. There are 3 indications of pretransplant renal replacement therapy in patients with end-stage liver disease and impaired renal function. The first is hepatorenal syndrome, in which type I is often benefited from renal replacement therapy. The second is impending hepatorenal syndrome combined with pulmonary edema/pneumonia. The third is impending hepatorenal syndrome combined with hepatic encephalopathy/uremic syndrome. Two latter indications require early application of renal replacement therapy. When renal replacement therapy is applied early in time before liver transplantation, the posttransplant outcome is quite comparable with those without hepatorenal syndrome. Therefore, early timely application of renal replacement therapy is reasonably recommended when it is indicated in patients waiting for liver transplantation.
When to Start Renal Replacement Therapy for Hepatorenal Syndrome

Hye Ryoun Jang

Nephrology Division, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Hepatorenal syndrome (HRS) is a reversible and functional renal failure. It occurs in patients with acute or chronic liver disease, and hepatic failure who are characterized with portal hypertension. HRS typically presents as acute kidney injury (AKI), but also can cause chronic kidney disease. Renal replacement therapy (RRT) is usually required in severe HRS, especially when hepatic encephalopathy is combined. Refractory fluid overload, hyperkalemia, metabolic acidosis, and symptomatic uremia are conventional indications of RRT. However, RRT is often required in HRS patients who lack traditional indications. Controversy regarding clinical outcomes of early vs. late RRT is ongoing despite numerous studies focusing on this issue. The timing of RRT is usually determined based on the volume status, comorbidities, and laboratory data. The concept of renal demand and renal capacity is relatively new. If metabolic demand exceeds renal capacity, RRT should be initiated even in early stages of non-oliguric AKI. In perioperative situations (before or after liver transplantation), early RRT should be considered in patients with systemic inflammatory response syndrome, pulmonary edema, and decreased reserve of cardiopulmonary or hepatic function. The modality of RRT is usually determined based on hemodynamic stability, neurologic status, and metabolic demand. Adequate timing of RRT and factors to consider when choosing RRT modality in HRS patients will be reviewed in this session.
DAY 2: Friday, June 21, 2019 (14:10-15:30)
ROOM B [2F] 203

KLTS Coordinator Session (K*)

Chairs:
Kyung-Ock Jeon (Severance Hospital)
Sunyoung Son (Gangnam Severance Hospital)
Recovery Management for Old Age Recipient

Man Ki Ju

Department of Surgery, Yonsei University Gangnam Severance Hospital, Seoul, Korea
Transplantation Counseling for an Elderly Liver Transplantation Patient

Hyung Sook Kim

The Catholic University of Korea Seoul ST. Mary's Hospital, Organ Transplantation Center, Seoul, Korea

고연령 간이식 대상자의 상담

김 형숙

가톨릭대학교 서울성모병원 장기이식센터

In Korea, the standard age of senior citizens is considered to be those over 65 years of age, respectively, according to laws related to senior citizens.

The age of recipients of liver transplants is also expected to advance as the number of people over 65 years of age is rapidly aging to 14.3% in 2018 and 41.0% in 2060 in Korea.

Even though similar outcomes can be achieved 1 year after liver transplantation in patients below 60 years of age, most studies have shown that 5-year post-transplant survival is significantly lower in recipients older than 60–70 years of age.

According to the 2017 KONOS Annual Report, the annual survival rate of the recipient of liver transplantation from a brain dead aged 65 to 74 in the country is 67.3%, while the annual survival rate for the recipient of a liver transplantation from a brain dead aged 75 or older is 37.8%. In contrast, the annual survival rate of the recipient of the liver transplantation by a living donor aged 65 to 74 was 84.6%, while that of the recipient of the liver transplantation by a living donor aged in recipients older than 75 years was 74.1%.

In general, early mortality increases in older patients with high MELD scores (>25–28) appear to be high. In the case of a good status of pre-transplantation recipient and planned living donor transplantation, the prognosis for transplants is not likely to be bad even if they are elderly liver transplant recipients.

Advanced age is significantly associated with the risk of death due to cardiovascular events and malignancy. Therefore, counseling for the aged transplant recipient will require careful consideration of the factors caused by aging, in addition to the liver transplant complications.
Acute Liver Failure

Dong Jin Joo
Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

급성간부전
주 동 진
연세대학교 의과대학 외과학교실

Acute liver failure (ALF) is a rare disease but it could be life-threatening and devastating condition with up to 30-50% mortality rate, which occurs mostly in patients who do not have preexisting liver disease. The incidence of ALF is around 10 cases per million persons per year in the developed countries. Some cases may be salvaged by vigorous medical treatment together with the liver's capacity for regeneration, but orthotopic liver transplantation remains the definitive therapy for medically refractory ALF.

Conventionally, fulminant hepatic failure is defined as a severe liver injury, potentially reversible in nature and with onset of hepatic encephalopathy within 8 weeks of the first symptoms in the absence of preexisting liver disease. But, the time gap between jaundice and hepatic encephalopathy differs according to the causes of liver failure.

Globally, hepatitis A and E infections are related to acute liver failure, with rates of mortality of more than 50% reported from the developing countries. ALF can be caused by hepatitis B infection. Particularly in Korea, acute on chronic liver failure caused by hepatitis B is not uncommon and sometimes ALF can occur in patients with reactivation of previously stable subclinical HBV infection without established chronic liver disease.

Another important cause of ALF is drug-induced liver injury. Drug-induced liver injury is responsible for approximately 50% of cases of acute liver failure in the United States. Acetaminophen is the most common hepatotoxic drug that could induce ALF in western countries. Unlike western countries, herbal medicine can be noticed the cause of ALF in many Asian countries. Other causes of ALF are hypoxia-induced liver injury, neoplastic infiltration, acute Budd–Chiari syndrome, heatstroke, mushroom ingestion, and metabolic diseases such as Wilson's disease. Rarely, pregnancy-related ALF can occur before deliver of baby, which may require early delivery of the fetus. However, in many cases, the cause of acute liver failure remains unknown, despite intensive investigation. These cases often follow a subacute presentation, and rates of survival are poor without transplantation.

Supportive therapies such as albumin dialysis units or bio-artificial livers are designed to provide a favorable milieu for regeneration by detoxifying waste molecules and providing synthetic function. These devices should bridge the patients until donor organs became available, or ideally, allow the patients to avoid liver transplantations altogether. But so far, there was no report to show survival benefit in these ALF patients. Thus, liver transplantation should be considered from the early period of ALF diagnosis.
References

간이식 후 환자관리

홍 승 희
삼성서울병원 장기이식센터

간이식은 B형간염, C형간염, 알코올성간질환 그리고 간암 등과 같은 다양한 원인에 의한 만성 간질환자나 급성간질환 환자들에게 시행되는 수술로서 국내에서는 매해 시행되는 간이식 건수가 증가하고 있다. 이렇듯 많은 수의 간이식이 시행될 수 있는 것은 이식 후 1년, 5년, 그리고 11년 생존율이 각각 86.82%, 77.88%, 71.57%로 높고 이식 후 삶의 질 또한 향상되기 때문일 것이다.

간이식을 성공적으로 받고 보다 건강한 삶을 유지하기 위해서는 이식 전 환자의 건강 상태도 중요하지만 이식을 성공적으로 마치기 위한 이식 전 환자 준비와 이식 후 관리 또한 매우 중요할 것이다. 이에 간이식 환자의 관리를 이식전 관리, 이식 직후 관리 그리고 퇴원 후 관리로 구분하여 알아보도록 하겠다.

이식 전 단계

- 환자가 간이식 수술을 받을지에 대한 결정을 돕기 위하여 간이식 상담이 필요하다. 간이식 상담에는 간이식 시기, 이식대기자 등록, 뇌사자 간이식 대상자 선정기준, 생체 간기증자의 법적, 의학적 적합 조건, 수술 전 KONOS 승인과 소요기간, 수술 후 입원기간, 약물복용, 이식 후 합병증 그리고 비용과 일시적인 사회활동의 중단 등에 대한 내용이 포함된다.
- 이식 전 검사를 시행한다. CT, MRI, Doppler US 등의 검사로 간 내부 악성종양 유무를 확인하고 혈관상태를 파악한다. 아울러 간암의 경우 다른 장기의 전이가 없는 것을 확인하기 위하여 PET CT, Chest CT 그리고 Bone Scan 검사를 시행한다. 간 이외 장기의 암여부를 확인하기 위하여 위내시경이나 대장내시경, 자궁경부암, 유방암 등의 검사도 시행한다. 수술에 위험을 초래할 수 있는 심혈관계와 폐상태에 대한 정밀검진도 시행한다.
- 간이식 후 발생할 수 있는 주요 감염에 대해 적절한 예방대학이 필요하므로 백신을 통해 예방 가능한 질병들에 대해서는 예방접종을 하는 것이 좋다. 특히 이식 후 사망률이 높은 감염 중의 하나가 폐렴이므로 폐렴구균과 독감에 대한 예방접종을 시행 한다.

이식직후-퇴원 전 단계

- 수술직후부터 퇴원 전까지의 단계로 중환자실에서 약 1주, 이식병동에서 약 2-3주간 입원하게 되는 시기이다.
- 혈액학적으로 높은 혈압, 고혈당, 간질환, 적혈구증과 같은 합병증의 위험이 높아 지속적인 심혈관 감시와 정서적 지지간호가 필요하다.
- 일부 환자에서 수술 직후 출혈, 혈관합병증(ex. Hepatic Artery Thrombosis, Portal Vein Thrombosis,
Hepatic Vein Thrombosis) 등의 이유로 재수술을 할 수도 있고 일차간이식 실패로 인한 재이식을 경험할 수도 있다.
- 담도합병증은 혈관합병증에 비해 빈도가 좀 더 많은 것으로 보고되고 있고 가장 흔한 것은 문합부위 담즙 누출이다.
- 퇴원 후 환자의 자기관리를 극대화하기 위하여 퇴원 전 다학제로 구성된 의료인의 집단교육을 시행한다. 집단교육의 내용으로는 사회복지사의 사회복지정보, 영양사의 영양관리, 약사의 약물복용 관리, 그리고 간이식파드네트워크의 혈액관리, 일상생활에서의 감염관리, 추후 병원외의 외래 방문과 혈액검사는 중요하게 그리고 문제발생시 이식팀과의 연락방법 등이 포함된다.
- 특히, 간이식 후 초기에 할 수 있는 근력운동을 교육하여 근육 감소를 방지하도록 한다.

퇴원 후 관리
- 퇴원 후 환자는 정기적인 외래진료를 통해 약물복용이행 등의 자기관리 확인, 혈액검사를 통한 저부반응, 감염상태, 그리고 면역억제약 복용의 효과를 확인 받고 수술상처나 배액관 등을 정밀하게 관리한다.
- 퇴원 초기에는 거부반응이나 감염 등의 문제로 재입원하는 기회가 높으므로 이러한 상황을 사전에 대비할 수 있는 능력에 대한 교육이 특히 필요하다.
- 매년 정기적인 약 조기검진이 되도록 교육한다.

간이식은 수술과 동시에 평생 동안 면역억제제를 복용해야 하고 건강을 유지 증진하기 위한 자기관리를 하는 노력이 필요하고 간이식 수혜자의 자기관리를 증진시키기 위해서는 간이식 수혜자의 유능성을 증대시키고 현재의 건강상태를 균형적으로 인식할 수 있도록 지속적인 교육이 필요하다.

환자교육은 환자 분위기를 감소시키고 환자의 만족도를 증진시킨다는 교육의 효과에 관한 많은 연구들이 있으며 특히 간이식 후 1년은 사회 적응을 위한 준비단계로 퇴원 후 적응을 위한 교육이 집중적으로 필요한 시기이므로 퇴원 전 이식학교육이 필요하다.

References
1. 2017 통계연보, KONOS
4. 윤지선, 임경춘, 정재심, 홍정자, 이순행 et al. 간이식 환자를 위한 퇴원 전 집단교육 프로그램 개발. 대한간기능학회지 2017;31:34-42.
8. 고다미, 간이식 수혜자의 수술 후 경과 시기에 따른 교육 요구도 비교 연구. 서울대학교간기능학회 간호학과 학기학과 논문 2012.
KLCA Symposium 1

A Developing Strategy to Improve Diagnosis of HCC

Chairs:
Jin Wook Chung (Seoul National Univ.)
June Sung Lee (Inje Univ.)
Surveillances for HCC in Patients with Non-Alcoholic Fatty Liver Disease

Vincent Wong
The Chinese University of Hong Kong, Hong Kong

Nonalcoholic fatty liver disease (NAFLD) is currently the most common chronic liver disease worldwide and affects around a quarter of the adult population in Asia-Pacific countries. Nonalcoholic steatohepatitis (NASH) is the active form of NAFLD with hepatic necroinflammation, more rapid fibrosis progression, and a higher risk of adverse clinical outcomes. While hepatocellular carcinoma (HCC) only affects a small fraction of NAFLD patients, the total number of cases can still be substantial when one multiplies the risk of HCC and the huge number of patients. As a result, NASH has already become the third most common cause of HCC in the United States. The number of patients undergoing liver transplantation for HCC secondary to NASH has also increased by 4-fold from 2002 to 2012.

Data on NASH-related HCC in Asia are scarce. In a study of 6508 Japanese patients with NAFLD diagnosed by ultrasonography, only 16 (0.25%) developed HCC at a median follow-up of 5.6 years. Although this may suggest that NASH-related HCC is unimportant in Asia-Pacific countries, we should not forget that this problem has only been emerging recently even in western countries. Since it takes decades before chronic liver diseases progress to cirrhosis and HCC, it is possible that there will be a time lag before we witness the wave of NASH-related HCC in Asia.

Although cirrhosis is one of the most important risk factors of HCC for most chronic liver diseases, a number of reports suggest that up to a third of NASH-related HCC develop from non-cirrhotic livers, a figure higher than that in other liver etiologies. There are several possible explanations for this phenomenon. First, there is some overlap in the signaling pathways of NASH and HCC. NASH may thus directly promote HCC development. Second, the proportion of NAFLD patients with cirrhosis is lower than that in other liver diseases. It comes as no surprise that non-cirrhotic HCC is also more common in NAFLD patients. Finally, some patients with NASH-related cirrhosis may be classified as cryptogenic cirrhosis when hepatic steatosis is no longer apparent. In any case, non-cirrhotic HCC has major clinical implications; it would be difficult to define a high risk group for HCC surveillance.
Are Emerging Biomarkers and Imaging Tools Better than Routine Abdominal Sonography for HCC Surveillance?

Do Young Kim

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

The reasons why prognosis of hepatocellular carcinoma (HCC) is poor along with pancreas cancer and lung cancer among solid cancers are decreased liver function due to accompanied hepatitis or cirrhosis and advanced stage at the time of diagnosis. Thus, the rate of application of curative treatments is not high. The way of increasing patient survival is to diagnose HCC as early as possible. The guidelines by Korean Liver Cancer Association (KLCA)/National Cancer Center and other international or regional guidelines recommend surveillance for HCC of 6-months interval using liver ultrasonography (US) and serum alpha-fetoprotein (AFP) in patients who are at risk of developing HCC, such as those with cirrhosis, chronic hepatitis B (CHB) or chronic hepatitis C.

For a method to be an effective surveillance one, the survival benefit should be proved. In only one randomized controlled trial conducted in China, there was 37% decrease of mortality in CHB patients who received surveillance using US + serum AFP compared to those who did not receive any surveillance. However, the study design and treatment algorithm were not appropriate, requiring a caution in the interpretation of results. Nevertheless, the current surveillance strategy with US+serum AFP seems to be effective in the early diagnosis of HCC. However, we can not conclude that this strategy improves patient survival because the studies were from single cohort without control group.

There is unmet need of developing imaging or novel biomarkers that can overcome the limitations of current US and serum AFP. In addition, there is also need of analyzing patient characteristics or morphological characteristics of liver in patients in whom it is difficult to diagnose early HCC, when applying US+serum AFP.

There were efforts to apply magnetic resonance imaging (HCC) with hepatobiliary-specific agent or unenhanced MRI in HCC surveillance to overcome the limit of US. Although it is obvious that these advanced imaging techniques can find early HCC which might not be detected by the current US, it is still controversial that enhanced or unenhanced MRI meet the criteria for HCC surveillance tool.

References

Hepatocellular carcinoma (HCC) can be diagnosed based on characteristic findings of arterial-phase enhancement and portal/delayed “washout” in cirrhotic patients. Several countries and major academic societies have proposed varying specific diagnostic criteria for HCC, largely reflecting the variable HCC prevalence in different regions and ethnic groups, as well as different practice patterns. In 2018, a new version of Korean practice guidelines for management of HCC was released by the Korean Liver Cancer Association (KLCA) and the National Cancer Center (NCC). In addition, the LI-RADS 2018 version was integrated into the HCC diagnosis, staging, and management practice guidance of the American Association for the Study of Liver Diseases (AASLD). Furthermore, Asian-Pacific Association for the Study of the Liver (APASL) and European Association for the Study of the Liver (EASL), changed the HCC guidelines with the advances in the imaging techniques in 2017 and 2018, respectively. The Liver Imaging Reporting and Data System (LI-RADS®) is a comprehensive system for standardizing the terminology, technique, interpretation, reporting, and data collection of liver observations in individuals at high risk for hepatocellular carcinoma (HCC). In this lecture, I will briefly review the new HCC diagnostic criteria endorsed by the 2018 KLCA-NCC Korea practice guidelines, in comparison with other recent guidelines, with special emphasis on the currently published LI-RADS algorithms.
KLCA General Meeting (K*)

DAY 2: Friday, June 21, 2019 (11:10-12:10)
ROOM D [2F] 205
Background & Aim: In this systematic review and meta-analysis, we aimed to clarify the effect of obesity on the occurrence of and mortality from primary liver cancer.

Methods: This study was conducted using a systematic literature search on MEDLINE, EMBASE, and the Cochrane Library until November 2018 using the primary keywords “obesity,” “overweight,” “body mass index (BMI),” “body weight,” “liver,” “cancer,” “hepatocellular carcinoma,” “liver cancer,” “risk,” and “mortality.” Studies assessing the relationship between BMI and occurrence of or mortality from primary liver cancer including hepatocellular carcinoma in prospective cohorts and those reporting hazard ratios (HRs) or provided data to allow HR estimation were included.

Results: A total of 28 prospective cohort studies with 8,135,906 subjects were included in the final analysis. These included 22 studies with 6,059,561 subjects for cancer occurrence and 7 studies with 2,077,425 subjects for cancer-related mortality. In the meta-analysis, an increase in BMI was associated with the occurrence of primary liver cancer (HR 1.69, 95% confidence interval [CI]: 1.50-1.90, I² = 56%). A BMI-dependent occurrence of primary liver cancer was reported. HRs were 1.36 (95% CI: 1.02-1.81), 1.77 (95% CI: 1.56-2.01), and 3.08 (95% CI: 1.21-7.86) for BMI > 25 kg/m², > 30 kg/m², and > 35 kg/m², respectively. Furthermore, increased BMI resulted in enhanced liver cancer-related mortality (HR 1.61, 95% CI: 1.14-2.27, I² = 80%).

Conclusion: High BMI increases liver cancer mortality and occurrence of primary liver cancer. Obesity is an independent risk factor for the occurrence of and mortality from primary liver cancer.

매년 2월 2일은 대한간암학회가 제정한 “간암의 날”이다. 2월 2일로 제정한 이유는 간암을 조기진단하기 위한 건강검진을 1년에 2번, 간암표지자인 AFP와 복부초음파 검사 2가지를 규칙적으로 시행하자는 의미이다.
간암은 한국인에게 많이 생기는 암 중 하나이다. 연령표준화발생률을 기준으로 살펴보면, 2015년에는 10만 명당 남자 29.5명, 여자 8.2명으로 남성에서 4위, 여성에서 6위를 차지하고 있다. 특히 암사망률이 높아 2015년 전체 암사망자 중 간암이 남성에서 2위, 여성에서 3위를 차지하고 있다. 특히 사회적으로 경제적 생산성이 높은 중년의 사망률이 높다는 점에서 간암은 국가적으로 큰 영향을 미치는 질환이 아닐 수 없다. 비록 과거 자료이지만, 2005년 간암으로 인한 사회경제적 부담은 2조 4,552억원으로 2조 3,963억원의 위암을 추월하고 1위를 차지하였으며, 암환자 1인당 부담 역시 6,700만원으로 췌장암에 이어 2위를 차지하였다. 간암은 상대적으로 사망
율이 높고, 더 젊은 나이에 사망하기 때문에 이로 인한 사회적 부담은 전체 암 중 가장 크다.

최근 들어 비만이 암 발생과 밀접한 관련이 있다는 보고가 많이 되고 있다. 우리나라의 비만 유병률은 2016년 기준 34.8%이며, OECD는 우리나라 고도 비만인구가 2030년 자금보다 두 배 늘어날 것으로 예상하였다. 특히 비만으로 인한 지방간이 우리나라에서 흔한 만성 B형, C형간염 환자들에서 간경변증 및 간암 발생을 증가시킬 수 있다는 점을 고려한다면 비만이 국내 간암 발생에 미치는 영향은 더욱 컸을 수 있다.

이에 대한간암학회는 제3회 "간암의 날"을 맞이하여 <비만과 간암의 관계>라는 주제 하에 비만이 간암에 미치는 영향 등에 관해 발표하였다. 2019년 대한간암학회가 비만과 간암의 관계에 대한 28개의 연구논문을 메타분석하였다.1-10 비만한 사람의 경우, 그렇지 않은 사람보다 간암 발생률이 1.69배 높고, 간암 사망률 역시 1.61배 높았다. 특히 비만한 정도가 심할수록 간암 발생률 및 간암 사망률이 비례하여 증가하였다. 체질량지수 25(kg/m²)이상인 경우 간암 발생률이 1.36배, 체질량지수 30(kg/m²)이상인 경우 1.77배, 체질량지수 35(kg/m²)이상인 경우 3.08배 높았다. 간암 사망률 또한 체질량지수 25(kg/m²)이상인 경우 1.25배, 체질량지수 30(kg/m²)이상인 경우 1.37배, 체질량지수 35(kg/m²)이상인 경우 2.82배 높았다(그림 1). 특히, 간암 발생의 고위험군인 바이러스간염 환자의 경우에도, 비만한 경우 비만하지 않은 경우보다 간암 발생률이 1.76배 증가하며, 체질량 지수가 증가할수록 그 위험이 증가하는 것으로 나타났다. 바이러스간염 환자의 경우 체질량지수가 25(kg/m²)이상인 경우 간암 발생률이 1.49배, 체질량지수가 30(kg/m²)이상인 경우 간암 발생률이 2.07배 증가하였다.

그림 1. 비만이 간암에 미치는 영향

이상을 정리하면, 비만은 간암의 발생과 사망률에 중요한 위험인자이며, BMI 25 이상의 비만은 간암의 발생과 사망률을 증가시킬 수 있고, 비만이 심해질수록 간암의 발생과 사망률은 더욱 증가한다. 또한, 만성 바이러스성 간염이 비만과 동반되면, 간암의 발생률을 증가시킨다.
References


DAY 2: Friday, June 21, 2019 (13:30-14:30)
ROOM D [2F] 205

LCSGJ-KLCA Joint Symposium 1

One Step Forward for Understanding Basic Knowledge

Chairs:
Yutaka Kawakami (Keio Univ., Japan)
Young Nyun Park (Yonsei Univ.)
Potential of Exosome-Carrying microRNAs in Liquid Biopsy

Takahiro Ochiya
Department of Molecular and Cellular Medicine, Tokyo Medical University, Tokyo Japan

Rapid advances in liquid biopsy techniques in recent years have led to research on the use of extracellular vesicles (EVs), in the diagnosis of diseases. The attraction of EVs as novel biomarkers is that they are present in various bodily fluids including blood, urine, saliva and breast milk, while disease-specific EVs have a high concentration among pathology-specific molecules. The analysis of EV biomarkers in blood or other fluid samples would enable preliminary diagnosis of diseases where tissue samples are difficult to obtain, and would eliminate the need for the direct tissue sampling of conventional biopsies, which would in turn be effective in reducing unnecessary biopsies. Meanwhile, the concentrated molecules in disease-specific EVs could be used together with diagnostics to promote personalized medicine. However, a number of issues need to be clarified and resolved, such as developing an EV liquid biopsy test for clinical use and identifying the molecules that make up disease-specific EVs. Here we will also present our current progress on EV-mediated circulating microRNAs for early detection of 13 species of cancer including HCC and dementia in Japan.

References

Cancer immunotherapy particularly immune-checkpoint inhibitors (ICIs) (anti-PD-1/PD-L1 and CTLA-4 Ab) have recently been established as one of the standard cancer therapies for a variety of cancers. However, the responses to ICIs are still limited (response rates are about 10-20%). Thus, the identification of biomarkers to select appropriate patients and appropriate immunotherapies as well as the improvement of immunotherapy efficacy possibly through combination strategies or T cell based adoptive cell immunotherapy (ACT) are needed.

The response to immunotherapies depends on immune status of patients particularly in tumor microenvironment (TME), which is defined by cancer cell genetic characteristics (e.g. immunogenic DNA mutations, immunosuppressive oncogenes and aneuploidy), patients’ genetic immune-reactivity (e.g. immune related gene SNPs, HLA types), and environmental factors (e.g. intestinal microbiota, smoking, UV, diet/obesity, stress). In general, for the patients with cancer cells having sufficient immunogenic antigens such as neo-antigens, ICI based combination immunotherapies may be effective, but for the patients without immunogenic antigens, gene engineered T cells (e.g. chimeric antigen receptor (CAR-T) or T cell receptor (TCR) gene transduced T cells) may be useful. Therefore, in addition to various ICI based combination immunotherapies, we have been developing T cell based ACTs including tumor infiltrating T lymphocyte (TIL) therapy for metastatic melanoma and chemo-resistant advanced cervical cancer, and CAR-T or TCR-T therapies for various solid cancers including hepatocellular carcinoma (HCC).

Anti-tumor T cells can be generated and expanded sufficient for clinical use from TILs of melanoma and cervical cancer. Clinical trials of ours and others showed that TIL therapy was effective for about 30% of melanoma patients even who failed to previous ICI therapy. For patients with other types of cancer, we have been developing CAR-T therapy targeting to two different tumor antigens. One of the CAR-Ts we are developing is targeting to human glypican-1 (GPC1), which is a cell surface molecule expressed on various cancers including lung cancer. GPC1 specific CAR-T showed strong tumor regression activity in both human cancer implanted xenogeneic tumor model and murine syngeneic tumor model. Furthermore, combination of anti-PD-1 Ab with GPC1-CAR-T was found to be more effective than either treatment alone.

For HCC patients, PD-1 Ab has been approved in the US, and combination immunotherapies such as PD-1/PD-L1 Abs plus anti-VEGF Ab or VEGF-R inhibitors are currently being evaluated. Transcriptome analyses of HCC tumor tissues defined immunological subtypes and suggested that some of the patients with either viral or non-viral cancers are T cell inflamed (relatively significant CD8+ T cell responses) and may respond to PD-1/PD-L1 inhibitor monotherapies, but others are T cell non-inflamed and may not respond to PD-1/PD-L1 inhibitors. In one of the T cell non-inflamed subtypes, stem cell like subtype, cancer cells express high amount of cell surface glypican-3 (GPC3). Then, we have also developed CAR-T targeting to human GPC3 which may be useful for the patients with ICI resistant stem cell like HCC subtype. These T cell based ACTs may be attractive strategies for the patients with various cancers including advanced HCC which may be resistance to various drug therapies including ICIs.
Oncolytic Virus-Based Therapy for HCC

Jeong Heo
Department of Internal Medicine, College of Medicine, Pusan National University, Busan, Korea

Oncolytic virotherapy (OVT) is the treatment using oncolytic viruses (OVs) for cancer. OVs are designed to replicate selectively in and destroy directly cancer cells and induce immune responses (Russell et al., Nature Biotechnology. 2012). Almost OVs are engineered viruses, selectively infect cancer cells including adenovirus, herpes virus, measles virus and vaccinia virus (VV) (Lichty et al., Nature Reviews Cancer. 2014). Telomelysin is engineered telomerase-specific replication competent oncolytic adenovirus, shown not only objective clinical responses, but also immune reactions in various solid tumors (Nemunitis et al., Mol Ther. 2010). Pexa-Vec (JX-594) is a Wyeth strain oncolytic VV, also shown both responses in HCC (Heo et al., Nature Medicine. 2013). OVs can be adopted into cancer immunotherapies. As recent developments and applications of immunology in cancer treatment, immune checker-points inhibitors (ICIs) including anti CTLA4 Ab, anti PD-1 Ab and PD-L1 Ab have been tried for various cancers including hepatocellular carcinoma. The limitations in efficacy of ICIs are related to poorly immunogenic tumors and highly suppressive tumor microenvironment (TME) (Liu et al., Oncoimmunology. 2016 and Fend et al., Cancer Research. 2017). OVs would lyse cancer cell and cause the release of various antigen, cytokine including type 1 interferon, which induce antitumor immunity and enhance T cell recruitment in non-immunogenic and immune-deserted TME. The combination strategies both OVT and ICIs would enhance the efficacy, safety and cost-effectiveness, compared to each alone treatment, in terms of dosages and treatment interval. OVs in various combination therapies have been evaluated for therapeutic efficacy in preclinical as well as clinical levels, which could affect almost all aspects of the cancer–immunity cycle, recruit tumor infiltrating lymphocytes to the TME and transform non-immunogenic and immune-deserted tumor into immune-competent tumor. The strategy of OVs and ICIs combination have increased therapeutic responses. The selection of virus, optimal dosing, route of administration and schedule in oncolytic virus treatment require further study. Clarification between tumor-specific T cell responses and the contribution of viral-specific T cell responses should be further investigated. The versatility and safety of oncolytic viruses would be the ideal agents for optimizing combination immunotherapy.
LCSGJ-KLCA Joint Symposium 2

Similarities and Differences in Treatment of HCC

Chairs:
Shoji Kubo (Osaka City Univ., Japan)
Seung Kew Yoon (The Catholic Univ. of Korea)
Recent Trends of Treatment for Intermediate Stage HCC: Japanese Experience

Masatoshi Kudo
Kindai University Faculty of Medicine, Osaka, Japan

Although transcatheter arterial chemoembolisation (TACE) is the standard of care for intermediate-stage hepatocellular carcinoma (HCC), there is a subgroup of patients who do not benefit from TACE. The treatment strategy for this subgroup of patients currently remains an unmet need. We performed a proof-of-concept study that lenvatinib may be favorable treatment as an initial treatment in intermediate-stage HCC patients with large or multinodular tumors exceeding the up-to-seven criteria.

This proof-of-concept study included 176 patients who received lenvatinib or TACE as an initial treatment and met the eligibility criteria [beyond the up-to-seven criteria, no prior TACE, no vascular invasion, no extrahepatic spread and Child-Pugh A]. Propensity score matching was used to adjust for patient demographics.

After propensity-score matching, outcome of 30 patients prospectively treated with lenvatinib (14 in clinical trials, 1 in early access program and 15 in real world setting) and 60 patients treated with cTACE as the initial treatment was compared. The change of ALBI score from baseline to the end of treatment were -2.61 to -2.61 for 30 patients in lenvatinib group ($p = 0.254$) and -2.66 to -2.09 in cTACE group ($p < 0.01$), respectively. The lenvatinib group showed a significantly higher objective response rate (73.3% vs. 33.3%; $p < 0.001$). Overall survival was significantly longer in the lenvatinib group than in the cTACE group (37.9 vs. 21.3 months; hazard ratio: 0.48, $p < 0.01$).

In patients with intermediate-stage HCC beyond the up-to-seven criteria with Child-Pugh A, who usually do not benefit from TACE, lenvatinib provides more favorable outcome than TACE.
Recent Trends of Treatment for Intermediate Stage HCC: Korean Experience

Ji Hoon Kim
Korea University College of Medicine, Seoul, Korea

Intermediate stage of hepatocellular carcinoma (HCC) in BCLC class is including very heterogeneous patients group in terms of not only liver function, but also tumor size. Therefore, same intermediate stage of HCC patients received different treatment modality and showed diverse prognosis. For example, HCC patient with four tumors in lateral lobe and child score 5 could receive surgical resection and might get good prognosis. However, HCC patient with four tumors in both lobe and child score 7 could receive TACE and the prognosis might be somewhat dismal compared with the patients described above.

Because of this heterogeneity, BCLC has been challenged to be the optimal staging method and many researcher including Bolondi L have been tried to optimize intermediate stage of BCLC. Moreover, BCLC recommended only TACE for proper treatment in intermediate stage of HCC patients. However, as I mentioned above, HCC patients with intermediate stage BCLC could receive surgical resection and could receive ablative therapy or liver transplantation sometimes. These practice for intermediate stage HCC patients generally showed diversity between nations.

In this LCSGJ-KLCA Joint Symposium, I will present past and current Korean experience of treatment of HCC patients with intermediate stage.
Recent Trends of Treatment for Advanced Stage HCC: Japanese Experience

Kazuomi Ueshima

Kindai University Faculty of Medicine, Osaka, Japan

In Japan, 4 molecular targeted agents are approved and available for hepatocellular carcinoma. Sorafenib and lenvatinib are the first-line agents and regorafenib and ramcirumab are the second-line agents. However, the immune checkpoint inhibitor nivolumab and pembrolizumab are not approved in Japan unlike Korea. For one year since lenvatinib was approved in March 2018, over 10,000 HCC patients have been treated with lenvatinib. Lenvatinib has changed clinical practice for advanced HCC dramatically. Clinically the first choice of treatment for advanced HCC with Child-Pugh A is almost lenvatinib due to its high response rate, different toxicities from sorafenib and its good cost-effectiveness. If the down-staging is obtained, loco-regional therapy such as resection, RFA or TACE is added radically. If lenvatinib is failed, sorafenib-regorafenib sequential therapy is performed but its effectiveness are limited. There is no second-line treatment for the patients who failed to lenvatinib but ramucirumab may be the candidate of effective second line treatment because of high activity of inhibition against VEGFR2 with high serum concentration. Ramucirumab may also be the standard agent for elderly patients due to its less toxicity. On the other hand, molecular targeted agents are not recommended for patients with Child-Pugh B, therefore hepatic arterial infusion chemotherapy or TACE as a loco-regional therapy is selected in case the patients have extrahepatic metastases if intrahepatic lesion is prognostic factor. The systemic chemotherapeutic agents for the patients with Child-Pugh B are now warranted. The effectiveness of nivolumab for Child-Pugh B HCC was reported. In the near future, nivolumab may be the first line agent for Child-Pugh B HCC.
Liver cancer is the third leading cause of cancer-related deaths worldwide, and hepatocellular carcinoma (HCC) represents 70% to 90% of all liver cancers. The burden of HCC is increasing worldwide. Its incidence and mortality rates have been steadily increasing. The crude annual rate of liver cancer mortality has increased over the last 30 years in Korea. Systemic therapies are indicated for advanced stage of HCC, not indicated for surgery or locoregional treatments. Systemic therapies include conventional cytotoxic chemotherapy, molecularly targeted therapy, and immunotherapy. Molecularly targeted therapies are the current mainstream of systemic therapy in Korea.

Sorafenib is the first approved molecularly targeted therapy agent for the treatment of advanced hepatocellular carcinoma and that targets vascular endothelial growth factor receptor-2 (VEGFR-2), platelet-derived growth factor receptor (PDGFR), and Raf/MEK/ERK. The Asia Pacific trial, phase III study, was the first sorafenib trial for the advanced HCC that included Korean patients. In the Asia Pacific trial, median overall survival (OS) was 6.5 months in patients treated with sorafenib, compared with 4.2 months in those who received placebo (hazard ratio [HR] 0.68 [95% CI 0.50-0.93]; \(P=0.014\)). Based on these results, sorafenib approved as first-line systemic chemotherapy for advanced HCC in Korea.\(^1\) The GIDEON study was a large-scale observational study involving 3,171 patients from 39 nations who were treated with sorafenib. The Gideon study reported that Median OS was different according to Child-Pugh class: 13.6 months for class A, 6.2 months for B7, 4.8 months for B8, and 3.7 months for B9.\(^2\) The Korean subset of the Gideon study, which included 497 patients from 11 sites, reported the median OS and time to progression (TTP) were 8.5 months and 2.5 months. In Child-Pugh A patients, the median OS and TTP were 10.2 months and 2.5 months. The most common adverse effects associated with sorafenib include hand-foot skin reaction (HFSR), diarrhea, hypertension, rash, fatigue, abdominal pain and nausea. The Korean data of the Gideon study reported that the most frequent treatment-emergent drug-related adverse event was hand-foot skin reaction (31.7%), followed by diarrhea (18.0%) and the safety profile did not appear to differ by Child-Pugh status.\(^3\)

Regorafenib is a multikinase inhibitor that targets kinases involved in angiogenesis, oncogenesis, and the tumour microenvironment. We participated in phase II and phase III clinical trials. But the Korean data of these trials were not separately analyzed. The RESORCE trial, phase III study, included patients who progressed after sorafenib treatment with Child-Pugh A and an ECOG score 0-1. Regorafenib improved OS with an HR of 0.63 (95% CI, 0.50 to 0.79; \(P < 0.0001\)); median survival was 10.6 months (95% CI, 9.1 to 12.1 months) for regorafenib versus 7.8 months (95% CI, 6.3 to 8.8 months) for placebo. Adverse events were reported in all regorafenib recipients (374 [100%] of 374) and 179 (93%) of 193 placebo recipients. The most common grade 3 or 4 adverse events were hypertension (15%), HFSR (13%), fatigue (9%), and diarrhea (3%) in regorafenib group. Based on this result, regorafenib was approved as second-line systemic therapy who progressed after sorafenib treatment.\(^4\) In subgroup analysis of patients from Asia, OS, PFS, TTP and treatment emergent adverse events were similar to overall patients.
Another multikinase inhibitor, lenvatinib, recently demonstrated non-inferiority of OS compared with sorafenib as first-line therapy for unresectable HCC. In phase III trial for advanced HCC patients with a tumor occupying less than 50% of the liver and no bile duct or main portal vein invasion, median OS was 13.6 months (95% CI, 12.1 to 14.9 months) for lenvatinib and 12.3 months (95% CI, 10.4 to 13.9 months) for sorafenib. The most common any-grade adverse events were hypertension (42%), diarrhea (39%), decreased appetite (34%), and decreased weight (31%), for lenvatinib. Based on these results, lenvatinib approved as first-line systemic chemotherapy for advanced HCC in Korea.

Nivolumab is a IgG4 anti-PD-1 (programmed cell death receptor-1) monoclonal antibody and works as an immune checkpoint inhibitor. A non-comparative phase I/II trial for patients with advanced HCC demonstrated an overall ORR of 20% (complete response 1%, partial response 18%) and a duration of response of 9.9 months. In subgroup analysis, median OS of sorafenib-experienced asian patients (n = 85), included 13 Korean patients, was 14.9 months. Currently, a randomized controlled multicenter phase III trial comparing nivolumab and sorafenib as first-line treatment for advanced HCC (CheckMate-459, ClinicalTrial.gov ID: NCT025276509) is ongoing.

In Korea, Sorafenib is approved for advanced stage of HCC with Child-Pugh class A and ECOG score 0-1. Lenvatinib is also approved for advanced stage of HCC not indicated for surgical resection. Regorafenib is approved for patients with progressive HCC after sorafenib treatment and with Child-Pugh class A and ECOG score 0-1. Nivolumab approved for patients with progressive HCC after sorafenib with Child-Pugh score 5 to 7. In Korea, many of the systemic therapy experience was from clinical trials and the real world data is limited except sorafenib.

References
KLCA Symposium 2

New and Emerging Systemic Therapies in Advanced HCC

Chairs:
Kwang-Hyub Han (Yonsei Univ.)
Seung Woon Paik (Sungkyunkwan Univ.)
Hepatocellular carcinoma (HCC) ranks among the most common and deadliest cancers worldwide. Incidence rates nearly doubled over the last decades and, to date, HCC is one of the fastest growing causes of cancer related deaths in the USA. Despite effective surveillance options less than 20% of patients are eligible for curative treatment, such as liver transplantation, resection, or radiofrequency ablation, at the time of diagnosis. During the past 10 years, drug development in advanced HCC stages has been significantly hampered by a pronounced phenotypic and molecular heterogeneity of the tumors, as well as a high toxicity of active compounds under clinical evaluation. The majority of patients with advanced HCC presents with a severely impaired liver function, which further requires a fine balance between anti-tumor activity and drug-induced toxicity. This lecture will summarize primary efficacy data and clinically relevant post-hoc analysis of the pivotal first-line phase-III trials in HCC.

Until recently, the multi-tyrosinekinase inhibitor sorafenib was the therapeutic standard of care in a first line setting since 2007. Median overall survival (OS) in the sorafenib arm was 10.7 months vs. 7.9 month in placebo-treated patients. Similar results were not only demonstrated in a parallel phase III study involving mainly Asian, predominantly hepatitis B-infected patients, but also in 8 subsequent phase III studies in which sorafenib served as control treatment. Notably, although currently no predictive biomarkers for response exist, several clinical factors including chronic hepatitis C infection or side effects including early dermatological events or hypertension favor a better response to the treatment.

Lenvatinib is another oral multi-tyrosinkinase inhibitor with activity against VEGFR1-3, FGFR1-4, PDGF, RET und KIT. The RESOURCE phase III study involving mainly Asian patients was conducted to demonstrate a non-inferiority of lenvatinib in comparison to sorafenib in a first line setting. The study achieved its primary endpoint with a median OS of 13.6 months in the experimental lenvatinib arm versus 12.3 months in the sorafenib arm (HR: 0.92; 95% CI 0.79-1.06). An interesting observation of this trial was the high objective response rate (ORR) for lenvatinib with 24.1% vs 9.2% for sorafenib despite the similar OS (independent review: ORR mRECIST 40.6% vs. 12.4%, ORR RECIST: 18.8% vs. 6.5%). Further, surrogate characteristics for survival such as progression free survival (PFS), Time-to-Progression (TTP) were consistently higher in the lenvatinib group than in the sorafenib group (PFS: 7.4 months vs. 3.7 months; TTP: 8.9 months vs. 3.7 months). Importantly, the study excluded patients with adverse prognostic tumor characteristics, e.g. main branch portal vein thrombosis or >50% tumor occupation of the liver. Nevertheless, results from the trial encourage the use of lenvatinib as an effective first line therapy in advanced HCC leading to inclusion in recent EASL and ESMO guidelines. Consequently, approval for lenvatinib in first line was recently granted by the FDA and EMA.
Second Line Treatments for HCC

Stephen L. Chan
Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong

An expanding number of drug treatment is available for advanced HCC, which include multi-targeted TKI, checkpoint inhibitors and monoclonal antibody. Following failure with first-line treatment, lenvatinib or Sorafenib, a number of second-line treatment has become available, including regorafenib, cabozantinib and PD-1 antibody. Ramucirumab has also been recently approved by US FDA for treating AFP-positive HCC in second-line setting. There are no head-to-head comparison amongst these second line treatments hence the decision is based on the mechanism of action, clinical trial data, toxicity of each agent.
Hepatocellular carcinoma (HCC) develops in the condition of uncontrolled growth of hepatic cells caused by the genetic alterations in complex signaling cascades. Therefore, we can expect the effect of targeted agents attacking important targets in carcinogenic pathways along with minimizing general adverse effects. However, we have failed to find the dominant signal pathways in hepatocarcinogenesis, yet.

Sorafenib is a multikinase inhibitor especially inhibiting serine/threonine kinases Raf-1/B-Raf, tyrosine kinases VEG-FR-2/-3 and PDGFR-β, which suppresses cancer progression and angiogenesis. Sorafenib is the first systemic therapy prolonged survival significantly in HCC patients. After that sorafenib not only established a proof of concept for the use of multi-kinase inhibitors strategy for the treatment of HCC, but also is the reference standard for systemic therapy for HCC patients.

Nevertheless, subsequent clinical trials using targeted agents have failed in succession for about 10 years. The agents which failed to prove their activity in HCC were sunitinib, linifanib, brivanib, nintedanib in the first-line treatment and axitinib, ramucirumab, brivanib, erlotinib, everolimus, tivantinib, ADI-PEG20 in the second-line treatment after sorafenib failure.

Recently, lenvatinib, another angiogenesis inhibitor, showed non-inferior overall survival in the 1st-line treatment compared with sorafenib in the REFLECT trial. Lenvatinib also showed rather superior response rate, progression free survival, time to progression and preferable toxicity profiles.

For the patients who failed sorafenib treatment, regorafenib and cabozantinib, mainly angiogenesis inhibitors overcame placebo control in RESORCE and CELESTIAL trials.

In addition, nivolumab showed meaningful results for HCC in phase II checkmate 040 trial. We have now 2 options in the 1st-line and 3 options after sorafenib failure in HCC, with angiogenesis inhibitor or immune checkpoint inhibitor.

However, the current effects of systemic treatments for HCC are far from satisfaction as ever. By looking at the trials currently conducted for HCC, we are discussing ways to improve the prognosis of HCC patients.
Combination of Interventional and Systemic Therapies for HCC: Current Status and Future Direction

Joong-Won Park
National Cancer Center, Korea

Combination therapy, a modality that combines more than one type of therapy or agent simultaneously or sequentially, is an effective cancer therapy. The rationale for combination therapy is to use drugs or modalities that work by different mechanism, thereby increasing the chances of a cure or long-term remission. Surgery or locoregional therapy (LRT) treats cancer that is confined locally, while systemic therapy kills the cancer cells that have spread to distant sites. Combination therapy can be generally useful for people with advanced cancers. Sometimes broad definition of combination therapy includes neoadjuvant therapy and adjuvant therapy.

For improving the outcomes of hepatocellular carcinoma (HCC) treatment, a various combination of surgery, LRT such as transarterial chemoembolization (TACE), transarterial radioembolization (TARE), radiofrequency ablation (RFA) and external beam radiation therapy (EBRT), and systemic therapy is attempted. In HCC therapy, unfortunately, the combination of systemic therapies has not yet been sufficiently validated. Combination therapy with TACE and systemic agents (sorafenib) has not proven to be superior to systemic agent alone, but some patients may benefit from combination therapy.

Theoretically, LRTs can increase tumor immunogenicity, which can result in an increase of tumor infiltrating cytotoxic T cells with systemic antitumor immune response. However, the evidence of this hypothesis is poor yet. Fortunately, initial results from studies combing LRTs with immunotherapies demonstrated especially promising results.

The combination of LRTs with systemic therapies may further improve response and survival rates in HCC treatment, and may change the current paradigm of HCC therapy.
Symposium 3

Hepatitis C Virus

Chairs:
Masao Omata (Yamanashi Prefectural Central Hospital, Japan)
Si Hyun Bae (The Catholic Univ. of Korea)
Long-Term Outcome of Direct-Acting Antiviral Treatment

Jung Il Lee
Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

만성 C형 간염에서 Direct-Acting Antiviral을 이용한 치료의 장기적 예후에 대한 고찰

이 정 일
연세대학교 의과대학 내과학교실

It has been reported that eradicating hepatitis C virus (HCV) infection decreases the liver related morbidity and mortality, reduces the risk of hepatocellular carcinoma (HCC) and improves the survival.\(^1\) Although direct-acting antivirals (DAAs) are very effective in the treatment of chronic HCV infection, its long-term benefits are still not clear. In addition, there has been some controversial reports over whether DAA therapy would increase the risk for HCC shortly after DAA treatment.\(^2\)

Recently, there has been a prospective cohort study reporting clinical outcomes in over 7,000 patients with chronic HCV after DAA treatment.\(^3\) The study demonstrated that HCV patients after DAA treatment would have decreased risk for liver-related mortality as well as reduced risk for HCC. When the analysis was performed for those with HCV related liver cirrhosis, DAA treatment in HCV patients could still reduce the risk for liver-related mortality and HCC development.

Nevertheless, further investigations may need in determining the benefits of DAA treatment in HCV patients that already experienced HCC. A recent study on early HCC patients after curative treatment suggested that DAA treatment would improve survival.\(^4\) However, another study recruiting cirrhotic patients that showed complete response to HCC treatment failed to demonstrate reduced HCC recurrence after DAA treatment.\(^5\) Another study suggested that the effect of DAA induced SVR on HCC occurrence might take time, and would not change the short-term HCC risk after DAA treatment.\(^6\)

Conclusion

It seems that DAA induced SVR would reduce liver-related mortality by reducing liver-related complication including HCC. However, beneficial role of DAA treatment as secondary prevention of HCC might need more evidences to draw a conclusion.
References


There are 71 million chronic hepatitis C (CHC) patients, in which a significant number of those develop cirrhosis or liver cancer. Approximately 399,000 people die each year from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (HCC). Viral eradication after interferon (IFN)-based therapy has been associated with an improvement of liver function and a reduced risk of developing HCC in CHC patients. The IFN-free direct-acting antiviral (DDA) combinations can cure more than 95% of CHC patients, thereby hopeful of the reducing the risk of death from liver cancer and cirrhosis.

Nevertheless, in the early years of their use, there are some negative reports on the effectiveness of DAA therapy in the recurrence of HCC. Following the reports of larger prospective studies, the risk of de novo HCC occurrence has been proven clearly to be lower after the achievement of sustained virological response (SVR), regardless of antiviral treatment. On the other hand, the risk of HCC recurrence following DAA treatment is controversial. The possible alterations in the immune system after clearance of the virus with the DAAs and how they may affect the conventional cancer immunity cycle are still under discussion. The aim of this presentation is to review published data on the risk of HCC occurrence and recurrence after viral eradication and provide an update on the risk and benefit of DAAs treatment revealed by clinical and basic researches so far.
Unmet Needs in the Era of Direct-Acting Antiviral Therapy

Ming-Lung Yu
Department of Internal Medicine, Kaohsiung Medical University and Hospital, Taiwan

Since the first directly acting antivirals (DAA) approved in 2011, the progress of DAA in HCV treatment is moving from IFN (IFN)-containing regimens to IFN-free regimens in 2013, which are currently standard-of-care. Currently, there are 14 DAAs approved in the treatment of HCV and at least 9 major combination regimens are applied in the clinical practice for HCV treatment. The two pan-genotypic DAA regimens sofosbuvir/velpatasvir and glecaprevir/pibrentasvir could cure all genotype with SVR rate of 96-99%.

However, even with such high SVR rate, there remains many unmet needs after SVR achieved:

1) The HCC risk remains. There are conflict data addressing the risk of HCC occurrence or recurrence after SVR by IFN-free DAA versus IFN-based regimens. Unexpected higher HCC risk after SVR by IFN-free DAA have been reported in Spain and France. By contrast, recent large scaled study from US and Japan did not observed higher HCC risk after SVR by IFN-free DAA. Nevertheless, even the risk of HCC is greatly reduced by achievement of SVR, a substantial number of patients remain at high risk of HCC, such as advanced fibrosis, old age, diabetes and persistently high levels of alfa-fetoprotein or liver enzymes. Recent studies demonstrated that HCV-induced epigenetic changes associated with liver cancer risk persist after SVR, suggesting HCC remains an unmet need after SVR.

2) The progression of hepatic decompensation after SVR remains among patients who have Child-Pugh class B or C decompensated liver cirrhosis before DAA therapy. These patients are still unable to de-listing from liver transplantation, especially for those with MLED score > 20.

3) Extrahepatic manifestations, although decreased in prevalence after SVR, will persist among substantial proportion of HCV patients after SVR, and need life-long monitoring/care.

4) Although current DAA regimens could achieve very high SVR rates of > 98%. The DAA failed patient number will accumulate year by year. The multiple drug resistance HCV strains will be very difficult-to-cure population in the near future.

5) Barriers to HCV elimination: Low disease awareness and accessibility in the care cascades of HCV treatment are the major hurdle on the way to HCV elimination. Finally, lack of HCV vaccine, HCV would never be controlled.
State-of-the-Art Lecture 2

Chair:
Jin Mo Yang (The Catholic Univ. of Korea)
Autoimmune liver diseases (AILD), autoimmune hepatitis (AIH), primary biliary cholangitis (PBC; formally known as primary biliary cirrhosis), and primary sclerosing cholangitis (PSC), have been considered to be a relatively uncommon etiology in Asia, where viral hepatitis is the diagnosis in the majority of patients with chronic liver diseases. However, recent findings demonstrate that prevalence of autoimmune liver diseases is increasing worldwide and therefore the importance of improving recognition and management of these diseases is increasing in Asia as well. In Korea, Professor Sook-Hyang Jeong, one of my best friend and colleague, published excellent papers regarding epidemiological studies of PBC and AIH in Korea. Recently, our group also published an increasing trend of prevalence of AIH, PBC and PSC in Japan.

The etiology of AILD are multifactorial, and involves the interaction of both genetic background and environmental triggers. Environmental insults in genetic susceptible individuals can develop aberrant immunological reactions and lead to autoimmune-mediated hepatocyte or bile duct injuries, indicating that AILD results from the combination of “bad genes and bad luck”. As innovative progresses of state-of-the-art techniques for identifying disease-susceptible genes such as genome-wide association studies (GWAS), a number of genes have been identified as contributing to development or progression of AILD. Despite the identification of genetic susceptible loci, it still remains obscure how these genetic elements can account for the pathological development of these diseases. Furthermore, a number of case-control studies, including a very recent study in PBC from Korea which is the first one in Asia, have identified several risk factors in the environment. Recent epidemiological studies clearly demonstrate a significant change in male-to-female ratio of patients with AIH and PBC, suggesting the alteration of environmental triggering factors for development over time.

From the clinical standpoint, it is crucial to always keep in mind the possibility of AILD in differential diagnosis when encountering patients with elevated liver enzymes. Detection of anti-mitochondrial antibody (AMA) in patients with chronic elevation of cholestatic enzymes establish a diagnosis of PBC. Since disease-specific biomarkers are lacking in AIH, a combination of exclusion of viral hepatitis, detection of anti-nuclear antibody (ANA), and typical histopathology are required to make a diagnosis of AIH. Similarly, characteristic cholangiographic findings such as band-like stricture and beaded or pruned-tree like appearance with presence of inflammatory bowel diseases in patients with chronic cholestasis are important for diagnosis of PSC.

Corticosteroids and ursodeoxycholic acid (UDCA) are established as first-line treatment options for AIH and PBC, respectively, while 20-30% of patients require second-line treatment due to incomplete responses or intolerance to the first-line. Azathioprine and mycophenolate mofetil are recommended as second-line therapy for AIH, and currently a phase 2/3 clinical trial with anti-BAFF receptor (VAY736) for AIH patients with incomplete responses to corticosteroids is underway. A very recent study from an international collaborative PBC study group (Global PBC group) indicated that PBC patients with incomplete responses to UDCA exhibited a significantly better prognosis compared to those without UDCA treatment, again unravelling the efficacy of UDCA. Obeticholic acid (OCA), a farnesoid X receptor (FXR) agonist, was approved for PBC with incomplete responses to UDCA in the US and Europe. In Japan,
bezafibrate has been used for those with incomplete responders. The efficacy of bezafibrate was recently confirmed by a randomized controlled study in France, and we also demonstrated a long-term efficacy of bezafibrate with a large-scale retrospective cohort in Japan. On the other hand, no medical treatment including UDCA has been proved to be effective for improving liver transplantation (LT)-free survival in PSC, and recurrence of PSC after LT seriously deteriorate long-term outcome. Nevertheless, a recent phase 2 clinical trial of Cilofexor (GS-9674), a non-steroidal FXR agonist, for non-cirrhotic PSC patients was very promising, and a global phase 3 trial will soon be launched. Another promising candidate drug for PSC is norURSO, a side chain-shortened C23 homologue of UDCA, which are or will be on global clinical trials including Asia.

Taken together, a series of new and promising drugs are coming in sight as novel treatment options for AILD, making individualized treatment possible based on stratification of risk for progression, and significantly improving overall survival as well as quality of life of patients. At the same time, global, Asian, and Korea-Japan collaborations is definitely warranted for more understanding of AILD.
Symposium 4

Cirrhosis

Chairs:
Rino Gani (Univ. of Indonesia, Indonesia)
Soon Koo Baik (Yonsei Univ. Wonju)
Liver cirrhosis, caused by chronic inflammation followed by fibrosis, is one of the prevalent refractory diseases in Japan, with more than 400,000 people suffering. Thus, a new therapy supporting liver fibrosis regression and regeneration, which the liver is inherently capable of, is urgently required. We started a clinical study for decompensated cirrhosis using autologous bone marrow cells in 2003 (Autologous Bone Marrow infusion, ABMi therapy). From the clinical study, we found BMC infusion improved liver cirrhosis and induced liver regeneration. ABMi therapy is effective for liver cirrhosis patient. Bone marrow cell included both mesenchymal stem cell (MSC) and macrophage, so we analyzed the mechanism of how and which bone marrow cell is effective to improve liver cirrhosis. In basic study with mice model using two photon microscopy, MSCs migrate to the lung work as “Conducting cells”, and bone marrow-derived macrophages that migrate to the damaged fibrotic liver area and change its polarity through interaction with MSCs function as “Effector cells”. Exosomes are critical as communication tools between MSCs and macrophages. Injecting only exosomes can achieve liver fibrosis regression and regeneration similar to MSC injection. On the other hands, we proceed Phase I/II clinical trial using allogeneic adipose tissue-derived mesenchymal stem cells (MSCs) for decompensated cirrhosis in 2017.

In this presentation, I will present status of MSC therapy for liver cirrhosis.

References


The Role of Albumin Related with Systemic Inflammation in Cirrhosis

Paolo Angeli
Unit of Internal Medicine and Hepatology (UIMH), University of Padova, Italy

Albumin was introduced in the treatment of patients with cirrhosis and ascites to increase the reduced plasma oncotic pressure, which, at that time, was thought to be a pivotal factor together with portal hypertension, in the pathogenesis of ascites. The following evolution of the knowledge showed that the renal functional abnormalities in cirrhosis are the final consequence of a reduction of effective circulating volume due to a marked splanchnic arterial vasodilatation. As a consequence, the rationale of the use of albumin in patients with cirrhosis and ascites was completely changed. Albumin is no more used on the basis of the plasma albumin concentration but in clinical situations that are or are going to be a sign of severe reduction of effective circulating volume such as: 1) prevention of post-paracentesis circulatory dysfunction, 2) prevention of hepatorenal syndrome in patients with spontaneous bacterial peritonitis (SBP), and 3) treatment of hepatorenal syndrome.

Albumin is very effective in preventing of post-paracentesis circulatory dysfunction and of hepatorenal syndrome in cirrhotic patients with SBP. In addition, albumin administration improves survival in patients with spontaneous bacterial peritonitis. In the treatment of hepatorenal syndrome, the use of albumin in combination with vasoconstrictor drugs is essential for the recovery of renal function and to improve slightly survival. More recently, it has been observed in a multicentre Italian RCT that albumin is capable to improve survival also in patients with responsive ascites. In these patients albumin reduces not only the rate of development of refractory ascites but also of SBP, infections other SBP, hyponatremia, hepatic encephalopathy and renal impairment. For sure, these effects can be due not only to its oncotic properties as plasma but to its several non-oncotic effects also. In particular, in the setting of SBP, albumin exerts a positive on cardiac output. Experimental and clinical data showed that the increase in cardiac output induced by albumin is not only related to its effect on cardiac pre-load but also to a cardiac positive inotropic effect. The inotropic effect of albumin in rats with cirrhosis and ascites was related to its effectiveness in counteracting the negative effects of oxidative stress- and TNF-α-induced activation of NF-κB-iNOS pathway and oxidative stress-induced alteration of β-receptor signaling in the cardiac tissue.

It seems easy to foresee that the role of albumin in the management of patients with cirrhosis and ascites will be once more defined in the near future.
Role of Cytoglobin, a Novel Radical Scavenger in Stellate Cell Activation and Hepatic Fibrosis

Norifumi Kawada
Osaka City University Medical School, Japan

Cytoglobin (CYGB) belongs to the globin family and is expressed in hepatic stellate cells (HSCs). In addition to its gas-binding and radical scavenging ability, we have been demonstrated that CYGB deficiency induced spontaneous fibrosis and cancer development in aged mouse liver and augmented their manifestation in mice treated with DEN- or CDAA-diet. On the other hand, HSC-specific overexpression of CYGB-mCherry protected mice from TAA-triggered liver fibrosis. These results obtained by in vivo studied confirmed that CYGB is an important molecule for maintenance of HSCs in a quiescent status. While we have been searching for molecules that triggered CYGB induction in human HSCs, we noticed that FGF2 is a key factor in inducing the alteration in both CYGB and αSMA expression in human HSCs. FGF2 initiated the phosphorylation of both JNK and c-JUN. C-JUN overexpression up- and down-regulated CYGB and αSMA expression, respectively. In ChIP analyses, phospho-c-JUN bound its consensus motif located -218 to -222 bases from the transcription initiation site in the CYGB promoter upon FGF2 stimulation. In contrast, TGFβ1 antagonized the effect of FGF2 via SMAD2-SP3 passway. In conclusion, CYGB is likely a critical molecule relevant to the maintenance of quiescent phenotype of human HSCs.
DAY 3: Saturday, June 22, 2019 (09:00-10:00)
ROOM BC [1F] 101-102

KAHBPS Symposium 1

Surgical Research in HBP Field—Challenges and Barriers

Chairs:
Il-Young Park (The Catholic Univ. of Korea)
Koo Jeong Kang (Keimyung Univ.)
Surgeon-Scientists: An Endangered Species?

Sundeep G. Keswani
Department of Surgery, Pediatrics & OB/Gyn, Baylor College of Medicine and Children’s Hospital, USA

Over the past several decades, federal funding to surgeon-scientists has been lagging, and our analysis suggests that this trend continues. This compounded by the current funding environment and its impact on research productivity, the future of basic research in academic surgery may be threatened. As the cost associated with conducting basic research continues to grow, the competition to obtain funding from the NIH and other extramural sources has become progressively difficult. This is especially true when considering the steady decline in the NIH pay line since 2003.

Although “success” in basic research is difficult to define, we use federal funding as a proxy, but accept that alternative revenue sources (private industry, philanthropy, clinical revenue) can sustain productive basic research programs. Nevertheless, achieving peer-reviewed federal funding is commonly accepted as indicative of a successful research effort. Based on this metric and the data presented previously by others, surgeon-basic scientists are falling behind and the future of this important aspect of academic surgery is uncertain. Recognizing that multiple challenges confront surgeon-scientists, the SUS formed a Basic Science Committee tasked with identifying the issues facing surgical investigators to inform potential solutions. In this talk, we will elucidate the findings of this committee that were published in the Annals of Surgery.

The changing academic and hospital environment has contributed to a prevailing perception that it is unrealistic for surgeons to succeed as basic scientists, and may have surgeons wondering whether it is even worthwhile to maintain and develop links between basic science and surgery. If such attitudes permeate surgical leadership, it will influence the justification for making the investment required to encourage young faculty along a path toward basic science inquiry and research independence. Current models for surgical training need to be evaluated and possibly changed to develop surgeon-scientists prepared to succeed in today’s competitive scientific environment. If we agree that fundamental investigation into the pathophysiology and treatment of surgical disease needs to include the active participation of surgeons, then academic surgery must act to address these challenges and ensure continued development of surgeon-scientists and the environment that promotes their success or we run the risk of becoming an “endangered species”.
Basic/Translational Research: How to Start and Grow?

Say-June Kim
Seoul St. Mary’s Hospital, The Catholic University of Korea, Korea

Firstly, I recommend that you write up a schedule with a series of milestones to accomplish by a specific date, and keep to it. You will need time to get an overview of what material is out there, find out what’s in your library, select relevant material, read it, take notes, and start putting it together — and to do a second wave of research to clear up points raised in the writing of your first draft. Next, have a research question in mind. Technically, your thesis should emerge from your research, when you have data in front of you. But you need a kind of “working thesis” while doing your research — a question you want to answer. As you come across new material, ask yourself if it looks like it will help you answer your question. Anything that looks relevant but doesn’t help answer your question you can put back. It’s tempting to gather a lot of background material, and some is necessary, but too much will waste your time without contributing to your research. Get one or two good sources for background and then keep focused by working towards an answer to your research question. Start your research with an idea of how you plan to collect and organize your notes and data. Use the human resources available to you as well as the material resources. Ask for help in finding and evaluating sources, or for help in figuring out what to do with the material you’ve collected so far.
Clinical Research to Reduce Pancreatic Fistula after Distal Pancreatectomy

Manabu Kawai, Seiko Hirono, Kenichi Okada, Motoki Miyazawa, Yuji Kitahata, Ryohei Kobayashi, Masaki Ueno, Shinya Hayami, Hiroki Yamaue

Second Department of Surgery, Wakayama Medical University, Japan

Objective: The appropriate pancreatic stump closure during distal pancreatectomy (DP) remains still controversial. Three clinical trials including one multicenter randomized controlled trial (RCT) have been conducted to evaluate the most appropriate pancreatic stump closure during DP.

Evaluation of stapler closure: In the first study, the risk factors of pancreatic fistula were investigated among three types of stump closure; hand-sewn suture (n=32), bipolar scissors (n=45), and stapler closure (n=45) in 122 DP. There was no significant difference regarding pancreatic fistula between the three types of stump closure (hand-sewn suture: 44% vs. bipolar scissors: 37.7% vs. stapler closure: 35.5%). However, this study reported that pancreas thicker than 12 mm significantly increased pancreatic fistula after DP using stapler closure.

Evaluation of pancreaticojejunostomy for pancreatic stump during DP: Second, a multicenter RCT (NCT01384617) was performed to evaluate whether pancreaticojejunostomy (PJ) of pancreatic stump decreases pancreatic fistula after DP compared to stapler closure. One hundred thirty-six patients were enrolled. Pancreatic fistula occurred in 23 patients (37.7%) in stapler closure group and 24 (38.7%) in PJ group (P=0.332) in intention-to-treat analysis. The incidence of clinically relevant pancreatic fistula was 16.4% for stapler closure and 9.7% for PJ (P=0.201). In a subgroup analysis for thickness of pancreas >12 mm, clinically relevant pancreatic fistula occurred in 22.2% of the patients in the stapler closure group and in 6.2% of the PJ group (P=0.080). This study could not clarify the impact of PJ for pancreatic stump. However, PJ for pancreatic stump might offer a potential reduction of pancreatic fistula in cases with thicker pancreas.

Evaluation of reinforced stapler during DP: In last multicenter single-arm, prospective, nonrandomized study (NCT02270554), 121 patients for DP were enrolled to evaluate whether reinforced stapler decreases clinically relevant pancreatic fistula after DP. Per-protocol analysis was performed using 105 patients. Clinically relevant pancreatic fistula occurred in 13 (12.4%) of 105 patients. Severe complication (Clavien classification IIIa or more) was 10.5% (11/105). Multivariate analysis revealed that staple line hemorrhage (P=0.006, odds ratio 8.6) were an independent risk factor for clinically relevant pancreatic fistula after DP. This study concluded that reinforced stapler did not reduce clinically relevant pancreatic fistula after DP.

Conclusion: As further steps adequately powered prospective randomized trials should be required to evaluate the most appropriate pancreatic stump closure during DP.
KAHBPS Symposium 2

Clinical Issues in Non-Hepatic Abdominal Surgery in Patients with Liver Cirrhosis

Chairs:
Hyung Chul Kim (Soonchunhyang Univ.)
Yang Won Nah (Univ. of Ulsan)
Management of Gallstones and Acute Cholecystitis in Patient with Liver Cirrhosis
- Medical Treatment: Indication and Result of Medical Treatment -

Ki Tae Suk
Department of Internal Medicine, Hallym University College of Medicine, Korea

Cholesterol gallstone disease is a common clinical condition influenced by genetic factors, increasing age, female gender, and metabolic factors. Although laparoscopic cholecystectomy is currently considered the gold standard in treating patients with symptomatic gallstones, new perspectives regarding medical therapy of cholelithiasis are currently under discussion, also taking into account the pathogenesis of gallstones, the natural history of the disease and the analysis of the overall costs of therapy. A careful selection of patients may lead to successful nonsurgical therapy in symptomatic subjects with a functioning gallbladder harboring small radiolucent stones. The classical oral litholysis by ursodeoxycholic acid has been recently paralleled by new experimental observations, suggesting that cholesterol-lowering agents which inhibit cholesterol synthesis (statins) or intestinal cholesterol absorption (ezetimibe), or drugs acting on specific nuclear receptors involved in cholesterol and bile acid homeostasis, might be proposed as additional approaches for treating cholesterol gallstones. In this review we discuss old, recent and future perspectives on medical treatment of cholesterol cholelithiasis.

Keywords: Cholesterol, Stone, Cirrhosis
병증이 발생할 경우 가까이에서 모니터링하고 수술하며 보존적으로 관리하는 것이 가장 좋다. 진행된 간질환이 있을 때 수술 위험이 낮아질수록 담석이 진단될 때 환자와 논의하여야며 치료 결정에 적극적으로 참여해야 한다.

내과 치료

증상이 경미하고 전형적인 담도성 통증을 의심하기 어려운 경우나, 환자가 수술을 원하지 않거나 혹은 수술을 시행하기 어려운 경우에는 내과적인 치료를 고려할 수 있다. 현재 담낭 탕식의 치료에 시도해볼 수 있는 비수술적 방법에는 담석을 용해시키는 방법으로 폐강 담낭총류계 또는 담낭 안에 적절 약물을 주입하여 담석을 용해시키는 방법이 있고, 담석을 분쇄, 제거하는 방법으로 체외충격파 쇄석술과 경피간담낭절제술을 이용하여 담석을 제거하는 방법이 있다. 그러니 최근 20년 간 복강경 담낭절제술이 보편화되면서 내과 치료의 비중이 감소하고 있는 추세에서 이들 중에서는 일부 환자에서 경구 담낭용해제를 투여하는 것 외에 나머지 치료는 치료 효과에 비하여 비용이나 합병증의 발생 위험이 높아 최근에는 거의 시행되고 있지 않다.

경구 담즙산 제제

경구 담즙산 제제는 담석의 용해요법에 가장 많이 사용되는 약물로 chenodeoxycholic acid (CDCA)와 ursodeoxycholic acid (UDCA) 등이 흔히 사용된다. 1972년 처음으로 CDCA가 방사선 투과성 담석의 용해에 이용되기 시작하였고 이후 1975년 천수성 담즙산인 UDCA가 CDCA의 부작용 없이 이 대체하여 담석 용해에 이용되게 되었다. 경구 담즙산 용해요법의 근거는 콜레스테롤 담석의 형성 과정에서 가장 중요한 기전이라고 할 수 있는 담즙내 콜레스테롤의 과포화를 억제시키는데 있다.5

CDCA나 UDCA를 경구로 투여하면 담즙산 저장고의 상당 부분이 CDCA나 UDCA로 대체되면서 담즙산 저장고의 용량이 확장되고, 콜레스테롤의 담즙 내 분비가 억제되어 담즙내 콜레스테롤의 포화도가 감소하게 된다. 이렇게 콜레스테롤이 불포화화된 담즙이 분비되어 담낭 내으로 들어가 담석의 표면을 둘러싸면 담석 내의 콜레스테롤이 미포 (micelle) 내로 용해되어 나오게 되어 담석의 용해가 일어나게 된다.

경구 담즙산 제제는 작용기전을 고려할 때 방사선 투과성 콜레스테롤 담석만을 용해시킬 수 있고 담석의 갈음 성분이 많은수록 용해되기 어렵기 때문에 순수한 콜레스테롤 담석보다는 색소성 담석의 비중이 높은 우리나라에서는 환자의 선택이 용이하지 않다. 담석 용해를 위한 CDCA의 효과적인 용량은 13-15 mg/kg/day인데, 최소 치료용량 이상의 용량에서 실패가 발생하여 현재는 담석용해 치료로 CDCA의 단독투여는 더 이상 추천되지 않는다. 대신에 CDCA의 복합제를 별도 용도 치료 효과를 높이기 위하여 UDCA 5-8 mg/kg/day의 병합요법이 이용되며, 국내에서도 CDCA 114 mg과 UDCA 114 mg의 복합제제(씨앤유®; Myungmoon Pharm. Co. Ltd, Seoul, Korea)가 시판되고 있다. 한편 UDCA는 천수성 담즙산으로 간 혹은 장내세균에 의하여 형성되는 3차 담즙산이다. UDCA는 천수성의 콜레스테롤 흡수가 담즙으로의 콜레스테롤 분비를 억제하여 담즙내 콜레스테롤 포화도를 40-60% 감소시킬 수 있다.6

담석 용해를 위해서는 10-14 mg/kg/day의 용량을 투여하는데 식사 후나 자기 전에 투여한다. CDCA와는 달리 간독성이 적고 혈중 콜레스테롤을 상승시키지 않으며, 설사는 1% 이하에서 발생한다. 현재 가장 많이 사용되고 있는 경구 담즙산 용해요법은 UDCA 단독요법이고, UDCA와 CDCA 병합요법도 사용되고 있다. 경구 담즙산 용해요법은 담낭 기능이 정상인 방사선 투과성 콜레스테롤 담석에 효과가 있다. 용해 효과는 6-12개월 후 영상진단으로 평가한다. 용해 효과는 담석의 CT 영상에서 예측할 수 있으며 CT에서 60 HU 미만의 담석에서 용해 효과가 가장 좋은 것으로 알려져 있다.7

References

Management of Gallstones and Acute Cholecystitis in Patient with Liver Cirrhosis  
- Surgical Treatment: What Should We Caution to Consider Surgery? -

Shang Yu Wang  
Chang Gung Memorial Hospital; Chang Gung University, Taiwan

Surgical treatments, both laparoscopic cholecystectomy (LC) and cholecystectomy via laparotomy (OC), are the mainstream treatments of several conditions related to biliary origin currently, including pain due to cholecystolithiasis, gallbladder polypoid lesions, choledocholithiasis with or without cholangitis, acute cholecystitis, and biliary pancreatitis. In addition, the timing of surgical treatment to individual aforementioned condition has also been proposed. Based on one of our recent study, patients who underwent percutaneous gallbladder drainage for acute cholecystitis and declined to elective cholecystectomy later still would encounter high risk of recurrence (up to 30%) with a median time of less than 5 months. The role of cholecystectomy for symptomatic gallbladder stones, therefore, cannot be replaced by other conservative treatment and LC is considered as the gold standard.

Cirrhosis is one of the most complicated human diseases and makes significant changes in physiology, local alteration of anatomy, modification of immune status, and other associated risks, which influence life expectancy. When it comes to surgical treatment of cholelithiasis, patients with cirrhosis were exposed to additional risks from 3 aspects: (1) relatively higher risk of cholelithiasis than general population, (2) relatively higher surgical risk, regardless to surgical procedures, and (3) increase surgical difficulty related to local condition, such as abundant collateral vessels around surgical field. Our previous investigation revealed that LC, once considered contraindicated in patients with cirrhosis, is a feasible procedure for most Child’s A and B patients with gallbladder stones and related conditions. Minor morbidity, an acceptable conversion rate, and shorter hospital stay can be achieved by applying LC to treat cirrhotic patients. However, appropriate preoperative preparations and meticulous operative techniques are required to reduce blood loss during laparoscopy and even mortality. Currently published studies, including retrospective case-controlled studies, prospective trials, and meta-analysis, also supported this point of view. In addition, LC is better than OC in several clinical aspects, including shorter operative time, reduced complication rates and reduced length of hospital stay. Considering to the possibility of future liver transplantation for cirrhotic patients, laparoscopic procedure may provide additional benefit of reducing postoperative abdominal adhesion, compared to open surgery. For the non-compensated cirrhosis, not only lack of study related to surgical outcomes (over 95% of currently reported cases were Child’s A and B) and conservative treatment still favored.

During the last decade, several surgical innovations, such as techniques related to LC, energy devices, and other related products related to hemostasis, have provided surgeons an arsenal to conduct delicate procedures with better outcome, especially in the intraoperative bleeding control and bile duct injuries related to LC. Several studies have mentioned those interesting issues. Besides, improved perioperative management also guarantees a better quality of care.

In our presentation, we are going to share our previous experience in LC for cirrhotic patients, review the current relevant evidences, and discuss perioperative management and the impact from the advance in current surgical techniques related to LC on the cirrhotic patients.
Clinical Outcomes and Prognosis of Emergency Surgery in Liver Cirrhosis Patient

Fausto Catena
Parma University Hospital, Italy

The increasing incidence of advanced chronic hepatic disease among patients with acute abdomen represents a great challenge for the emergency surgeon.

The severity of liver insufficiency, the grade of portal hypertension, the type of emergency of surgery to be performed, and severity of other comorbidities are relevant predictors of postoperative mortality and morbidity. Accurate patient history and examination together with scrupulous laboratory and imaging tests analysis are able to detect liver insufficiency with or without portal hypertension and all related affections.

A correct use of existing specific scores (Child-Pugh or MELD) consents to stratify patients’ severity in order to timely treat all potential complications.

Coagulation disorders and hypovolemia are the most insidious intraoperative and postoperative challenges. For this reason, during resuscitation it is mandatory a careful use of intravenous fluids and an appropriate targeted utilization of blood derivatives.

Two acute care surgery golden rules for high risk patients must be applied: first choose the quickest procedure, second use the less invasive operative strategy. According to this policy laparoscopic techniques should be employed extensively.

Moreover, all new technologies such as energy devices, staplers, hemostatics should be used without any concerns about costs.

Surgeons have to be aware about particular risks like severe bleedings from porto-systemic veins shunts even during abdominal wall dissection.

Liver and spleen anatomy can be different and standard surgical procedure such as splenectomy can be technically demanding in case of huge splenomegaly.

Finally, after surgery these patients in the postoperative course have an ongoing risk of liver/renal insufficiency.
Elective Cancer Surgery in Patients with Liver Cirrhosis

Sae Byeol Choi

Korea University Guro Hospital, Seoul, Korea

Liver cirrhosis has been associated with increased postoperative mortality and morbidity. Therefore surgical indications in patients with cirrhosis were limited due to complications associated with portal hypertension. Liver cirrhosis is a heterogenous disease, the severity of which has been evaluated with Child Pugh score and MELD score.

In patients with liver cirrhosis, extrahepatic malignancy could be developed. Preoperative optimization and evaluation of liver function as well as malignancy work up is essential to treat the malignancy. In this review, gastric cancer, colorectal cancer and periampullary cancers necessary pancreaticoduodenectomy or pancreas surgery are reviewed. In cancer surgery, the extent of surgery is expanded compared with the operation for benign disease.

In gastric cancer, the standard surgery is gastrectomy with lymph node dissection. Radical operation with D1 or D2 lymph node dissection can be tolerated in class A gastric cancer patients. D1 lymph node dissection is recommended in class B patients, and radical gastrectomy is very dangerous, even fatal for class C patients. In Colorectal cancer patients with liver cirrhosis have poorer overall survival compared to those without liver cirrhosis; however, the recurrence rates are similar. It might be due to the mortality from the liver, and surgical treatment should be actively considered for patients with MELD-Na score <10. On the other hand, in periampullary cancers requiring pancreaticoduodenectomy or pancreas surgery, El Nakeeb et al have reported surgical outcomes after pancreaticoduodenectomy in patients with liver cirrhosis. Patients with periampullary tumours and well-compensated chronic liver disease should be routinely considered for pancreaticoduodenectomy at high volume centers with available expertise to manage liver cirrhosis. Pancreatoduodenectomy is associated with an increased risk of postoperative morbidity in patients with liver cirrhosis; therefore, it is only recommended in patients with Child A cirrhosis without portal hypertension.

The perioperative morbidity and mortality following non-hepatic surgical procedures in patients with cirrhosis are significant. Preoperative assessment of these patients for co-morbidities and liver function is essential if surgical outcomes are to be improved. Both Child score and MELD score is useful to prognosticate these patients in short term surgical outcomes.

References

4. Teh SH, Nagorney DM, Stevens SR, Offord KP, Therneau TM, Plevak DJ, Talwalkar JA, Kim WR, Kamath PS. Risk fac-
KAHBPS Special Lecture

Chair:
Hee Chul Yu (Chonbuk National Univ.)
The Journey from Scientific Idea to Funded Grant: A Surgeon’s Approach

Sundeep G. Keswani
Department of Surgery, Pediatrics & OB/Gyn, Baylor College of Medicine and Children’s Hospital, USA

In the morning lecture, we elucidated the challenges that are facing surgeons to become effective surgeon-scientists. Now that those problems are more defined, how does one begin the journey of taking your insightful surgical observations from an conceptual idea to a fundable proposal? Much like everything else that we do as surgeons it becomes better with practice, and it is facilitated when we have a methodologic approach to the procedure. Just like with any other surgery we will highlight and define an algorithmic approach to formulating a hypothesis and translating it into a grant that can be used in most scientific situations. This is a very extensive topic. However, this overview of taking an idea to a fundable proposal will give attendees a solid foundation on which to move your projects forward in order to make more impact. The overview will include how to generate a hypothesis, how to formulate appropriate specific aims to test a hypothesis, and then the components of most grants with an operative approach to achieving your goals.
DAY 3: Saturday, June 22, 2019 (14:30-15:30)
ROOM BC [1F] 101-102

KAHBPS Symposium 3

Focus Review of Advanced Gallbladder Cancer Treatment

Chairs:
Dong Wook Choi (Sungkyunkwan Univ.)
Sang-Jae Park (National Cancer Center)
The Operative Indication of Advanced Gallbladder Cancer: How Much Advance Is the Limitation?

Masayuki Ohtsuka, Hideyuki Yoshitomi, Katsunori Furukawa, Tsukasa Takayashiki, Satoshi Kuboki, Shigetsugu Takano

Department of General Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

Currently surgical resection is considered to be the only hope for long-term survival in patients with advanced gallbladder cancer (GBC) despite a recent improvement of non-surgical therapy. However, because the lesion is often advanced by the time of diagnosis, only a small subset of GBC patients qualifies for surgery.

In order to select patients eligible for surgical resection, both technical and oncological factors should be considered. Surgical resection for advanced GBC is recommended only if a potentially curative resection is possible. Therefore, cases with peritoneal dissemination or metastasis to distant organs other than the liver are contraindications for surgical resection. In addition, cases with invasion of the hepatic artery (HA) and/or portal vein (PV) to be unable to reconstruct, or cases with extensive hepatic invasion and/or liver metastasis to be unable to excise due to insufficient remnant liver volume are judged to be “technically unresectable”. Excluded these cases, all patients with “technically resectable” disease should be potential candidates for surgical intervention.

However, advanced GBC often spreads to surrounding structures, such as the liver, the duodenum, the colon and the hilar structures (bile duct, hepatic artery, portal vein), and the prognosis of such cases is apparently poor even if radical surgical resection is achieved. In fact, our data indicates that the 5-year survival rate after surgical resection in 55 patients with advanced GBC (≥ T2) confined to the gallbladder is 46%, while it is only 20% in 64 GBC patients with a spread to extra-gallbladder. In particular, out of these 64 GBC patients with invasion to adjacent structures undergoing aggressive surgery with vascular and multivisceral resection, patients with obvious hepatic metastasis, patients with invasion of HA and/or PV requiring combined resection, and patients with invasion to more than three organs had significantly unfavorable prognosis. Curative resection was possible in only 9 of 15 patients with obvious hepatic metastasis, only 9 of 14 patients with invasion of HA and/or PV, and 10 of 15 patients with invasion to more than three organs. There were only three 2-year survivors in cases with obvious hepatic metastasis, only one in cases with invasion of HA and/or PV, and only one in cases with invasion to more than three organs. Therefore, advanced GBC cases with obvious liver metastasis, cases with invasion of HA and/or PV requiring combined resection, or cases with invasion to more than three organs should be regarded as “oncologically unresectable”. This may be the limitation of surgical resection.

On the other hand, down-sizing chemotherapy has a potential to overcome this oncological limitation of surgical resection for advanced GBC. We experienced a patient with advanced GBC spreading to three organs such as the liver, the bile duct and the hepatic artery. This case was judged as “oncologically unresectable”, so that chemotherapy was applied. After 4 courses of gemcitabine treatment, invasion of the hepatic artery was markedly improved, and surgical resection was performed. This patient survived more than 5 years. This strategy is expected to expand the surgical indication and to improve patient survival.
Recent Advances in the Chemotherapy in Advanced Gallbladder Cancer: Palliative vs. Neoadjuvant Chemotherapy

Hei-Cheul Jeung
Medical Oncology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Gallbladder cancer (GBC) is the most common and aggressive malignancy of the biliary tree. GBC remains a highly lethal disease, with only 10% of all patients presenting at a stage amenable to surgical resection.

Systemic chemotherapy is the mainstay for the treatment of advanced biliary tract cancer. Combination of Gemcitabine plus cisplatin become the standard of care for advanced biliary tract cancer. However, chemotherapy has demonstrated modest survival prolongation effect in GBC and most published series are small and include heterogeneous population of patients with GBC, cholangiocarcinoma, and occasionally some pancreatic and hepatic cancers which respond differently to chemotherapy. Moreover, most studies reported are performed in patients with adenocarcinoma, the most common histology of GBC. There is paucity of data regarding treatment of advanced adenosquamous or squamous cell gallbladder cancers, and in clinical practice these patients are treated similarly. Reported overall response rates with chemotherapy in GBC patients are in the range of 50 to 60 percent. There is limited data assessing the impact of treatment on overall survival (OS). In the only randomized trial comparing chemotherapy (gemcitabine plus oxaliplatin [GEMOX] or 5-FU/leucovorin) against best supportive care alone in 81 patients with inoperable GBC, median OS was 4.5, 4.6, and 9.5 months in the supportive care, FU/leucovorin and GEMOX groups, respectively.

As for neoadjuvant therapy, currently outside the setting of a clinical trial, neoadjuvant therapy is not recommended for surgically resectable gallbladder cancer. Trials with a neoadjuvant strategy may provide opportunities for the development of predictive markers to guide personalized treatment in patients with gallbladder and biliary tract cancer.

Combination therapy using cytotoxics and molecular-targeted agents has been tested in GBC. However, its efficacy remains limited. It has not yet been clarified whether second-line chemotherapy can improve the prognosis of advanced GBC. Several problems exist when assessing the results of previous reports concerning advanced GBC. In the presentation, the current evidence in advanced of systemic therapy of GBC will be highlighted, and a view at possible future prospects linked with molecular profiling, immunotherapy, and targeted therapies will be provided.
Case Presentation

Chi-Young Jeong
Department of Surgery, Gyeongsang National University Hospital, Gyeongsang National University Postgraduate School of Medicine, Jinju, Korea

Background: Gallbladder cancer (GBC) is highly aggressive disease. Although surgical resection is the only curative treatment for GBC, multidisciplinary approach has received much attention in recent years.

Case presentation: The first case is 50 years old man. He underwent an extended cholecystectomy for GBC (pT2N2M0). We recommended adjuvant chemotherapy, but he denied. Sixteen months later, when a recurrence lesion was detected in peri-gastric area, we performed radical antrectomy, transverse colon segmental resection, segment 3,4 (s3,4) wedge resection and pancreas head partial resection. After surgery we started chemotherapy with gemcitabine and cisplatin. After a year of chemotherapy, the lesions suspected metastatic recurrence again appeared in para-aortic lymph node and we started chemo-radiotherapy. After 8months of Chemo-radiotherapy, the para-aortic lesion decrease on imaging, but lesions suspected metastatic recurrence appeared in right adrenal gland, for which palliative chemotherapy was administered. The second case is 75 years old women. She underwent extended cholecystectomy with transverse colon segmental resection for GBC (pT3N1M0). We recommended adjuvant chemotherapy, but he denied. Four months later, the lesion suspected peritoneal seeding was detected. The third case is 66 years old man. In pre-operative image, GBC with liver invasion and multiple metastatic lymph nodes in periportal, perihepatic and para-aortic were detected. He underwent extended cholecystectomy for GBC (pT3N2M0). The fourth case is 66 years old man. He underwent extended cholecystectomy for GBC (pT3N0M0). We performed surveillance without further treatment. Since then, he has remained free of recurrent disease of 33 months follow up.

Conclusion: We hear report four cases of advanced GBC. The multidisciplinary treatment may be a promising option in selected patients with advanced GBC.
DAY 3: Saturday, June 22, 2019 (10:20-11:20)
ROOM D [1F] 106

Special Session

National Health Insurance
Big Data Research (★K)

Chairs:
Hyoung-Soo Kang (National Health Insurance Service)
Jaeyoun Cheong (Ajou Univ.)
National Health Insurance Big Data Analysis: Process and Example

Seong Yong Park
Big Data Center, National Health Insurance Service, Korea

NHIS, as a single insurer, take responsibility for operation of National Health Insurance (NHI) scheme, such as eligibility review of the insured, imposition and collection of contributions, insurance benefit, and negotiation of medical fee schedule with healthcare service providers.

The Korean National Health Insurance Big Data (NHID) features a whole population cohort which can be used for research purposes. National Health Insurance Big Data is made out of many resources. Database of beneficiary, contributions, medical service utilization, health screening service, long-term care service is integrated into NHID through individual ID linkage.

National Health Insurance Big Data can be used in various areas. NHIS supports for research that contributes to evidence-based policies and provides customized health service and so on.

NHIS created a public research DB, only after a de-identification process, to improve the accessibility of data, and provides big data and support for research that contributes to evidence-based policies, relates to issues of public concern, and improves data availability, conducted by a professional societies or public institutions.

NHIS provides a various health services, such as one-stop service which includes an annual physical diagnosis, an assessment of potential health risks and a customized treatment plan to counteract any health risks, monitoring indicators for the prevention of cardiovascular disease, and a health map service for an adequate allocation of healthcare resources and design an effective system.

NHIS is expecting to prevent disease and cut medical costs and predict disease outbreak and improve overall health services using health big data. NHIS' final goal may be summarized that every people can live without the burden of disease. NHIS believes that the more trials we should put for exceeding the public data boundary lines, the faster our final goal can be accomplished.
국민보험공단 빅데이터를 이용한 간질환 연구: 간암 검진 연구  

백 용 한  
성균관대학교 의과대학 내과학교실

우리나라에서 간암은 2번째로 사망률이 높은 암종이며, 특히 40~50 대에서는 암관련 사망 원인 1위 질환으로, 간암으로 인한 사회적 손실이 매우 크다. 이러한 사회적 손실을 줄이기 위하여 2003년부터 간암 고위험군에 대한 국가 암조기검진사업이 시행되고 있다. 다른 암종과 달리 간암은 거의 대부분 고위험군에서 발생하며 현재 우리나라에서는 20세 이상 만성 B형 간염, 만성 C형 간염, 간경변증 환자에 대하여 초음파 검사 및 혈청 alpha–fetoprotein (AFP)을 주기적으로 시행하고 있다. 그러나, 현재 시행되고 있는 국가 간암 검진의 현황 및 효과에 대하여 평가에 대한 연구는 부족한 실정이다. 이에 본 연구에서는 1) 국가간암검진을 포함한 간암검사실의 수검 현황 및 패턴을 파악하고, 2) 고위험자들의 간암 발생 패턴 및 간암 감시검사로 인해 간암이 조기 발견되었는지 알아보고자 하며, 3) 간암감시검사로 인하여 생존율의 개선이 있었는지를 평가하고자 한다.

본 연구에서는 국민건강보험공단 빅데이터를 분석하여 간암감시검사의 효과 및 간암 환자의 예후를 향상시키는 수검 암종을 정의하고자 하며, 크게 아래 두 가지 분석을 통하여 접근하고자 한다. 첫째는 2003년부터 2016년까지 국민건강보험공단 검진DB의 간암감시 검진자료를 이용하여 국가간암검진의 대상자분석을 통하여 수검률, 검진여부에 따른 조기간암 진단률, 검진여부에 따른 사망률 등을 분석하여 국가간암검진의 수검률 향상 및 사망률 감소를 위한 방향을 제시하고자 한다. 둘째로 국민건강보험공단의 맞춤형 데이터베이스를 이용하여 국가간암검진을 포함한 간암감시검사 여부를 조사하여 간암감시검사의 효과 및 개선방향을 분석하고자 한다.

이용 자료는 국민건강보험공단의 2002년부터 2016년까지의 건강보험청구자료를 활용하는 예정이다. 본 연구의 대상자는 40세 이상의 성인 중에서 2002년 12월 31일 1일자 간암 발생이 없는, 2003년부터 2016년 사이 국민건강보험공단 간암 발생자 원인분석에 의한 간암경험자를 대상으로 한다. 간암의 경우 간세포암 (C22.0)으로 정의하였고 조기 간암의 경우는 간암 관련 치료 중 간암을 진단 받은 후 처음 받은 치료수술 또는 간화성질환 흥행으로 정의하였다. 수검 패턴 및 수검 패턴에 따른 간암 발생을 분석하고 대상자의 특성 및 조기 간암 발생의 차이를 확인한다.

본 자료는 국가적으로 시행하고 있는 국가간암검진사업 및 간암감시검사를 평가하는 데 중요한 자료가 될 것으로 판단된다. 다만, 본 연구는 임상 변수가 제한적인 공공자료로 이용한 연구이므로, 완전한 간암 사업과의 연동이 불가하기 때문에 자료의 해석에 주의가 필요할 수 있다.
Role of Statins on Development and Progression of Non-Alcoholic Fatty Liver Disease: A Nationwide Nested Case-Control Study

Jung Il Lee\textsuperscript{1,2}, Hyun Woong Lee\textsuperscript{1,2}, Kwan Sik Lee\textsuperscript{1,2}, Hye Sun Lee\textsuperscript{3}, Ju-Young Park\textsuperscript{3}

\textsuperscript{1}Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; \textsuperscript{2}Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; \textsuperscript{3}Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Korea

Objective: Use of statins in nonalcoholic fatty liver disease (NAFLD) may reduce cardiovascular morbidity, whereas their effects on NAFLD itself is not well known. We aimed to investigate the role of statins on development of NAFLD and progression of significant liver fibrosis.

Design: This study included 11,593,409 subjects from the National Health Information Database of the Republic of Korea, entered in 2010 and followed up until 2016. NAFLD was diagnosed by calculating fatty liver index (FLI) and significant liver fibrosis was evaluated using BARD score.

Results: Among 5,339,901 subjects that had FLI <30.0 and included in non-NAFLD cohort, 164,856 subjects eventually had NAFLD developed and matched with 824,280 control subjects. Use of statin was associated with reduced risk of NAFLD development compared to that of the nonusers (AOR [adjusted odd ratio] 0.66; 95% CI [confidence interval] 0.65-0.67) in dose dependent manner, and independent of associated DM (AOR 0.44; 95% CI 0.1-0.46, with DM; AOR 0.71; 95% CI 0.69-0.72, without DM). From 712,262 subjects with FLI >60 and selected as NAFLD cohort, 111,257 subjects showed BARD score $\geq$2 and defined as liver fibrosis cases and matched with 556,285 control cases. Use of statins reduced risk of significant liver fibrosis compared to that of the nonusers (AOR 0.43; 95% CI 0.42-0.44) dose dependently, independent of DM (AOR 0.31; 95% CI 0.31-0.32, with DM; AOR 0.52; 95% CI 0.51-0.53, without DM).

Conclusions: Statins would decrease the risk of NAFLD occurrence and development of liver fibrosis in NAFLD subjects independent of accompanying DM.

Keywords: Stains; Nonalcoholic fatty liver disease; Liver fibrosis; Dyslipidemia
서론

정맥류 출혈, 조절되지 않는 복수, 간신증후군 및 간성뇌증은 진행된 비대상성 간경변 환자에서 나타나는 합병증으로 사망률과 간세포암종의 발생율을 높인다고 알려져 있다. 많은 선행연구에서 비대상성 간경변이 발생하는 경우 간세포암종 발생의 위험도는 매년 7~8% 증가한다고 알려져 있으며, 사망률은 매년 20~50%로 알려져 있다. 그러나 최근 의료수준의 발전에 따라 출혈, 말초로 인한 사망률이 줄었으며, 간세포암종의 진단율도 오랜 변 관에서 발생하였다. 무엇보다 만성 B형 간염에서 항바이러스제의 사용은 간질환의 진행과 간암 발생의 낮춘다고 알려져 있다.2,3 최근 항바이러스제의 광범위한 사용에 따라 만성 B형 간염 환자와 초기 간경변 환자에서 항바이러스제의 사용 후 간세포암종 발생 및 사망률에 대한 clinical outcome이 많이 알려져 있다. 그러나 아직 비대상성 환자에서 항바이러스 사용에 따른 간세포암종 발생 및 사망에 대한 clinical outcome에 대하여는 알려진 바가 적다. 일부 소규모 환자를 대상으로 비대상성 환자에서 항바이러스제 사용에 따른 clinical outcome에 대한 연구가 보고되었으나 대상환자가 적고 관찰기간이 짧은 문제가 있다. 본 연구는 전국민이 단일의료보험에 속하는 한국의 자료를 이용하여 항바이러스를 사용하는 비대상성 간경변환자에서 clinical outcome에 대하여 살펴보고자 하였다.

Method

Study population

연구의 분석 대상은 2007년~2014년 동안 보험기준에 따라 B형 간염 항바이러스제를 최초로 처방 받은 환자 286,871명을 대상으로 하였다. 항바이러스제를 처방 받은 286,871명 중 앞선 1년 동안 항바이러스제 사용이 없고 추적관찰기간이 5년 이상 가능한 2008년~2009년에 항바이러스제를 사용한 환자를 대상으로 하였다. 연구대상기간(2008년~2009년) 동안 만성 B형 간염 환자의 보험급여 기준은 변경되지 않았으며, 골게 기준은 아래와 같다. HBeAg(+)로서 HBV-DNA≥100,000 copies/ml이거나, 또는, HBeAg(-)로서 HBV-DNA≥10,000 copies/ml인 만성활 동성 B형간염 환자에서 AST(Aspartate Transaminase) 또는 ALT(Alanine Transaminase)가 80단위 이상인 환자, 만 성 B형 간염의 초치료로는 lamivudine, clevudine, entecavir, tenofovir와 pegylated interferonα가 가능하다.

Inclusion criteria

2007년부터 2014년까지 만성 B형 간염 환자의 보험급여 기준에 합당하여 경구용 항바이러스제를 90일 이상 사용한 사람을 대상으로 하였다. 최초 경구용 항바이러스제를 사용한 이후 최소 5년 이상 추적관찰 자료가 있는 환자만을 대상으로 하였다. 비대상성 환자들의 정의는 조절되지 않은 복수로 인하여 3리터 이상의 복수 천차를 받은 경우, 정맥류 출혈로 인하여 내시경지혈술을 받거나 약물 치료를 받은 경우, 간성뇌증으로 인하여 lactulose 응용을 시행한 경우, 간신증후군으로 치료를 받은 경우로 하였다.
Exclusion criteria
항바이러스제를 사용하는 시점으로 1년 이내에 경구용 항바이러스제 (lamivudine, clevudine, adefovir, telbivudin, entecavir, tenofovir)를 사용한 병력이 있는 경우, 비대상성 합병증(조절되지 않는 복수, 정맥류 출혈, 간신증후군, 간성뇌증)이 2년 이내에 발생된 경우, 항바이러스제 처방 이전에 암을 진단받은 경우, 추적관찰 기간이 5년 미만인 경우를 제외하였다.

Baseline biochemical data.
분석 대상자는 비대상성 합병증이 최초 발생된 B형 간염 환자 중에서 비대상성 합병증 발생 전후 간단 이내에 혈청 HBsAg 양성, 혈청 HBV-DNA PCR > 2,000 U/L, and ALT/AST >80 U/L 이상인 경우였다.

Results
1. 대상 환자 선별
2007년부터 2014년까지 항바이러스제를 혈청 HBsAg 양성, 혈청 HBV-DNA PCR > 2,000 U/L, and ALT/AST >80 U/L 이상으로 암이 발생한 환자로 하였다 (Figure 1). 처음 항바이러스제를 투여하는 당시 대상성 간질환을 보이는 환자 48,365명과 항바이러스계를 투여 당시 비대상성 합병증이 동반되었던 환자 2,682명을 대상으로 하였다 (Table 1). 대상자의 평균 연령은 43.5세였으며, entecavir를 사용한 경우가 24.1%로 가장 많았으며, lamivudine를 사용한 경우가 많았다. 항바이러스제를 처방 받은 환자의 26.9%는 관찰기간 동안 75% 이상의 복약 순응도를 보였다. 비대상성 간경변을 동반하는 경우 불응성 복수가 75.4%로 가장 많았으며, 이에 정맥류 출혈이 많았다.

2. Clinical course of compensated hepatitis B patients under NUC treatment
만성 B형 간염 및 대상성 간경변 환자에서 항바이러스제를 사용 후 첫번째 비대상성 합병증이 발생하는 빈도는 연간 1.2~2.0%였으며, 대상성 정맥류 출혈의 발생 빈도는 연간 7.4%였다. 항바이러스제를 사용한 대상성 간질환 환자에서 간암 발생은 연간 1.7~3.5%였으며, hepatitis cell carcinoma 발생 빈도는 5년 누적 발생 빈도는 11.5%로 비대상성 합병증 발생빈도보다 높았다 (p <.0001). Compensated HBV patients에서 연간 사망율은 약 0.55~0.71%였으며, 5년 누적 사망률은 3.1%, 누적 생존율은 96.9% 였다.

3. Clinical course of compensated hepatitis B patients under NUC treatment
비대상성 간경변 환자에서 항바이러스제를 사용 후 두번째 비대상성 합병증이 발생하는 빈도는 연간 2.05~46.8%였다. 대상성 간경변 환자에서 간암 발생은 연간 0.55~0.71%였으며, hepatitis cell carcinoma 발생 빈도는 5년 누적 발생 빈도는 11.5%로 비대상성 간경변 환자에서 5년 누적 간암 발생 빈도는 24.1%였다. Decompensated HBV patients에서 연간 사망율은 약 2.61~19.1%였으며 5년 누적 사망률은 32.6%, 누적 생존율은 67.4%였다.
4. Mortality according to decompensated event

비대상성 합병증의 종류에 따른 사망률을 비교하였다 (Table 3). 불응성 복수가 발생한 경우 연간 13.6%~24.3% 였으며, 첫해 사망률이 가장 높았다. 1년 사망률은 24.3%, 5년 누적사망률은 89.5% 였다. 정맥류 출혈이 발생한 경우 연간 15.1%~23.1% 였으며, 첫해 사망률이 가장 높았다. 1년 사망률은 23.1%, 5년 누적사망률은 87.0% 였다. 간 신증후군이 발생한 경우 연간 10.5%~23.2% 였으며, 첫해 사망률이 가장 높았다. 1년 사망률은 23.2%, 5년 누적사망률은 92.8% 였다.


References

DAY 3: Saturday, June 22, 2019 (14:30-15:40)

Common Concerns

Hapatologists and Surgeons (*K)

Chairs:
Yung Sang Lee (Univ. of Ulsan)
Sung Su Yun (Yeungnam Univ.)
Assessment of Surgical Risk in Patients with Cirrhosis

Ki Tae Yoon

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University College of Medicine, Yangsan, Korea

The pathophysiology of chronic liver disease and portal hypertension predisposes the patient with cirrhosis to complications related to surgical procedures. Invasive surgery is frequently required in the patient with cirrhosis and perioperative management is challenging. Although morbidity and mortality rates correlate with progression of portal hypertension in this population, Child-Pugh classification and the MELD score can provide some prediction of risk in counseling patients and their families. A multidisciplinary approach to these patients is critical for optimizing all phases of perioperative care, including planning, preoperative evaluation, intraoperative management, and postoperative recovery. Studies of larger cohorts with matched controls and randomized controlled trials are needed to improve our understanding and management of surgical risk in cirrhotic patients.

Keywords: Liver cirrhosis, Surgery, Risk

서 론
간경변증 환자에서 수술 위험성 평가
윤 기태
부산대학교 의과대학, 양산부산대학교 병원, 내과학학교실, 소화기내과

The pathophysiology of chronic liver disease and portal hypertension predisposes the patient with cirrhosis to complications related to surgical procedures. Invasive surgery is frequently required in the patient with cirrhosis and perioperative management is challenging. Although morbidity and mortality rates correlate with progression of portal hypertension in this population, Child-Pugh classification and the MELD score can provide some prediction of risk in counseling patients and their families. A multidisciplinary approach to these patients is critical for optimizing all phases of perioperative care, including planning, preoperative evaluation, intraoperative management, and postoperative recovery. Studies of larger cohorts with matched controls and randomized controlled trials are needed to improve our understanding and management of surgical risk in cirrhotic patients.

Keywords: Liver cirrhosis, Surgery, Risk

본 론
1. Child-Pugh Classification

수술 전 이환율과 사망률에 관한 평가에서 Child-Pugh 분류체계가 주로 이용되어 왔다. Child-Pugh 분류체계는 빌리루빈, 알부민, 프로트롬빈 시간, 복수 및 간성혼수의 정도에 의한 점수의 합으로 평가되고 있다. 이 분
류체계를 이용하여 간경변증 환자의 수술 후 사망률을 조사한 연구들에서 수술 후 30일 사망률을 Child-Pugh A 10%, Child-Pugh B 30%, Child-Pugh C 76~82%로 보고하고 있다. 현재 수술 전 협진에서 간경변증 환자의 수술 후 예후는 이와 같은 근거에 의하여 이루어지고 있다. 그러나 Child-Pugh 류체계는 간경변증 환자들의 예후를 예측하는 데 있어서 몇 가지 한계점이 가지고 있다. 첫째, 5개의 구성 요소 중 복수와 간성혼수 2가지 순위적인 요소로 객관적이지 못하며, 둘째, 모든 요소들이 가중치 없이 동일하게 취급되고 있고, 셋째, cut-off value가 통계적인 근거 없이 임의적으로 설정되었으며, 넷째, Child-Pugh 류체계는 세 가지 빈에 없는데 같은 등급 내의 환자들 간의 수술 성공률이 동등하다고 하더라도 같은 등급 내에서도 서로 다른 예후를 보일 수 있다는 점 등이 제기되어 있다.

2. ASA Physical Status Classification

ASA 분류체계는 1940년대 초부터 수술과 관련된 마취의 위험성 평가에 사용되어 왔다. 이 분류체계는 임상 환경에서 수술 결과와 대략적 상관관계가 있는 질병의 상태 수준을 나타내는 것으로 결과의 예측적으로 예측자라기로 보다는 질병의 상태의 중증정도로 간주할 수 있다. ASA I은 정상, ASA II는 경증 전신질환이 있는 환자, ASA III는 중증 전신질환이 있는 환자, ASA IV는 생명을 위협하는 전신질환이 있는 환자, ASA V는 단기생존이 가능한 환자, ASA VI는 뇌사상태의 환자로 정의된다. 이 분류체계는 다시 주관적인평가가 이루어질 수 있는 특성으로 관찰자간의 평가결과 일치성이 좋지 않을 수 있는 문제점이 있다. 또한 증상도 질환에 대한 분류가 없고, 경증 및 중증 질환에만 해당되는 분류만 있다. 이런 약점에도 불구하고 마취 영역에서 간경변증 환자에서 수술 위험 예측지표로 사용 및 연구되고 있다.

3. MELD Score

경경정맥 간내 문제단락술 (transjugular intrahepatic portosystemic shunt)을 시행하는 환자들의 예후를 예측하기 위해 개발된 model for endstage liver disease (MELD) 점수는 간이식 환자에서 장기 배정의 우선 순위를 결정하는 모델로 도입되었다. MELD는 혈청 빌리루빈 및 크레아티닌치와 프로트롬빈 시간의 국제표준화율 (international normalized ratio, INR)를 이용하여 계산할 수 있다. MELD 점수는 간이식을 대기하는 환자들의 단기 및 중기 사망률을 정확히 예측하는 것으로 알려져 있다. MELD 점수를 이용하여 간경변증 환자의 수술 후 사망률을 예측한 연구들이 보고된 바 있다. 수술 전 MELD 점수가 16점 미만인 환자는 16점 이상인 환자보다 수술 후 사망률이 낮았으며, 한 연구에서는 수술 후 사망률이 MELD 점수에 따라 선형 증가하는 것으로 나타났다. 140명의 수술을 받는 간경변증 환자를 대상으로 한 연구에서 MELD 점수가 30일 사망률을 예측할 수 있는 유용한 인자였으며 MELD 점수가 1점 올라갈 때마다 MELD 점수 1~10을 가진 환자는 1%, MELD 점수 11~20을 가진 환자는 2% 사망률이 증가하였고, 그 외의 대조군 연구에서도 MELD 점수가 CTP 점수에 비해 간경변증 환자들의 복강 내 수술 후 사망률을 예측하는 데 유용하다고 보고하였다. 심장 수술을 받는 간경변증 환자들 대상으로 한 연구에서는 MELD 점수 13점 이상이 나쁜 예후와 연관이 있다고 보고되었다. MELD 점수는 간절제술을 시행하는 환자들의 예후를 예측하는 데에도 매우 유용한 것으로 알려져 있다. MELD 점수는 Child-Pugh 점수와 달리 객관적인 변수들로 이루어져 있고, 중요도에 따라 변수들에 가중치를 두고 있으며, 임의적인 cut-off value를 사용하지 않고, MELD 점수가 1점 올라도 위험성이 바뀌지 않아 EXPRESS 적응이 훨씬 더 빠르게 적용할 수 있다. 따라서 최근에는 수술을 받는 간경변증 환자들의 예후 판정에 Child-Pugh 분류체계보다 MELD 분류체계를 이용하는 추세이다. 그러나, 복수 및 정맥류 출혈과 같이 심한 환경적 압박을 가지지 않는 환자에서는 MELD 점수 구성 요소인 복수유출 및 INR이 비교적 정상으로 유지되는 환자에서 MELD의 경우 수술 위험성을 충분히 반영하지 못할 수도 있으며 이와 같은 경우에는 Child-Pugh 분류체계가 더 유용한 도구가 될 수 있다.

결론

간경변증 환자들은 수술 후 이환율과 사망률이 높아 수술 전 평가에 보다 세심한 접근이 요구된다. 임상적 외과 수술이 계획된 간경변증 환자들에게 예후를 예측하는 것은 표준화되지 않았으며 전방향 연구의 시행을 통한
명확한 근거의 제시도 쉽지 않다. 그럼에도 Child-Pugh 분류체계와 MELD 점수는 환자와 보호자들의 수술 전 상담에 있어 유용한 예측 정보를 제공할 수 있으며, 이러한 접근은 수술 계획, 수술 중 관리 및 수술 후 복원의 모든 단계를 최적화하는데 중요하다. 간경변증 환자에서 수술 후 위험도를 조금 더 정확히 예측할 수 있는 지표에 대한 연구는 향후 더 필요하다.

References
Determination of Preoperative Liver Function and Extent of Resection

Bong-Wan Kim
Liver transplantation and Hepatobiliary Surgery, Ajou University Medical School, Suwon, Korea

It is necessary for the safe liver resection that the liver reserve function should be assessed accurately in the preoperative stage. There are many methods developed to assess the liver reserve using laboratory and/or radiological studies. General scoring methods such as Child-Pugh score or MELD score using a liver function tests correlates with incidence of the post-hepatectomy liver failure, however, unable to evaluate the liver reserve among the patients with low score and discriminate between normal liver and early cirrhosis. Drug clearance tests using indocyanine green (ICG) could overcome the weakness of the general scoring methods. ICG clearance tests reflects portal blood flow and the compliance of the liver. The ICG clearance test could provide credible global liver function, discriminate liver reserve between normal liver and early cirrhosis, and predict the safe range of the liver resection according to the clearance rates.

Radiological image study of the scintigraphy using 99mTc galactosyl human serum albumin (99mTc GSA) could provide liver regional function over the global liver function. Assessment of the regional liver function could be useful when the liver function is inhomogeneous, such as tumor thrombus in segmental/lobar portal vein or bile duct.

Current various methods for the assessment of the liver reserve could render the liver resection safer and expand the indication of the liver resection for the patients with borderline liver function.
HBV 감염에 의한 간경화 및 간세포암은 국내 전체 간이식 원인의 약 80% 를 차지하고 있으며, 이식 환자에서의 B형 간염 재발은 이식편의 소실을 유발시키고 생존율을 감소시키기 때문에 그 예방이 매우 중요하다. 간이식 후 적절한 예방요법을 시행하지 않는 경우 대체로 1개월 이내에 HBV에 재감염 되며 이로 인한 mortality rate 는 50% 이상에 달하는 것으로 알려져 있다.

1990년대 이후 HBV 재발 예방을 위해 lamivudine, adefovir, entecavir, tenofovir 등의 항바이러스제와 고용량 Hepatitis B immunoglobulin (B형 간염 면역글로불린, HBIG)을 장기간 투여하는 방법이 도입되면서 HBV의 재발률이 획기적으로 감소하였으며 이식 후 생존율이 역시 큰 폭으로 향상되었다.

현재 간이식 후 HBV 감염 예방을 위해 의료기관마다 다소의 차이는 있으나 HBIG과 항바이러스제의 병용 투여가 대부분의 기관에서 예방 요법의 근간으로 자리잡았다.

그러나 HBIG 투여의 경우 비용이 많이 들고 주사로 투여해야 하기 때문에 이로 인한 불편함 및 합병증 발생 가능성이 있다. 또한 최근 도입된 항바이러스제인 entecavir, tenofovir 등의 경우 높은 효능을 보여 여러 randomized study에서 HBIG 중단 후 항바이러스제 단독 투여 시에도 기존의 병용 투여 못함은 예방 효과가 있음을 보고되고 있어 이에 대한 관심이 높아지고 있다.

HBIG과 항바이러스제의 병용 투여가 도입된 이후 HBIG의 사용량 감소 및 중단을 위한 여러 노력들이 이루어졌는데 anti-HBV vaccination 도 그 중 하나이다. Active immunization 을 통해 endogenous HBsAb를 형성하여 HBIG 투여 중단의 근거를 마련할 수 있다는 이론적 배경에도 불구하고 적절한 vaccination 스케줄, 면역억제 상태에서의 효과판정 기준 등은 아직까지도 확립되어 있지 않다.
Common Concerns

Optimal Hepatitis C Virus Treatment Strategy for Patients Waiting for Liver Transplantation

In Hee Kim

Department of Internal Medicine, Chonbuk National University Medical School, Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Jeonju, Jeonbuk, Korea

Introduction

Chronic hepatitis C virus (HCV) infection-related advanced liver cirrhosis and hepatocellular carcinoma (HCC) are leading indications for liver transplantation (LT), accounting for 10% to 50% in Western countries and approximately 5% in Korea as causes of LT. However, HCV recurrence after transplantation is inevitable if it is not fully eradicated prior to transplantation. HCV reinfection can cause significant damage to the liver graft resulting in poor patient survival.

The advent of safe and highly effective, direct-acting antiviral agents (DAAs) has had great implications in the field of HCV transplantation, and changed the management of both patients on the waiting list and those with HCV graft re-infection after LT. Recent large cohort studies reported that HCV-related disease burden is decreasing in the DAA era with decreasing need for LT listing, wait-list mortality, need for LT, and post-transplant morality. The present review discusses the optimal DAA-based hepatitis C treatment strategy for patients on the waiting for LT.

DAAs treatment in pre-LT phase

The goals for treating HCV infection before LT can be improvement of liver function to avoid liver transplantation, stabilization of liver function to reduce waitlist mortality, prevention of HCV re-infection of the graft after LT.

1. DAAs in LT candidates

DAAs should be used with caution in LT candidates with severely impaired liver function (Child-Turcotte-Pugh [CTP] class B and C) or with severe renal dysfunction (estimated glomerular filtration rate [eGFR] <30 ml/min), as both conditions may affect the metabolism of some DAAs. Sofosbuvir (SOF), ledipasvir (LDV), velpatasvir (VEL),
and daclatasvir (DCV) can be used in patients with cirrhosis without dose adjustments, regardless of liver impairment. However, the protease-inhibitor containing regimens, such as 3D (Paritaprevir/r, ombitasvir, dasabuvir), 2D (Paritaprevir/r, ombitasvir), simprevir (SIM), grazoprevir/elbasvir (GZR/EBR), glecaprevir/pibrentasvir (GLE/PIB), sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX), can be safely used only in patients with compensated cirrhosis (CTP class A); but, they should not be recommended in patients with decompensated cirrhosis (CTP class B and C). In cases of pre-LT eGFR below 30 ml/min, SOF should be preferably planned after LT. Drug-drug interactions (DDI) between a specific DAA and any other co-administered drug, should be carefully evaluated when planning any antiviral regimen. Possible DDI should be checked on international websites (www.hep-druginteractions.org/) or discussed with a clinical pharmacologist.

2.DAA treatment in patients listed for decompensated cirrhosis

Sustained virologic response (SVR) and improvement of liver function

In the US-based SOLAR-1 trial, 108 patients with genotype 1 or 4 infection and decompensated cirrhosis (59 CTP class B and 49 CTP class C) were randomly assigned to 12 weeks or 24 weeks of the daily fixed-dose combination of LDV (90 mg)/SOF (400 mg) plus ribavirin (RBV) (initial dose of 600 mg, increased as tolerated). The SVR12 rate was 87% in CTP class B patients who received 12 weeks of treatment and 89% in those who received 24 weeks of treatment. Similarly, the SVR12 rates were 86% and 87%, respectively, with 12 weeks and 24 weeks of antiviral therapy in the CTP class C patients. In the majority of participants with CTP class B or C disease, the MELD and CTP scores decreased between the baseline and post-treatment week 4. The frequency of serious adverse events increased with treatment duration in both the CTP class B group (10% week 12; 34% week 24) and the CTP class C group (26% week 12; 42% week 24). Most of the serious adverse events were related to RBV. Therapy was discontinued in 7% of CTP class B patients and 8% of CTP class C patients in the 24-week treatment arm.

In the multicenter (Europe, Canada, Australia, and New Zealand) SOLAR-2 trial, 160 genotype 1- or 4-infected patients with decompensated cirrhosis were randomly assigned to the same combination of LDV/SOF plus RBV (initial dose of 600 mg, increased as tolerated) for 12 weeks or 24 weeks. The SVR12 rate was achieved in 85% after 12 weeks of treatment (90% CTP class B, 75% CTP class C) and 90% after 24 weeks of treatment (98% CTP class B, 77% CTP class C). The baseline CTP and MELD scores were improved in the majority of patients receiving treatment; however, some participants experienced worsening hepatic function. Among non-transplanted patients whose MELD score was ≥15 at baseline, 80% (20/25) had a MELD score <15 at SVR12. Among those with a MELD score <15 at baseline, 4% (2/56) had a MELD score ≥15 at SVR12.

The ALLY-1 trial evaluated the efficacy and safety of 12 weeks of daily DCV (60 mg) and SOF (400 mg) plus RBV (600 mg with possible escalation to 1000 mg as tolerated) among patients with advanced cirrhosis (n=60, CTP class A/B/C 20%/53%/27%, G1 75%). In patients with advanced cirrhosis, SVR12 rates by genotype were as follows: 82% (37/45) genotype 1, 80% (4/5) genotype 2, 83% (5/6) genotype 3, and 100% (4/4) genotype 4. The SVR12 rates by severity of cirrhosis were 92% among those with CTP class A cirrhosis, 94% among those with class B, and 56% among those with class C cirrhosis.

In a real-world study that took place in the United Kingdom, patients with decompensated cirrhosis infected with HCV genotype 1 were treated with LDV/SOF, or with DCV and SOF, for 12 weeks with or without RBV. The SVR12 rates were as follows: 85% (11/13) after 12 weeks of LDV/SOF without RBV; 91% (136/149) after 12 weeks of LDV/SOF with RBV; 50% (2/4) after 12 weeks of DCV and SOF without RBV; and 88% (30/34) after 12 weeks of DCV and SOF with RBV. However, in patients with decompensated cirrhosis infected with HCV genotype 3, the SVR12 rates were as follows: 60% (3/5) after 12 weeks of DCV and SOF without RBV, and 71%
(75/105) after 12 weeks of DCV and SOF with RBV. Approximately one-third of patients saw an improvement in their MELD scores; one-third had no change; and one-third suffered deteriorating liver function 12 weeks after treatment. Improvement in the MELD score was more frequent in treated patients than in untreated patients. Longer-term follow-up of the same group of patients confirmed that treatment was clinically beneficial in patients with advanced liver disease.

In the ASTRAL-4 study, 267 patients with genotype 1, 2, 3, 4, or 6 infection and decompensated cirrhosis (CTP class B) were randomly assigned (1:1:1 ratio) to one of the following groups: 12 weeks of daily fixed-dose combination SOF (400 mg)/VEL (100 mg); 12 weeks of SOF/VEL plus weight-based RBV (1000 mg/d, weight <75 kg; 1200 mg/d, weight ≥75 kg); or 24 weeks of SOF/VEL. Among patients with genotype 1 infection, the SVR12 rates were 88%, 96%, and 92%, respectively (88%, 94% and 93% in patients with genotype 1a infection; 89%, 100% and 88% in patients with genotype 1b infection). The SVR12 rates were 100%, 100% and 75% in patients with genotype 2 infection; 50%, 85%, and 50% in patients with genotype 3 infection; 100%, 100%, and 100% in patients with genotype 4 infection. At post-treatment week 12, 42% of patients had an improvement in the CTP score, 42% had no change, and 11% had an increased CTP score. Of the patients with a baseline MELD score <15, 51% had an improved MELD score at week 12 post-treatment, 22% had no change in their MELD score, and 27% had a worse MELD score. Of the patients who had a baseline MELD score ≥15, 81% had an improved MELD score, 11% had no change in their MELD score, and 7% (2/27) had a worse MELD score. Importantly, data are almost non-existent for patients with the most advanced forms of disease (CTP score >12 or MELD score >20), who were excluded from the studies.

Effects on post-LT recurrence

The effects of pre-LT DAA treatment on post-LT recurrence were explored in a study in which 61 HCC patients with CTP class A cirrhosis were treated with SOF and RBV. All patients were infected with genotype 1 or 4 and were treated for either 48 weeks or until LT. The “on treatment” response was very high (93% had HCV RNA less than the lower level of quantification (LLOQ) at week 4) and post-LT SVR12 was achieved in 70% of treated patients. In the same study, a “post hoc” analysis showed a dramatic post-LT SVR12 of 96% in the subgroup of 29 patients that had remained HCV RNA negative for at least 30 days before LT. Indeed, of the 29 patients who had HCV RNA below LLOQ for at least 30 days, only one (3%) suffered HCV recurrence after LT compared with 9 out of 14 patients (64%) with HCV RNA below LLOQ for less than 30 days. These results suggest that the removal of the infected liver, after achieving viral clearance for a minimum of 1 month, is adequate for preventing HCV recurrence after LT.

Impact on de-listing in LT candidates

Several studies assessed the impact of DAA treatment prior to LT on delisting of LT candidates. In a multicenter European real world study of patients receiving DAA treatment, 40% (41/103) were transplanted, whereas only 20% (21/103) were delisted and an additional 13% (13/103) were put on hold (inactivated) after a median period of 60 weeks. The probability of being delisted was very high in patients with a MELD score <16 (about 35%) and minimal in those with a MELD score >20 (about 5%). Baseline MELD categories (MELD 16–20: HR = 0.120, P=0.0005; MELD >20: HR = 0.042, p <0.0001), continuous 12-week delta MELD (HR = 1.349; p <0.0001), and continuous 12-week delta albumin (HR = 0.307; P=0.0069) were independent predictors of inactivation on waiting list and subsequent delisting. Among patients with a MELD score <16, the probability of inactivation was 27%, 86%, and 100% in patients with 12-week delta MELD <2, 2 to 4, and >4, respectively. In contrast, in patients with a baseline MELD score ranging from 16 to 20, the probability of inactivation was 11% in patients with 12-week delta MELD <2, but 17% and 43% in patients with 12-week delta MELD of 2–4 or 4, respectively. Eventually,
among patients with a baseline MELD score >20, inactivation was observed only in 2 patients with a 12-week delta MELD >4. In a similar Spanish study, 24% (29/122) of patients were delisted after DAA-based therapy. No patients with a baseline MELD score >20 were delisted.

**Optimal timing for pre-LT DAA treatment**
To establish whether pre-LT DAA treatment is justified, the following factors should be considered: 1) The risk of death on the waiting list, which is proportional to the MELD score; 2) the possibility of clinical improvement after DAA treatment, which may favor the delisting of some patients, typically those with low MELD scores; 3) the awareness that a mild improvement in MELD score after DAA may not be enough for delisting and may work as a disadvantage for patients that lose priority on the waiting list (MELD purgatory effect in patients with high MELD score); 4) the cost-effectiveness considerations; and 5) the potential side effects as some case series show liver failure during DAA±RBV. Statements made by the European Liver and Intestine Transplant Association (ELITA) recommends the following with respect to DAA treatment in LT candidates. First, patients with baseline a MELD score <16 (typically CTP class B) have a high chance (35%) of being delisted because of clinical improvement, and therefore should be treated while listed. Second, patients with baseline MELD scores between 16 and 20 (mostly CTP class C) have a chance of being delisted due to clinical improvement of about 12%. They should be started on DAAs while listed, and possible clinical improvements should be assessed after 12 weeks of therapy. Patients showing a significant improvement of MELD score >3 points and albumin >0.5 g/dl after 12 weeks on DAAs should be considered for possible delisting during the follow-up period. Third, patients with baseline MELD scores between 21 and 25 (typically advanced CTP class C) have limited MELD improvement. For these patients, a case-by-case multidisciplinary decision is advised. Fourth, patients with high MELD scores >25 are not recommended to undergo pre-LT DAA treatment; however, post-LT treatment is preferable due to their poor prognosis, significant risk of death pre- or post-LT, unknown probability of improvement, potential DAA toxicity, and rapid access to LT. A US study developed microsimulation model from LT integrated data and suggested that treating HCV before, instead of after, LT would only increase life expectancy in patients with a MELD score ≤23–27, depending on the United Network for Organ Sharing region. In a recent study assessing the optimal timing of hepatitis C therapy in LT eligible patients with cost-effectiveness analysis, pre-LT treatment was reported to be cost-effective for patients without HCC with a MELD score ≤20, while antiviral treatment after LT was cost-effective in patients with a MELD score >20. Overall, patients with decompensated cirrhosis and MELD score <20 on the LT waiting list should be considered for DAA treatment. However, patients with a MEDL score >20 may be less likely to see improvement and may be better to undergo transplantation than DAA treatment.

3. **DAA treatment in patients listed for HCC**
In patients with HCC, without cirrhosis or with compensated cirrhosis, who have an indication for LT, the ideal timing for antiviral therapy (before or after LT) remains controversial. Lower SVR rates were reported in patients with HCC treated with DAAs than in patients without HCC or in patients with HCC treated after LT (74% vs. 91% and 94%, respectively). Post-LT treatment of HCV was reported to be cost-effective in patients with HCC. The 1-year rate of removal from the LT waiting list due to tumor progression is estimated to be up to 10% in centers following the Milan criteria, and up to 20% in those following the extended criteria. Similarly, the risk of death from HCC recurrence after LT is as high as 10% in centers adopting the Milan criteria, and up to 20% in those adopting the extended criteria. The response to therapeutic interventions for HCC while the patient is on the waiting list further affects the prognosis either pre- or post-LT. These competing risks should be considered to avoid futile DAA treatment. This scenario is further complicated by the previous alarming reports regarding a possible increased risk of HCC recurrence after DAA treatment. However, prospective studies and systematic review
did not show higher risk of HCC recurrence after DAAs in patients with successfully treated HCC.\textsuperscript{18-21} In addition, a recent study from the Italian Liver Cancer Group suggested that DAAs significantly improved overall survival when compared with no DAA treatment in patients with HCV-related cirrhosis as well as in those who underwent successful previous treatment of early HCC.\textsuperscript{22} Thus, despite conflicting data, DAAs are considered as safe and do not increase the risk of dropout for tumor progression in patients with HCC listed for LT. According to the recommendations from ELITA statements, pre-LT DAA treatment should be restricted to those with the following features: 1) a low risk of post-transplant HCC recurrence, regardless of the model for assessing the risk (i.e. Milan criteria, alpha-fetoprotein model or other predictive models of recurrence at listing); 2) no signs of HCC progression while on HCC bridging therapy, and 3) expected waiting time $>3$ months.\textsuperscript{12}

**DAAs treatment in Post–transplant Phase**

HCV infection can be treated post-LT either soon after the transplant, taking advantage of the removal of the infected native liver, or at the time of disease recurrence, carried out in the past. In either case, some DAAs have a limited use due to their DDI with various immunosuppressants (IS), as well as the many other drugs often prescribed to LT recipients.

1. **DAAs in LT recipients**

   LT recipients should take life-long IS, and the possible DDI between DAAs and IS must be checked. DCV+SOF, LDV/SOF, and SOF/VEL have no significant DDIs with any IS and antimitabolites. Regimens containing protease inhibitors, such as 2D and 3D combinations, strongly interact with all major IS. SIM strongly affects the metabolism of cyclosporine A (CsA) and, to a lesser extent, of tacrolimus (Tac) and mTOR inhibitors via CYP3A4 inhibition. A 40%-50% increase in the Tac levels is to be expected during co-administration with GZR, while a 15-fold increase in GZR AUC and a 2-fold increase in EBR AUC is expected if co-administered with CsA. A 5-fold increase in GLE AUC with higher doses (400 mg) of CSA and 9.4-fold increase in VOX AUC with CsA are expected. Therefore, SIM, GZR, EBR, and VOX should not be co-administered with CsA. Monitoring the blood levels is required when SIM, GZR, and EBR are combined with Tac or mTOR inhibitors. Two-dimensional (2D) and 3-dimensional (3D) combinations require monitoring of all major IS. GLE/PIB should not be recommended in patients requiring stable CsA doses $>100$ mg/day. Finally, DCV+SOF, LDV/SOF, SOF/VEL should be the preferred regimens after LT due to no or minimal DDI. Any other drug co-administered with DAAs after LT should be checked for possible DDI, such as antifungal agents, antibiotics, cardiovascular drugs, CNS drugs, recreational drugs, and even hormonal treatments.

   Renal dysfunction is another common problem after LT, which limits the use of SOF. Safe and effective doses of sofosbuvir in persons with an eGFR $<30$ mL/min have not been established and is out of the license recommendations. However, in the TARGET 2.0 real-world cohort study, progressive deterioration of renal function and renal symptoms were reported in patients with severe renal impairment receiving a SOF-based regimen, although efficacy was comparable to that observed in patients without renal impairment.\textsuperscript{23} Thus, SOF-free regimens should be preferred in patients with severe renal impairment. If there is no other choice beside a SOF-based regimen, close monitoring is required, and treatment should be rapidly interrupted if renal function deteriorates. Although tolerability and efficacy of GZR/EBR are satisfactory in patients with renal insufficiency, their use is not recommended after LT due to major DDI with many IS. This is also true for the 3D combination.

   The issue of increased risk of rejection following HCV clearance is also a major consideration. Close monitoring of calcineurin inhibitors/mTOR is recommended, particularly at the end of DAA therapy, when the cessation of DDIs and the improved metabolic capacity of the liver may alter the exposure to various IS.
2.D AAs treatment in post-LT recurrence

SVR

In the SOLAR-1 trial, transplant recipients with HCV genotype 1 or 4 recurrence were treated with the fixed-dose combination of LDV (90mg)/SOF (400 mg) for 12 or 24 weeks with RBV. The RBV dose was weight based for patients without cirrhosis or with compensated cirrhosis (1000 mg [<75 kg] to 1200 mg [= 75 kg]). For patients with CTP class B or C cirrhosis, RBV was initiated at 600 mg/d, followed by dose escalation as tolerated. In patients treated for 12 weeks with RBV, the SVR12 rates were 96% (53/55) in those without cirrhosis and 96% (25/26), 85% (22/26), and 60% (3/5) in those with CTP class A, B, and C cirrhosis, respectively. The SVR12 rates were not higher in patients treated for 24 weeks with RBV: 98% (55/56), 96% (24/25), 88% (23/26), and 75% (3/4), respectively. Similar results were reported in the SOLAR-2 study in patients with genotype 1 receiving the same treatment regimens. In patients treated for 12 weeks with RBV, the SVR12 rates were 93% (42/45) in patients without cirrhosis and 100% (30/30), 95% (19/20), and 50% (1/2) in those with CTP class A, B, and C cirrhosis, respectively. In patients treated for 24 weeks, the SVR12 rates were: 100% (44/44), 96% (27/28), 100% (20/20), and 80% (4/5), respectively. Twenty-five of the 27 patients infected with genotype 4 (93%) achieved SVR12.

An observational cohort HCV-TARGET study assessed the safety and efficacy of DAA regimens in liver or kidney recipients from real-world data. Among the 279 participants treated with LDV/SOF for 12 weeks or 24 weeks, the SVR rates were 97% (152/157) in those with RBV and 95% (116/122) in patients without RBV. The rate of therapy discontinuation due to an adverse event was 1.3%, highlighting the safety of the drug combination. Acute graft rejection occurred during or after cessation of therapy in 1.4% of patients, suggesting the need to monitor IS levels throughout the DAA therapy period.

The ALLY-1 trial evaluated the efficacy and safety of a 12-week course of daily DCV (60 mg) and SOF (400 mg) plus RBV (600 mg with possible escalation to 1000 mg as tolerated) among 60 patients with cirrhosis (CTP class A, B, or C) and 53 patients with recurrent HCV infection after LT. Seventy-six percent (86/113) of participants had genotype 1 infection, including 77% (41/53) in the post-transplantation group. The SVR12 rate was 94% (50/53) among those with recurrent HCV infection post transplantation.

In another study, LT recipients with HCV recurrence were treated with the fixed-dose combination of SOF/VEL for 12 weeks without RBV. The global SVR12 rate was 96% (76/79; 2 relapses). By genotype, SVR12 rates were 95% (genotype 1), 100% (genotype 2), 97% (genotype 3), and 100% (genotype 4). There was relapse in one genotype 1 patient, out of a total of 15, and one genotype 3 patient, out of 35.

In the MAGELLAN-2 trial, 80 LT recipients and 20 kidney transplant recipients without cirrhosis were treated with the 12-week course of the daily fixed-dose combination of GLE (300 mg)/PIB (120 mg). All genotypes were represented, except genotype 5; 57% of participants had genotype 1 infection and 24% had genotype 3 infection. Any stable immunosuppressive regimen was allowed, except CsA >100 mg/d and prednisone >10 mg/d. SVR was achieved in 98% (98/100) of patients with no virologic breakthroughs on treatment and 1 post-treatment relapse. This regimen offers a RBV-free option for noncirrhotic liver or kidney transplant recipients. Although GLE/PIB has not been studied in transplant recipients with compensated cirrhosis, this regimen may be considered in patients who are RBV ineligible. Due to the frequency of DDIs and the need for IS dose adjustments, treatment regimens, including a protease inhibitor, are not optimal for post-LT HCV treatment. However, in LT-recipients with impaired kidney function, the combination of GLE/PIB for 12 weeks is an alternative to SOF-based regimens.

Optimal timing for DDA therapy after LT

In the IFN/RBV era, pre-emptive therapy was found to be ineffective and difficult to manage, due to severe hematological side effects and risk of rejection in the early post-LT period. Given the far better risk-benefit ratio of
DAA therapy, those principles of management can be reconsidered. The results from phase 3 studies show that excellent SVR rates can be achieved in post-transplant patients with HCV-related chronic hepatitis and compensated cirrhosis; however, the SVR rates are 10% to 30% lower in patients with decompensated cirrhosis compared with those without decompensation. Although very early DAA-based pre-emptive therapy may be an attractive option to manage HCV recurrence, no large data are currently available on the efficacy and safety of this approach. Of note, in the very early post-transplant phase, the optimal use of DAAs may be hampered by reduced postoperative liver function, impaired renal function, and DDIs. At present, pre-emptive DAA therapy cannot be recommended on a routine basis. DAA treatment of HCV recurrence should be initiated early after LT, ideally as early as patients become stabilized (generally after the first 3 months post-transplant), because the SVR rates diminish in patients with advanced post-transplant liver disease.

3. HCV positive donor in DAAs era

The use of HCV-positive liver or kidney grafts in HCV-positive recipients has been encouraged by healthcare professionals, based on the fact that 5-year liver or kidney graft function is similar to that observed with organs from HCV-negative donors.27, 28 Yet HCV-positive organs have remained under-used due to a reluctance on the part of healthcare professionals. Given the scarcity of donated organs and the frequency of death on the waiting list, strategies that could improve the available supply of high-quality liver grafts are severely needed. DAA regimens have proved to be highly effective to treat HCV, even in the setting of post-transplantation. The question arises as to whether transplant communities should consider the utilization of HCV-positive donors into HCV-negative recipients.29 The transplantation from HCV-positive donors into HCV-negative recipients has both advantages and disadvantages. Advantages include increase pool of currently available donors, decrease wait-time mortality for very sick recipients (FHF, high MELD >30), potentially younger donors without other comorbidities, highly successful DAA regimens, as well as similar long-term graft and patient outcome than HCV-negative donors. Whereas, disadvantages include 100% risk of transmission of HCV for recipients, high cost of DAA, limited access to DAA regimens, requirement for preapproval by drug companies or insurance companies, possible interaction between DAA regimens and immunosuppression, as well as ethical/society barrier. The advancement in the high pan genotypic efficacy of DAA regimens may render HCV-positive liver grafts safer, extending the use of such grafts even in HCV-negative recipients, and ultimately enabling a substantial expansion of the donor pool. Recent pilot studies showed that kidney transplantation from HCV-positive donors into HCV-negative recipients, followed by the use of DAAs, can provide potentially excellent allograft function with a cure of HCV infection.30, 31 The post-DAA era has seen increased utilization of HCV-viremic donor livers, including HCV-viremic livers into HCV-negative recipients. Early graft outcomes are similar to those of HCV-negative recipients.32, 33 These results support the utilization of HCV-viremic organs in selected recipients, both with and without HCV infection. However, the potential to induce an infection raises ethical concerns and requires a rigorous process of obtaining informed consent from potential recipients.

Conclusions

The recent advent of DAAs has dramatically increased the chances of curative treatment for the transplant population. As more HCV patients achieve cure with DAA regimens, the rate of LT wait-listing for HCV complicated by decompensated cirrhosis has already been on a decline. However, the timing for treatment of the infection remains controversial; the question remains, whether to pursue HCV eradication before LT to improve liver function, delist some patients and prevent graft infection, or whether to pursue treatment as early as possible after LT, rather than waiting for hepatitis C recurrence. Patients with decompensated cirrhosis and MELD score <20 on the LT
waiting list should be considered for DAA treatment. However, patients with MEDL score >20 may be less likely to improve and might be better served by transplantation than DAA treatment. DAA treatment of HCV recurrence should be initiated early after LT, ideally as early as possible when the patient is stabilized. DAAs should be used with caution in LT candidates or recipients with severely impaired liver function (CTP class B and C) or with severe renal dysfunction (eGFR <30 ml/min), as both conditions may affect the metabolism of some DAAs. In LT recipients, the potential DDI between DAAs and IS should also be verified. Moreover, in the DAA era, the use of HCV-positive donors may represent a potential approach to safely expanding the donor pool.

References


Joint Symposium 1

Unresolved Issues in HCC: Medical and Interventional Radiology

Chairs:
Yun Hwan Kim (Korea Univ.)
Jaeseok Hwang (Keimyung Univ.)
Adjuvant Therapy after Curative Treatment: Enough or Still Lacking?

Su Jong Yu, Yun Bin Lee, Eun Ju Cho, Jeong-Hoon Lee, Yoon Jun Kim, Jung-Hwan Yoon
Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea

Hepatocellular carcinoma (HCC) is a common malignancy in the world. Although resection and various loco-regional therapies can achieve eradication or complete ablation of early stage HCC, HCC recurrence after curative treatments is still common. Although candidates for medical ablation usually exhibit compensated hepatic functional status, the frequent recurrence of HCC after successful ablation contributes to short survival. Therefore, attempts to prevent HCC recurrence are essential to prolong survival. Efforts in preventing HCC recurrence after curative therapies include prevention of early recurrence by improving liver immunity and eliminating microscopic tumor foci or micro-metastases, and prevention of late recurrence from multi-centric carcinogenesis by reducing the hepatitis activity and using antiviral therapies based on viral suppression/eradication. However, sorafenib, a tyrosine kinase inhibitor, was not an effective intervention in the adjuvant setting for HCC following resection or ablation in a phase 3, double-blind, placebo-controlled study (STORM). In recent clinical trials, adjuvant cytokine-induced killer (CIK) cell-based immunotherapy increased progression free- and overall survival after curative treatment of HCC. More recently, phase 3 randomized placebo controlled clinical trials to examine the recurrence-preventing effect of immunotherapies including immune checkpoint inhibitors (ICIs) after curative treatment in patients with HCC who are at high risk of recurrence after curative hepatic resection or ablation are in progress (nivolumab, NCT03383458; durvalumab monotherapy or in combination with bevacizumab, NCT03847428; and pembrolizumab, NCT03867084). Treatments to prevent recurrence as well as early detection and early curative treatment are extremely important to improve the prognosis of patients with HCC. Thus, further research on this issue should be carried out.
**Direct Acting Antiviral and HCC in Chronic Hepatitis C: Friend or Foe?**

**Hyung Joon Kim**

Department of Internal Medicine, Chung Ang University Hospital, Korea

만성 C형 간염에서 직접 작용 항바이러스약제와 간세포암종 : 친구 혹은 적?

김 형 준
중앙대학교병원 내과학과

---

**Introduction**

Although several robust scientific evidences sustain the beneficial role of SVR after interferon therapy in the natural history of cirrhosis with a decreased incidence of Hepatocellular Carcinoma (HCC), currently a hot debate about the impact of DAAs on HCC development animates the scientific community. In spring 2016 this topic became particularly hot for the publication of two papers suggesting a potential increase of HCC occurrence and recurrence rates in patients undergoing DAA schedules. In addition to DAAs not offering IFN’s direct antiproliferative property, it was hypothesized that DAAs may also adversely impact immune surveillance, resulting in higher HCC risk. Since those publications, more than 100 papers, letters or communications have been published until now. The purpose of this review is to describe the interaction between DAA therapy for HCV and HCC incidence, HCC recurrence, and DAA efficacy.

**Risk of Incident de novo Hepatocellular Carcinoma After Direct-Acting Antiviral Agent Treatment**

In studies included more than 30,000 HCV patients, overall, SVR resulted in an approximately 70% reduction in HCC risk; this effect was evident early (within 3–6 months) and increased over time. Patients who were treated but failed to achieve SVR with DAA remained at high risk for HCC. The relative benefit of SVR persisted after accounting for demographic and clinical differences between patients approximately 70% reduction in HCC risk; this effect was evident early (within 3–6 months) and increased over time. Patients who were treated but failed to achieve SVR with DAA remained at high risk for HCC.

In a retrospective cohort study of more than 60,000 US Department of Veterans Affairs (VA) patients with chronic HCV, DAA recipients tended to be older than IFN recipients, were more likely to have cirrhosis, and were more likely to have comorbid conditions, such as diabetes and alcohol abuse, that elevate the risk for HCC. After adjusting for these confounders in multivariate analysis, the risks for HCC after DAA and IFN treatments were no different (adjusted hazard ratio [aHR], 1.12; 95% CI, 0.95-1.32). Other studies comparing DAA- and IFN-treated patients have come to similar conclusions. Large cohort studies also confirm that patients with DAA-induced SVR have a significantly lower risk for HCC compared with treatment failure or no treatment. A study of more than 20,000 VA patients found that DAA recipients who achieved SVR had a more than 70% lower risk for HCC.
compared with nonresponders (aHR, 0.28; 95% CI, 0.22-0.36).

**Risk of Hepatocellular Carcinoma Recurrence After Direct-Acting Antiviral Agent Treatment**

Meta-analyses show that IFN-based antiviral therapy after curative HCC treatment reduces the likelihood of cancer recurrence and improves survival. Although data have demonstrated decreased risk of incident HCC after DAA therapy in patients with HCV cirrhosis, there continues to be debate about the risk and aggressiveness of HCC recurrence after DAA therapy in patients with a history of HCC. The first such study included 58 patients with previously treated HCC, of whom 16 (27.8%) experienced recurrent tumor after a median follow-up of 6 months from DAA initiation. A simultaneous publication reported HCC recurrence in 17/59 patients (28.8%). These recurrence rates were alarmingly high compared with historic controls, and some recurrences appeared to be temporally associated with DAA exposure. The available data are conflicting, and the published studies show different and relevant methodological limitations: heterogenous cohorts, potential misclassification of HCC, the absence of an adequate control group, short follow-up time and different length of follow-up. There are no conclusive data that DAA therapy is associated with increased or decreased risk, differential time to recurrence, or aggressiveness of recurrent HCC in patients with complete response to HCC therapy.

**Timing of Direct-Acting Antiviral Agent Treatment After Hepatocellular Carcinoma Complete Response**

One of the most consistent correlates for early recurrence is the interval between HCC complete response and DAA initiation, with shorter intervals being associated with higher risk of recurrence. Reig and colleagues found higher recurrence (41% vs 23%) in patients treated within 4 months of HCC complete response. DAA therapy should not be withheld from patients with complete response to HCC therapy; however, DAA therapy can be deferred 4–6 months to confirm response to HCC therapy. Patients with complete response to HCC therapy who are treated with DAAs have a continued risk of HCC recurrence and require HCC surveillance, which should be conducted indeﬁnitely with dynamic contrast-enhanced computed tomography or magnetic resonance imaging every 3–6 months.

**Conclusion**

DAAs dramatically enhanced our ability to cure chronic HCV and prevent its downstream complications. Several large cohort studies demonstrate that DAA-induced SVR reduces the risk for de novo HCC. However, the residual risk for HCC after SVR means that surveillance is still required for patients with advanced fibrosis and cirrhosis. Additional well-designed studies are needed to determine the consequences of DAA therapy in patients with previously treated HCC, although the initial concern that DAAs increase recurrence risk has generally not been borne out in subsequent studies.
How to Overcome Long-Term Decline in Survival of HCC Patients Treated with Ablation

Shuichiro Shiina
Department of Gastroenterology, Juntendo University, Japan

Image-guided percutaneous ablation is considered best in the treatment of early-stage hepatocellular carcinoma (HCC). Ablation is potentially curative, minimally invasive, and easily repeatable for recurrence. In our early study, we performed 2,982 RFA treatments on 1,170 primary HCC patients and the 1-, 3-, 5-, 7-, and 10-year survival rates of all 1,170 HCC patients were 96.6%, 80.5%, 60.2%, 45.1%, and 27.3%, respectively (Shiina S, et al. Am J Gastroenterol 2012). Multivariate analysis demonstrated that age, anti-HCV, Child-Pugh class, tumor size, tumor number, serum DCP, and serum AFP-L3 were significantly related to survival. A recent nationwide survey in Japan showed long-term survivals were similar between surgical resection and RFA. A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small HCC (SURF trial) recently demonstrated that the 3-year RFS of patients underwent surgery and RFA was 49.8%, 47.7%, respectively (hazard ration [HR] 0.96, 95% CI 0.72-1.28; \(P=0.793\)).

It is true that survival of HCC patients declines gradually after ablation. Even in small HCC, survival becomes lower in the long run. However, this is not specific to ablation. The situation is almost the same in surgical resection. In liver cancer, a survival declines considerably even after 5 years while in stomach cancer, colorectal cancer and many other cancers, recurrence and death are rare after 5 years. According to the cancer survival rates at Japanese Association of Clinical Cancer Centers, in liver cancer, 5- and 10-year survival rates were 32.2%, and 15.3%, respectively while in stomach cancer, they were 70.9%, and 69.0%, respectively and in colorectal cancer, they were 72.1%, and 69.8%, respectively.

There are two main reasons why the survival declines. One is frequent recurrence of HCC. It is due to micro-metastasis, metachronous multicentric carcinogenesis, and local tumor progression. The other is gradual deterioration of liver function. It is due to loss of liver tissue by treatments and advance of underlying liver cirrhosis.

In order to overcome the long-term decline in survival, to improve outcomes of ablation is most important. Various innovations have been introduced in the field of ablation, such as a dedicated US transducer for puncture, a dedicated procedure bed, multimodality fusion imaging and US contrast agents. New-generation MWA systems incorporating antenna cooling and high-power generation have been receiving considerable attention. New-generation MWA can create a more predictable ablation zone, a larger ablation volume in a shorter procedure time. However, MWA antenna has some problems; it is difficult to insert into the liver. It cannot be seen clearly by US. It is easily broken. Further studies are needed from viewpoints of adverse events and long-term survival.

Incidentally, ablation is highly operator-dependent. Its skills and outcomes are very different from operator to operator. In order to disseminate skills and know-hows for ablation, we have held domestic training programs 12 times, with a total of 201 participants. We also have held international training programs six times, which were successfully completed with 91 participants in total. Programs are composed of comprehensive lectures, live demonstrations and case studies. In the live demonstrations, RFA and new-generation MWA are performed on a
wide variety of cases. In the case studies, difficult to ablate cases from participants’ hospitals are presented and discussed. Our programs may be useful to provide opportunities to understand basic concepts and learn essential technical tips in ablation.

Sophisticated ablation, which is potentially curative, minimally invasive and easily repeatable for recurrence, would be superior to conventional surgery in some selected cases.

Another important way to improve long-term outcomes in HCC is to treat underlying liver disease. It may suppress recurrence of HCC and prevent deterioration of liver function. In our institution, the B-HCC prognosis improved dramatically ($P<0.001$) over time, whereas the prognosis of C-HCC improved moderately ($P=0.01$). The difference in antiviral therapy feasibility may explain the difference in the survival improvement in the two groups. Compared with NA, which can be administrated even to B-HCC patients with impaired hepatic function without serious adverse effects, IFN-based therapies were associated with a higher adverse effect rate and a lower SVR rate, especially with advanced liver fibrosis. Incidentally, the 5-year survival rate of C-HCC patients treated with IFN-based therapy during HCC treatment was actually 87.1% in our institution. Introduction of direct acting antivirals (DAA) results in sustained virological response (SVR) rates of >90% in treated patients whatever the stage of liver fibrosis with an excellent safety profile. In the era of DAA which can eradicate HCV in more than 90% of patients, the C-HCC prognosis will improve significantly.
KAHBPS-KLTS-KLCA Joint Symposium 2

Unresolved Issues in HCC: Surgical and Radiation Oncology

Chairs:
Hee Jung Wang (Ajou Univ.)
Jinsil Seong (Yonsei Univ.)
Will Laparoscopic Approach Be Almighty Weapon in Surgery of HCC?

Jong Man Kim

Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Introduction

Liver resection is an excellent treatment option for selected patients with hepatocellular carcinoma (HCC). Open compared with laparoscopic surgery has been considered as being “more suitable” for liver resections. Additionally, the concern of excessive bleeding during laparoscopic liver resection (LLR), attributed to the inability to apply manual compression of bleeding vessels, was also invalidated. Two international LLR consensus conferences convened, the first in Louisville, Kentucky in 2008,11 and the second in Morioka, Japan in 2014.12 The first conference stated that minor LLRs are safe and should be a standard practice. Second conference showed not only non-inferiority of LLR compared with open liver resection (OLR) but also superiority of LLR in several parameters

Outcomes in HCC

There is critical to demonstrate that LLR is at least noninferior to OLR in oncologic outcomes. Previous most reports in the literature show comparable overall survival (OS) and disease-free survival (DFS) rates between LLR and OLR. Not only was LLR established as an oncologically noninferior operation compared with OLR but also some investigators demonstrated superior results with LLR. The investigators attributed these results, favoring LLR over OLR, to two factors: first, less blood loss in the LLR group; blood loss is known to be a risk factor for HCC recurrence. Second, in contrast to significant mobilization and tissue manipulation before and during parenchymal transection for the OLR, the laparoscopic resections were performed using the anterior approach, with parenchymal transection taking place before any significant mobilization. Thus, a no touch technique is performed, which may be associated with improved oncologic outcomes.

Resections in cirrhotic patients

Liver resections in cirrhotic patients are associated with a relatively high hospital mortality of 1% to 4%, even at high-volume centers. Therefore, LLR in cirrhotic patients is conceptually perceived as being risky, and in many centers, Child–Pugh B patients are precluded from laparoscopic resections.

HCC in difficulty segments

HCC in the posterior-superior liver is considered as difficult and inaccessible parts for LLR. Recent study reported that LLR was associated with less blood loss and shorter hospital stay. There were no statistically significant differences between the 2 groups in operative time, postoperative complications, rate of negative resection margins, and the 3-year OS and DFS rates.
Conclusion

Comparable oncologic outcomes (R0 rate, 5-year DFS, and 5-year OS) have been reported for LLR for HCC compared with OLR using case controls, propensity score matching, and meta-analyses. Further studies will need to define which patients with advance cirrhosis or HCC in the difficult area are suitable for an laparoscopic approach.

References

Priority Policy for Patients with HCC Awaiting Liver Transplantation: Unresolved Issue?

Dorry L. Segev

Johns Hopkins University, USA

Historically, exception points for hepatocellular carcinoma (HCC) in the United States led to higher transplant rates and lower waitlist mortality for HCC candidates compared to non-HCC candidates. As of October 2015, according to changes in US policy, HCC candidates must wait 6 months after initial application to obtain exception points. We have studied 2013-2017 SRTR data. Based on this, we identified 39 350 adult, first-time, active waitlist candidates and compared deceased donor liver transplant (DDLT) rates and waitlist mortality/dropout for HCC versus non-HCC candidates before (October 8, 2013-October 7, 2015, prepolicy) and after (October 8, 2015-October 7, 2017, post-policy) the policy change using Cox and competing risks regression, respectively. Compared to non-HCC candidates with the same calculated MELD, HCC candidates had a 3.6-fold higher rate of DDLT prepolicy (aHR = 3.49 3.69 3.89) and a 2.2-fold higher rate of DDLT postpolicy (aHR = 2.09 2.21 2.34). Compared to non-HCC candidates with the same allocation priority, HCC candidates had a 37% lower risk of waitlist mortality/dropout prepolicy (asHR = 0.54 0.63 0.73) and a comparable risk of mortality/dropout postpolicy (asHR = 0.81 0.95 1.11). Following the policy change in the United States, the DDLT advantage for HCC candidates remained, albeit dramatically attenuated, without any substantial increase in waitlist mortality/dropout. In the context of sickest-first liver allocation, the revised policy seems to have established allocation equity for HCC and non-HCC candidates.
Radiation Therapy for Early HCC: Will It Be a Good Option in Practice?

Sang Min Yoon

Department of Radiation Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Currently recommended curative treatment options for hepatocellular carcinoma (HCC) include hepatic resection, liver transplantation, and percutaneous ablative therapies. However, these treatments can only be applied to the limited groups of patients according to baseline hepatic function, availability of organs, and tumor location. Therefore, alternative non-invasive local treatments should be considered in such cases.

With remarkable recent advances in radiation therapy techniques, including four-dimensional computed tomography, intensity-modulated radiation therapy, image-guided radiation therapy, and controlling respiratory movements during radiation therapy, stereotactic body radiation therapy (SBRT) has been regarded as a good alternative treatment option for early HCCs that are not suitable for curative treatments. Many prospective and retrospective studies have evaluated the ablative role and safety of SBRT for small HCCs and showed that SBRT results in an excellent local tumor control and minimal treatment-related toxicity.

Here, we summarize recent updates and discuss the future perspectives of the role of SBRT for early HCC.
Asian Forum

Korea-Japan-Taiwan

Chairs:

Jin Mo Yang (Korea)
Tetsuo Takehara (Japan)
Jia-Horng Kao (Taiwan)
The introduction of direct-acting antivirals (DAAs) substantially increased the rate of sustained virologic response. In Japan, IFN-free DAA treatment has been introduced in 2014. First IFN-free DAA treatment is asunaprevir (ASV); an NS3/4A inhibitor + daclatasvir (DCV); an NS5A inhibitor. After that, many IFN-free DAA treatments were approved until now. For patients with HCV genotype 1, which is a major HCV genotype in Japan, ASV+DCV, ombitasvir (OBV)/paritaprevir (PTV)/ritonavir (r) and ASV/DCV/beclabuvir (BCV) were used, and ledipasvir(LDV)/sofosbuvir(SOF), grazoprevir (GZR)+Elbasvir (EBR) and glecaprevir (GLE)/pibrentasvir (PIB) are used. Nowadays, SVR rates of any IFN-free DAA treatments exceed 95%. However, resistance-associated substitutions (RASs) emerge in patients with virologic failure (VF) after IFN-free DAA treatment to create a new issue. Since an NS5A inhibitor is a key drug for IFN-free DAA treatment and RASs generated by an NS5A inhibitor show cross resistance to other NS5A inhibitors, we should pay attention NS5A RASs, especially, after VF.

To examine emerging RASs, we deep sequenced HCV and compared HCV RASs between before and after VF. We treated 322 and 1258 hepatitis C patients with ASV+DCV or LDV/SOF, respectively. With ASV+DCV treatment, 19 (5.9%) patients experienced VF including 4 NR (non-response), 8 BT (break through) and 10 relapses. Among them, 14 patients’ HCV RASs could be analyzed at both time point before and after treatment. All 14 patients infected with HCV genotype 1b and did not receive any NS5A inhibitors before ASV+DCV treatment. Although some patients carried HCV with L31M/V-Y93H RASs at baseline as a minor clone, no patients carried HCV with L31M/V-Y93H RASs as a major clone. In contrast, HCV with L31M/V-Y93H RASs was detected as a major clone in 13 patients at the time of VF. The other 1 patient carried HCV with P32del at the time of VF, which was not detected at baseline. The HCV with P32del was also detected as a major clone post 24 weeks after treatment. With SOF/LDV, 13 (1.0%) patients experienced VF including 3 NR and 10 relapses. Among them, 9 patients’ HCV RASs could be analyzed at both time point before and after treatment. All 9 patients infected with HCV genotype 1b and did not receive any NS5A inhibitors before SOF/LDV treatment. One patient did not carry a signature RAS at the L31 or Y93 position at baseline but Y93H was found at the time of VF. Among the other 9 patients, 5 had HCV with L31V/F-Y93H, 3 had HCV with Y93H, and 1 had HCV with L31M at baseline. All 8 patients who were positive for baseline Y93H either harbored this substitution at a high frequency before treatment or exhibited an increase in frequency after treatment. One patient who carried HCV with L31M at baseline developed HCV with P32del at the time of VF; the P32del was not detected at baseline. The P32del HCV was detected as a major clone for more than a year after VF.

Among the VF patients with sequenced HCV after treatment with ASV+DCV or SOF/LDV, 4 patients carrying HCV with L31V/F-Y93H or Y93H were re-treated with GLE/PIB, and all of them achieved SVR. On the other hand, in the phase III trial of GLE/PIB in Japan, 2 of 33 DAA-treated patients had the P32del mutation before treatment, and the treatment was not effective in both cases. Effective treatment was not established for patients carrying HCV with P32del. So we next examined treatment options for chronic hepatitis C patients carrying HCV
with P32del using humanized liver chimeric mice.

After inoculation of sera from the patient carrying HCV with P32del after SOF/LDV treatment or DAA-naïve patient carrying wild-type HCV without any RASs at L31, P32 or Y93 into chimeric mice, serum HCV RNA levels increased and developed persistent HCV infection in both inoculated mice. Two-week NS5A inhibitor (LDV, EBR) monotherapy decreased serum HCV RNA levels to undetectable levels in mice infected with wild-type HCV, but not at all in mice infected with P32del HCV. Three-week IFN monotherapy decreased serum HCV RNA levels by 2.8±0.2 log IU/ml from baseline in mice infected with wild-type HCV as same as those in mice infected with P32del HCV. To examine the efficacy of a combination therapy, mice in each group were divided into three treatment groups. One group received 3 weeks of LDV+GS-558093 (a NS5B inhibitor), another group received 3 weeks of simeprevir(SMV)+GS-558093 treatment, the other group received 3 weeks of SMV+pegIFN. In mice infected with wild-type HCV, all three combination therapies rapidly deceased serum HCV RNA levels to below the sensitivity. In contrast, in mice infected with P32del HCV, LDV+GS-558093 reduced serum HCV RNA levels only by 1.0±0.5 log IU/ml from baseline. SMV+GS-558093 reduced serum HCV RNA levels by 3.0±0.4 log IU/ml from baseline and SMV+pegIFN reduced serum HCV RNA levels to below the sensitivity. Combination therapy with an NS3/4A protease inhibitor and a nucleotide NS5B inhibitor or pegIFN alfa-2b may be a treatment option for HCV-infected patients with P32del.
Current Status and Emerging Issues in Liver Diseases in Taiwan

Chun-Jen Liu
Department of Internal Medicine, Graduate Institute of Clinical Medicine and Hepatitis Research Center; National Taiwan University College of Medicine and Hospital, Taiwan

Hepatitis B virus (HBV) infection and related liver diseases are a heavy disease burden worldwide, particularly in Asia-Pacific region. Thus, Taiwan has been fighting this virus since the late 1970s, and successful results have been achieved. Currently, the HBsAg carriage rate drops to below 1% in the young generation after implementation of nationwide vaccination program. After 15-year active treatment of patients with CHB through government reimbursement of peg-interferon and oral nucleos(t)ide analogue (NUC), incidence of HBV-related morbidity and mortality was documented to be decreased gradually.

The World Health Assembly adopted the Global Health Sector Strategy on viral hepatitis since 2016 (Chen DS, 2019). The Taiwanese people and government follow the strategy and make great efforts towards the elimination of chronic hepatitis C. Efforts from experts, public health officers, legislators, and the government leaders have culminated in a consensus of reaching the WHO goals in 2025—i.e., 5 years earlier than the 2030 deadline set by WHO. Accordingly, the Taiwan Hepatitis C Policy Guideline 2018–2025 was approved and published at the beginning of 2019. The government will provide US$1.7 billion in the coming 8 years for the control of hepatitis C. Actions will include lowering the barriers of access to care, screening strategies, continuum of care, preventive measures for high-risk populations, improving liver health literacy on the prevention of new infections and reinfections, liver disease management, outcome evaluation of policy and interventions, and innovation, research, and development.

Non-alcoholic fatty liver disease (NAFLD) is an emerging disease burden in Taiwan accompanying westernization of lifestyle and food. The prevalence of fatty liver is increasing; however definite prevalence or number of patients suffering from severe form of NAFLD such as steatohepatitis and cirrhosis is still lacking in Taiwan. Moreover, there is no approved medication for the treatment of NAFLD. Lifestyle modification and control of metabolic derangement remain the key strategies for the management of NAFLD.

Reference

Current Status and Emerging Issues in Liver Diseases in Korea

Yoon Jun Kim
Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

There are several issues raised recently in the hepatology field in Korea. Wide use of nucleos(t)ide analogues brings rapid decrease of decompensated patients due to chronic hepatitis B virus (HBV) infection. On the other hand, the crude incidence of primary liver cancer associated with HBV infection has been increased during recent decades in Korea. Elimination program of hepatitis C virus (HCV) was initiated with massive use of direct antiviral agents. However, active screening for hidden HCV infection is important for HCV elimination. Nonalcoholic fatty liver disease (NAFLD) has become prevalent in Korea in the last decade. The Korean society needs to quickly control the increasing prevalence of NAFLD and reduce its complications. Vaccination for hepatitis A virus (HAV) has been implemented as one of the national vaccination programs despite the epidemiological transition of HAV in Korea. Recent epidemic of HAV warns the effectiveness of the program. These topics will be discussed in the lecture.
Cirrhotic Portal Hypertension: From Arterial Vasodilatation to Systemic Inflammation

Han-Chieh Lin
Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital and, National Yang-Ming University, Taiwan

Chronic liver injury will eventually lead to development of cirrhosis. Increased intrahepatic resistance due to distorted liver structure during hepatic fibrosis is the initial trigger for the development of cirrhotic portal hypertension. The classical hemodynamic derangement in cirrhotic portal hypertension included peripheral and splanchnic arterial vasodilatation with the development of hyperdynamic circulation that is characterized by increased cardiac output and decreased peripheral and splanchnic arterial resistances. Previous studies have shown that, following the development of portal hypertension, intestinal bacterial translocation occurred. This phenomenon would lead to the development of systemic inflammatory response. In addition, the bacterial translocation associated endotoxemia will further exacerbate the hyperdynamic circulatory derangements with increased in intrahepatic resistance. A number of studies have shown that increased plasma endotoxin level following bacterial translocation in cirrhosis with portal hypertension play in part a role for the pathogenesis of cirrhotic cardiomyopathy, hepatopulmonary syndrome, kidney injury, and encephalopathy. It is also known that systemic inflammation is a hallmark of acute on chronic liver failure. Currently, there is no specific treatment to block bacterial translocation. The role of long-term antibiotic prophylaxis is still under debate. Fecal microbiome transplantation has shown some potential beneficial effects, but its long-term outcome is not known. It is now recognized that cirrhotic portal hypertension may be regarded as a systemic inflammatory multi-organ syndrome.
USG Session 1

Upgrading the USG Education (*K)

Chair:
Soon Koo Baik (Yonsei Univ. Wonju)
Current Status of Ultrasonography Education Program and Ultrasonography Specialist Certificates of KASL

Hyung Joon Yim
Division of Gastroenterology, Department of Internal Medicine, Korea University Medical College, Seoul, Korea

As abdominal ultrasonography help physician to visualize the organs and structures in the abdomen, it became one of basic and essential initial evaluation tools of abdomen currently. As of 2019, upper and lower abdominal ultrasonography can be reimbursed to health insurance system. In addition, resident of Internal Medicine should learn ultrasonography and get proper training for applying the Board Certified Internal Medicine Specialist.

With this regard, Korean Association for the Study of the Liver (KASL) launched “the Quality Management Committee of Abdominal Ultrasonography” in 2018. The committee is responsible for qualification of internists performing abdominal ultrasonography and issuing the certificate of abdominal ultrasonography subspecialist. For getting the certificate, experience of 200 cases of abdominal sonography and 9 points of educational credits are mandatory. Among the 9 points, 4 points should be obtained from the ultrasonography educational session sponsored by KASL. Last year, 20 doctors obtained the certificate. KASL will receive the application for the upper abdominal ultrasonography subspecialist in September this year. All the applying documents should be submitted to the electronic management system of the KASL website.

The Korean Association of Internal Medicine indorsed the Korean Association of Clinical Ultrasound and the Korean Society of Gastroenterology for the education of abdominal ultrasonography trainer. KASL approves the qualification for abdominal ultrasonography trainer together with the Korean Society of Gastroenterology. For obtain the qualification for abdominal ultrasonography trainer, 9 points of educational credits are also needed. Experiences as a speaker or a chair at ultrasonography session of academic meeting are also required in addition to 200 cases of abdominal sonography practice. Last year, a total of 78 doctors obtained the certificate. In addition, 9 doctors applied to the certificate this year.

Currently, KASL opens ultrasonography educational sessions at the Liver week and the Korean Digestive Diseases Week. In the other hands, 3 times of hands-on workshops are held separately.

Residents of Internal Medicine can learn basic skills of performing abdominal ultrasonography through class room lectures and hands-on practice workshops. Three hour education can replace the experience of abdominal sonography of 17 patients.

In conclusion, this ultrasonography sessions are planned to educate the ultrasonography and to issue the educational credits, eventually for the better qualification of knowledge and technique of ultrasonography for members of KASL and trainees. KASL is making every effort to provide more opportunity for better ultrasonography education.

References
How Do I Teach Abdominal USG for Trainee?

Yun Soo Kim

Department of Gastroenterology and Hepatology, Gil Medical Center, Gachon University, Incheon, Korea

Learning Abd USG for Physician:
How Did I Learn Abd USG?
- My Experience

Why Trainees Feel Difficult?

Indirect Image
Changing Orientation (Direction)
Obstacles for scanning: artifacts, poor sonic window...

Understanding Limitation of USG
Trainees:
- Medical students
- Medical Residents
- Clinical Fellows

How Do I Teach Abd USG for Trainee

Lecture: Liver, Biliary & Pancreas
- 모식도, CT USG image 비교
- Hands-on: standard images
  - Pathologic conditions

모식도 – CT – USG

Courses – The Liver Week 2019

June 20-22, 2019 | BEXCO, Busan, South Korea
Hands-on

- Normal: junior residents
- Clinical correlation
- procedures: biopsy, abscess drainage, RFA
Ablation therapy for liver and pancreatic cancer is performed under ultrasound imaging guidance. Contrast-enhanced ultrasound (CEUS) is used for tumor delineation and efficacy evaluation in local ablation therapy. Sonazoid gives us long lasting Kupffer phase imaging in which bubble signals are emitted from Kupffer cells after phagocytosis. Vascular phase imaging is used for differential diagnosis of the tumor and Kupffer phase imaging is used for delineation of the tumor and ablation area.

At the same time, ultrasound fusion imaging with CT, MRI and PET has an important role in the safe and effective ablation therapy. Multi planar reconstruction (MPR) imaging of these modalities which is consistent with real time ultrasound imaging can cover weak points of ultrasound imaging.

Needle navigation technology is also indispensable to monitor the needle tip during puncturing and ablation procedures even when the needle tip could not be visualized well on real time ultrasound imaging.

RFA and MWA for liver cancers and IRE (irreversible electroporation, NanoKnifeTM) for pancreatic cancer can be performed safely and effectively using contrast-enhanced ultrasound and fusion imaging technologies.
USG Session 2

Diversifying the Field of USG for Training (HK)

Chair:
Won Young Tak (Kyungpook National Univ.)
Setting-Up an Abdominal USG Facility and Training Program

In Hee Kim

Department of Internal Medicine, Chonbuk National University Medical School and Hospital, Jeonju, Korea
복부 초음파 지도인증의
- 대한소화기학회, 대한간학회, 대한췌담도학회에서 공동으로 인정

• 복부초음파 지도인증의 - 복부초음파의 진단과 판독을 수행할 수 있는 능력을 갖춘 소화기 관련 의사
• 자격 취득 기준
  1. 대한소화기학회 또는 대한간학회 또는 대한췌담도학회 회원으로 하여의 자격을 모두 만족하여야 한다.
  2. 최근 5년간 대학내과학회, 대한소화기학회, 대한간학회, 대한췌담도학회, 또는 임상초음파학회의에서 인정하는 복부초음파 지도 관련 교육과 9 평점 이상의 교육평점을 취득해야 한다.
  3. 최근 5년 이내에 200건 이상의 복부초음파 검사를 시행하고 판독해, 이를 담보로 받을 수 있는 문서와 영상물 또는 복부초음파 지도인증의 인증위원회에서 요구하는 자료를 제출해야 한다. 특히, 최소 3년 이상의 실습 경력이 필요하여야 한다.
  4. 최근 5년간 대학내과학회, 대한소화기학회, 대한간학회, 대한췌담도학회 또는 임상초음파학회에서 주관하는 학회(학자)에 최소 1회 이상 참여한 자는, 최소 3년 이상의 실습 경력이 필요하다.

• “복부 초음파 세부전문의”: 초음파 진단과 판독에 적합 수준 이상의 능력을 갖춘 임상의사
• 자격취득기준
  1. 최근 5년 이내에 200건 이상의 복부 초음파를 시행하고 판독한 경우, 이를 담보로 받을 수 있는 문서와 영상물 또는 세부전문의 심사위원회에서 인정하는 자료를 제출해야 한다.
  2. 최근 5년 이내에 대한간학회 세부전문의 심사위원회에서 인정하는 초음파 검사 관련 평점의 교육평점을 취득해야 한다.

초음파실 Setting-Up을 위한 기본 준비사항

1. 초음파실 공간 확보
   • 적절한 크기의 공간
   - 입수
   - 환자대기실, 탈의 및 개인 물품보관실
   - 초음파 검사실
   - 기타 물품보관실
   - 휴게실 등

2. 초음파 검사 장비
   • 초음파 검사 장비(본체, 탐촉자)
   • 각 회사에서 소개하는 초음파 장비의 특성, 기능, 가격, A/S 등의 조건을 비교
   • 실제 초음파 장비를 사용해본 검사자들의 의견 수렴
   • 관심있는 초음파 장비에 대해 시연 요청
   • 최종 초음파 장비 선택 후 병원 측에 구입 요청

3. 초음파 검사 관련 물품 및 환경
   • 접수 및 검사실 컴퓨터, 책상, 의자 등
   • 초음파실의 청대 및 시트
   • 피검사자용 가운, 수건
   • 초음파 검사용 젤리, 젤리 보관용 옷장
   • 검사 시 적절한 간접 조명 및 조명 조절 장치

초음파실  Setting-Up을 위한 기본 준비사항

1. 초음파실 공간 확보
   • 적절한 크기의 공간
   - 입수
   - 환자대기실, 탈의 및 개인 물품보관실
   - 초음파 검사실
   - 기타 물품보관실
   - 휴게실 등

2. 초음파 검사 장비
   • 초음파 검사 장비(본체, 탐촉자)
   • 각 회사에서 소개하는 초음파 장비의 특성, 기능, 가격, A/S 등의 조건을 비교
   • 실제 초음파 장비를 사용해본 검사자들의 의견 수렴
   • 관심있는 초음파 장비에 대해 시연 요청
   • 최종 초음파 장비 선택 후 병원 측에 구입 요청

3. 초음파 검사 관련 물품 및 환경
   • 접수 및 검사실 컴퓨터, 책상, 의자 등
   • 초음파실의 청대 및 시트
   • 피검사자용 가운, 수건
   • 초음파 검사용 젤리, 젤리 보관용 옷장
   • 검사 시 적절한 간접 조명 및 조명 조절 장치
4. 초음파실 인력 및 역할분담

- 간호사(간호조무사): 환자 접수, 안내, 검사 준비
- 방사선사: 초음파 검사 장비 및 기타 물품 관리
- 검사 보조자(진공, 전임의): 환자 정보(검사 목적, 이전 검사 결과 등) 파악, 예비 초음파 검사 시행
- 검사저(지도전문의, 교수): 초음파 검사 시행, 관독, 교육

초음파실을 Setting-Up 할 때의 고민...

소화기내과 복합적인 초음파실 공간 확보
- 장점: 소화기 검사실(내경계, 섬유화 검사)이나 진료실과의 연계성, 새로운 장비, 복합적인 운영
- 단점: 병원의 소극적인 지원(예산, 인력 등)

기존 영상의학과 초음파실을 공동 이용
- 장점: 최소한의 투자, 초기 setting-up이 용이, 주변 동료(영상의학과 의사, 방사선사)의 긴밀한 협조
- 단점: 합소한 공간, 오래된 장비, 다른 소화기 검사실과 연계성 부족

초음파실 Setting-Up

- 검사 시간
  - 시행 초기: 6개월간, 주 2 sessions (오전, 밤, 수)
  - 현재: 주 6 sessions (오전, 밤, 수, 금/오전, 토, 목, 금)

초음파실에서 시행될 수 있는 각종 검사와 시술들

- 복부초음파 진단 검사 - B mode와 도플러 초음파 검사
- 간조직 검사
- 복수, 천자 및 흉수 천자 위치 표기나 시술
- 간종양의 흡인과 치료, 캐터 삽입
- 조영초음파 검사
- 알코올 주입술
- 고주파 열치료술

내용

벽부 초음파 Training Program

- 복부 초음파 Setting-Up
- 복부 초음파 Training Program

벽부 초음파 Training Program

- 교수 교육
- 전문의 교육
- 내과 전문의
- 복부 초음파 세부 전문의
교수 교육 – 기관 경험이

- 기관 내 영상의학과 복부전담 교수의 지도
  - 대상: 소화기내과 교수 (2인)
  - 초청강의, 초음파 환관 및 Hands-on (주 2회, 2 session)
  - 실제 검사 시행
  - 6개월 정도 소요
- 복부초음파 관련 교재, On-line 교육자료 활용
- 학회 초음파 교육 강의, Hands-on 참석
  - 복부 초음파 저도관련 교육 9명점 이상
- 복부 초음파 시행
  - 주 1 SESSION 이상, 200건 이상

전임의 및 전공의 교육: 기관 경험이

- 복부초음파 study 모임
  - 대상: 소화기내과 전임의 및 내과 전공의
  - 시간: 주 1회 (매주 월요일 정시시간, 30분)
  - 복부 초음파 관련 교재(복부 초음파 아틀라스, 한국의학) 리뷰
  - 2개월 (8-4월)
- 복부초음파 관련 On-line 교육자료
  - 교수(지도전문의) 지도하 초음파 검사 참관 및 검사 시행
    - 전공의: 25건/년 이상, 전임의: 100건/년 이상
- 학회 초음파 교육 강의의 Hands-on, 이수 권고
  - 전공의: 초음파 교육 1회/년 이상
  - 전임의: 복부초음파 세부전문의 교육 3회/년 이상

복부 초음파 STUDY 모임

- 기간: 18주

http://www.kasl.org/?code=academy

복부 초음파 교육에 유용한 On-line 교육자료

- 대한간학회 홈페이지 – 교육자료실, CME
- http://www.kasl.org/bbs/?code=academy

1. 복부 초음파 기본 스탠드
2. 복부 초음파 검사의 실제
3. 복부 초음파 검사스캔시의 trouble shooting
4. 간의 정상구조 및 기본 스탠드
5. Standard report system for US results
6. 다양한 간질환의 초음파 소견
7. 초음파 검사에서 발견된 간질 및 간종괴의 감별
초음파 검사 시행 및 전공의 교육

<table>
<thead>
<tr>
<th></th>
<th>월</th>
<th>화</th>
<th>수</th>
<th>목</th>
<th>금</th>
</tr>
</thead>
<tbody>
<tr>
<td>오전</td>
<td>교수1</td>
<td>교수2</td>
<td>교수3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>전임의1</td>
<td>전임의2</td>
<td>전임의3</td>
<td>전임의1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>전임의2</td>
<td>전임의3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>오후</td>
<td>교수4</td>
<td>교수5</td>
<td>전임의2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>전임의3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 초음파 검사 건수: 15~20건/session

결론

- 외부 환경 변화에 대한 능동적 대처 필요
- 원내 현실의 강점, 약점을 파악하여 초음파실 Setting-UP
  - 공간, 장비, 기타 물품, 인력 등
- 초음파 Training Program
  - 지도를 담당할 교수 교육, 지도 전문의
  - 전공의, 전임의 교육, 내과 전문의, 복부 초음파 세부전문의
  - Off-line 교육(자체 초음파 study 모임, 학회 초음파 교육, Hands-on)
  - On-line 교육(학회 홈페이지 교육자료실, CME)

감사합니다.
Tips for Selection and Maintenance of USG Machines

Hyun Joo Kim¹, Han Jong Yu²

¹GE Healthcare Korea, ²Canon, Korea
Assessment of Hepatic Fibrosis with 2-dimensional Real-Time Shear Wave Elastography (SWE)

Joo Hyun Sohn
Gastroenterology & Hepatology, Hanyang University College of Medicine and Guri Hospital, Seoul, Korea

Contents

- Introduction
- Measuring Liver Stiffness (LS) by 2D-SWE
- Roles of 2D-SWE in Chronic Liver Disorders
  - Assessing Liver Fibrosis
    • Various CLD
    • Viral hepatitis (CHB, HCV)
    • Non-viral CLD
  - Assessing Portal Hypertension
  - Assessing Esophageal Varices
  - Assessing the HCC Risk and Prognosis in CLD
  - Spleen Stiffness (SS) by 2D-SWE
- Summary

Elastography (Elasticity Imaging)

1. Ultrasound-based elastography:
   1) One-dimensional (1-D) transient elastography (TE) (Sandrin et al. 2003)
   2) Two-dimensional (2-D) static ultrasound elastography (Friedrich-Rust et al. 2007)
   3) Acoustic radiation force impulse (ARFI) imaging (Fahey et al. 2003; Palmeri et al. 2008)
   4) Supersonic shear imaging (SSI) (Muller et al. 2009)
   5) Shearwave dispersion ultrasound vibrometry (SDUV) (Chen et al. 2008)
   6) Spatially modulated ultrasound radiation force (SMURF) imaging (McAlaevey et al. 2009)
   7) Sonoeleastography (Taylor et al. 2000)

2. MR (magnetic resonance) elastography
   (Klatt et al. 2006; Muthupillai et al. 1995)

Non-invasive methods for liver fibrosis: advantages and disadvantages

US Elastography: TE vs. 2-D SWE

1st generation, Prototype

2nd generation, SWE
Merits of 2-D SWE vs. TE

- The integration into a conventional US machine with conventional US probes during a routine standard US scan (Aixplorer version 3, Supersonic imagine, France).
- The real-time liver echo images and measurement of the liver stiffness (expressed in kilopascals, kPa) simultaneously.
- The exact localization of the ROI during B-mode US, avoiding large vessels, cysts, other structures.
- A color-coded 2-D quantitative mapping of shear elasticity, displayed in color over a conventional gray-scale B-mode image (blue to red according to low to high kPa).
- It has a larger region of interest (ROI, Q-BoxTM, 300-700mm² area) and higher range (1~150 kPa) of measured values than TE.
- No limitation of stiffness measurement in patients with ascites.
- LS measurements by SWE: Higher applicable, reliable, reproducible, success rates than TE.

2D Real-time SWE in various chronic liver diseases: Role in predicting liver fibrosis

Table 1: Basic characteristics of patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57±12</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>45/35</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23±3</td>
</tr>
</tbody>
</table>

Diagnostic performance in all patients with various CLD

<table>
<thead>
<tr>
<th>Diagnostic performance in all patients with various CLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUROC</td>
</tr>
<tr>
<td>P</td>
</tr>
</tbody>
</table>

Diagnostic performance in viral CLD

<table>
<thead>
<tr>
<th>Diagnostic performance in viral CLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUROC</td>
</tr>
<tr>
<td>P</td>
</tr>
</tbody>
</table>

2D Real-time SWE in chronic liver diseases (CLD): Correlation with liver fibrosis and cut-off values

Table 1: Liver stiffness cutoff values for the diagnosis of advanced fibrosis (F≥3) and cirrhosis (F≥4) based on MRE (kPa = 70)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cutoff Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>6.77±1.72</td>
</tr>
<tr>
<td>F1</td>
<td>9.98±3.99</td>
</tr>
<tr>
<td>F2</td>
<td>15.80±7.73</td>
</tr>
<tr>
<td>F3</td>
<td>22.09±10.09</td>
</tr>
</tbody>
</table>

Diagnostic performance and cut-off values of LS by 2D SWE in various CLD

Table 1: Diagnostic performance of liver stiffness by MRE (F ≥ 2), advanced fibrosis (F ≥ 3), and cirrhosis (F ≥ 4) based on MRE (kPa = 70)

<table>
<thead>
<tr>
<th>Disease</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>0.906</td>
</tr>
<tr>
<td>F1</td>
<td>0.934</td>
</tr>
<tr>
<td>F2</td>
<td>0.960</td>
</tr>
</tbody>
</table>

Etiology: HBV/HCV/Alcohol/NAFLD/Other

Jeong: 23 (32.9%)/18 (25.7%)/10 (14.3%)/4 (5.7%)/13 (18.6%); F0-21.4%)
Diffuse: 24 (20%)/44 (36.7%)/10 (8.5%)/19 (15.6%)/23 (18.8%)/F0-15.2%}

Examples: 2-D SWE Images and LS

M0: Normal LS ≤ 1.9 kPa
M1: CHB, F1, LS 5.2 kPa
M2: CH, F2, LS 10.5 kPa
M3: CH, F3, LS 12.2 kPa
M4: AC, F4, LS 20.2 kPa
M5: LC, ascites, LS 60.5 kPa

Examples: 2-D SWE Images and LS

M0: Normal LS ≤ 1.9 kPa
M1: CHB, F1, LS 5.2 kPa
M2: CH, F2, LS 10.5 kPa
M3: CH, F3, LS 12.2 kPa
M4: AC, F4, LS 20.2 kPa
M5: LC, ascites, LS 60.5 kPa
Assessment of liver fibrosis by 2-D SWE: An individual patient data-based meta-analysis (n=1134).

A meta-analysis (n=1,134): Cut-off Values for Liver Fibrosis

<table>
<thead>
<tr>
<th>Fibrosis Stage</th>
<th>AUROC</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>F2</td>
<td>86.4%</td>
<td>91%</td>
<td>93%</td>
</tr>
<tr>
<td>F3</td>
<td>91%</td>
<td>93%</td>
<td>96%</td>
</tr>
<tr>
<td>F4</td>
<td>93%</td>
<td>96%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Accuracy of 2D-SWE: Summarized ROC curves and diagnostic performance by AUROC

Diagnostic performance and Cut-off Values of LS by 2D SWE in CHB

Diagnostic performance and Cut-off Values of LS by 2D SWE in CHC
Diagnostic performance and Cut-off Values of LS by 2D SWE in non-viral liver diseases

In NAFLD patients, there is a relatively high failure rate (2.7%–13%) because of the higher BMIs. Diagnostic performance in predicting each fibrosis stage was relatively low, and the cut-off values of the fibrosis stages varied between the studies.

SWE > TE in AUROC for the diagnosis of F2, F3, F4 Fibrosis

In HCV, HBV, or NAFLD patients, AUROCs were 4.7%–11.5% larger using 2D-SWE for the diagnosis of F2 fibrosis (absolute differences, p=0.001 in HBV patients, p<0.001 in all patients).

AUROCs were 1.4%–12.0% larger using 2D-SWE for the diagnosis of F3 fibrosis (p=0.003 for all patients)

For the diagnosis of F4 cirrhosis, AUROCs were about 1.4%–8.7% larger using 2D-SWE versus TE (p<0.001 in HCV patients, p=0.012 for all patients)

The gain in AUROC with 2D-SWE when compared with TE was largest in HBV patients and smallest in HCV patients.

Comparison between 2D SWE vs. TE

Paired TE and 2D-SWE evaluations were performed in 518 (38.8%) among 1341 total patients.

Comparison with TE vs. SWE vs. MRE: a Meta-Analysis

NAFLD (n=13,046; 28/64 studies: TE(19), SWE(4), MRE(5))

The summary AUROC values using FibroScan M probe, XL probe, SWE, and MRE for diagnosing Advanced Fibrosis were 0.88, 0.85, 0.95, and 0.96 (FS vs. SWE, MRE, all p values < 0.01).

MRE and SWE may have the highest diagnostic accuracy for staging fibrosis in NAFLD patients.
**Portal Hypertension (PH)**

**Diagnosis Modalities**

**Invasive**
- HVPG (Hepatic Venous Pressure Gradient) measurement is a relevant gold standard for assessing the degree of portal hypertension (PHT).
- HVPG = WHPG - FHVP

**Non-invasive**
- CT angiography
- MR angiography
- USG
- Doppler US
- EUS
- Liver Stiffness by US (TE, SWE)
- MR elastography of liver, spleen
- Portal scintigraphy using $^{99m}$Tc
- Biomarkers

---

**Role of TE in the evaluation of PH:**

Relationship between liver stiffness by TE and HVPG

- The correlation was excellent for HVPG values less than 10 or 12 mmHg ($r = 0.81, \ P < 0.0003$ and $r = 0.91, \ P < 0.0001$, respectively), but it was not optimal for HVPG values ≥10 or ≥12 mmHg.
- TE cannot measure the complex hemodynamic changes, characteristics of severe PH and is not useful in monitoring the hemodynamic response to drug therapy. (Castera L. J Hepatol 2008;48:835)
- TE is unsuccessful and limited to use in cirrhotic patients with perihepatic ascites.

---

**Diagnostic performance of TE**

Clinically significant portal hypertension (CSPH, HVPG ≥10 mmHg)

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Diagnostic</th>
<th>Presence of</th>
<th>Liver stiffness (KPa)</th>
<th>SE %</th>
<th>SP %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron et al. 1996</td>
<td>81</td>
<td>Direct</td>
<td>4</td>
<td>0.20</td>
<td>80</td>
<td>90</td>
</tr>
<tr>
<td>Vazquez</td>
<td>61</td>
<td>HVPG &lt; 10</td>
<td>77</td>
<td>0.22</td>
<td>85</td>
<td>87</td>
</tr>
<tr>
<td>Capron</td>
<td>38</td>
<td>HVPG &gt; 10</td>
<td>74</td>
<td>0.22</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>Gamba</td>
<td>40</td>
<td>HVPG &gt; 10</td>
<td>76</td>
<td>0.22</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>Laurence</td>
<td>44</td>
<td>HCV</td>
<td>55</td>
<td>0.22</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>Gamba</td>
<td>38</td>
<td>HCV</td>
<td>55</td>
<td>0.22</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>Ross</td>
<td>180</td>
<td>HCV</td>
<td>61</td>
<td>0.22</td>
<td>88</td>
<td>90</td>
</tr>
</tbody>
</table>

HVPG = WHPG - FHVP


---

**Role of 2D-SWE in Portal Hypertension**

- 92 among 115 cirrhotic patients were eligible for analysis
- LSM using real-time 2D-SWE is well correlated ($r = 0.65, \ p<0.001$) with the value of HVPG in cirrhotic patients regardless of the presence of ascites.
- SWE is a new reliable non-invasive tool to predict both clinically significant and severe portal hypertension, even in cirrhotic patients with ascites.

---

**2D-SWE Role in predicting CSPH and SPH**

Table 1: Performance of 2D-SWE in predicting clinically significant portal hypertension (CSPH, HVPG ≥10 mmHg)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>SENS (95% CL)</th>
<th>SPEC (95% CL)</th>
<th>PPV (95% CL)</th>
<th>NPV (95% CL)</th>
<th>LR+ (95% CL)</th>
<th>LR- (95% CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSPH</td>
<td>87% (76-96)</td>
<td>89% (81-96)</td>
<td>91% (87-94)</td>
<td>84% (76-92)</td>
<td>5.2 (3.8-6.9)</td>
<td>0.1 (0.1-0.2)</td>
</tr>
<tr>
<td>SPH</td>
<td>78% (69-86)</td>
<td>91% (83-96)</td>
<td>92% (89-95)</td>
<td>88% (81-94)</td>
<td>7.5 (5.7-11.1)</td>
<td>0.1 (0.1-0.2)</td>
</tr>
</tbody>
</table>


---

**2D-SWE in predicting CSPH (HVPG ≥10)**

Table 1: Performance of 2D-SWE in predicting clinically significant portal hypertension (CSPH, HVPG ≥10 mmHg)

| CSPH | 87% (76-96) | 89% (81-96) | 91% (87-94) | 84% (76-92) | 5.2 (3.8-6.9) | 0.1 (0.1-0.2) |


2D-SWE role in predicting CSPH (HVPG ≥10 mmHg) in alcoholic hepatitis/NASH/others: 89/12/27/30 (56.3/7.6/17.1/19%) n=158

JY Jeong, YS Cho, JH Sohn. World J Gastroenterol 2018; 24(34): 3849-3860

---

These are the slides from the Liver Week 2019 conference on Portal Hypertension (PH) diagnosis modalities and the role of TE and 2D-SWE in evaluating PH. The slides detail various diagnostic methods and their performance metrics.
SWE as a Quantitative Biomarker of CSPH: A Systematic Review and Meta-Analysis

Role of SWE in Detecting Esophageal Varices

Comparison between LS by SWE and Other Common Predictors for Esophageal Varices in Patients With Compensated Cirrhosis

Role of SWE in evaluating Esophageal Varices in Patients With Compensated Cirrhosis

Diagnostic accuracy of 2D-SWE for predicting EV

2D-SWE Role in Evaluating the Risk of HCC: Korean patients with CHB (n = 291)

- Measured by 2D-SWE between 2011 and 2012
- 291 eligible subjects among 446 CHB patients
- Median follow-up for 3 years
- Mean age: 48.8 years
- Cirrhosis in 14%
- Antiviral treatment in 36.7%

- Based on a multivariable analysis, older age (<50 years) and higher LS value (≥10 kPa) were independently associated with the risk of EV (HR: 4.39, p=0.023 and HR: 4.69, p=0.036, respectively).
- The cumulative incidence rate of HCC was significantly higher in patients with higher LS values (≥10 kPa) than in those with lower LS values (p=0.001).
- The cumulative rates of HCC at 1-, 2-, and 4-years were 0.9%, 1.6%, and 2.5%, respectively, in patients with LS values ≥10 kPa, and 2.4%, 5.5%, and 21.5%, respectively, in patients with LS scores ≤9 kPa.
- The time-dependent AUCs of LS measurement by SWE for HCC development at 1-, 2-, 3-, and 5-year were 0.76, 0.61, 0.77, 0.75, and 0.70, respectively.
SWE predicts HCC risk in CHC patients after SVR24 (n=196)

PLoS ONE 13(4):e0195173. April, 2018
https://doi.org/10.1371/journal.pone.0195173

The estimated 1- and 3-year recurrence-free survival rates after RFA were 63.4 and 37.6%, respectively;
SWE-not significant

The estimated 1- and 3-year overall survival rates after RFA were 96.4 and 85.8%, respectively.

Cut-off value of LS 13.3 kPa:
3-year overall survival rates: 96.3 vs. 76.8%
(hazard ratio = 4.30 [1.26 – 14.7]; p = 0.020).

→ LS values measured by 2D-SWE was a significant predictive factor for overall survival after RFA for HCC.

LSM by 2D-SWE:
Prognostic Value after RFA for HCC

Parameters of Success of Valid SS Measurement

Valid spleen stiffness values were obtained in 164 of the 310 patients (52.9 %).
Valid liver stiffness values were obtained in 292 of the 310 patients (94.2%).
* Valid results were defined as interquartile range divided by median (IQR/M) of less than 0.3, the index of validity used for TE

Spleen Stiffness(SS)
Measurement by 2D-SWE (Examples)

SS Measurement Using 2D-SWE:
Predictors of Valid Measurement

A 50-year-old male patient with normal SS value: 19.4 kPa
A 57-year-old female patient with liver cirrhosis who underwent endoscopic variceal ligation (EVL): splenomegaly and increased SS value: 37.8 kPa

* Splenomegaly: Splenic index = a value of 44.4 cm^2 or greater

TheLiver Week 2019

234  June 20-22, 2019   |   BEXCO, Busan, South Korea
SS values:
According to spleen size and liver stiffness groups.

F0, F1 fibrosis group: 20.4 ± 5.7 (normal)
F2 and F3 fibrosis group: 31.9 ± 13.4 kPa
F4 cirrhosis group: 40.2 ± 10.5 kPa.

The no splenomegaly group: 23.7 ± 8.7,
The splenomegaly group: 35.1 ± 14.4 kPa.

Role of SS Measurement by 2D-SWE in Ruling Out the Presence of High-Risk Varices in Cirrhotic Patients

AUROC of LS and SS were 0.628 and 0.792, respectively. (SS> LS)

A Meta-analysis: Comparison of LS and SS for Esophageal Varices Diagnosis (LS< SS)

Summary: Take-home Messages

- 2D-SWE is a very useful non-invasive tool in evaluating liver fibrosis, portal hypertension, esophageal varices, and HCC.
- 2D-SWE is at least equal or slightly superior to TE in general (diagnostic performance, less limitation, etc.).
- However, large prospective multicenter studies are still limited and more clinical data are needed.
Image-guided percutaneous ablation is considered best in the treatment of early-stage hepatocellular carcinoma (HCC). Our 20-year outcomes show that ablation is a curative treatment and enables long-term survival. Since the ethanol injection period, we have had strong arguments regarding which treatment is superior for HCC, surgical resection or percutaneous ablation. A recent nationwide survey in Japan showed long-term survivals were similar between surgical resection and RFA. A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small HCC (SURF trial) recently demonstrated that the 3-year RFS of patients underwent surgery and RFA was 49.8%, 47.7%, respectively (hazard ration [HR] 0.96, 95% CI 0.72-1.28; \(P=0.793\)).

Various innovations have been introduced in the field of ablation, which would further improve outcomes. We developed a dedicated US transducer for puncture, with which we have performed RFA on 12,000 cases of liver tumors. A new version of this transducer with a better US image will be introduced into the market this year. Our dedicated procedure bed can keep a patient in an optimal position. Multimodality fusion imaging and US contrast agents are essential in our daily practice of ablation. We use these techniques in more than half of the cases. New-generation MWA systems incorporating antenna cooling and high-power generation have been receiving considerable attention. New-generation MWA can create a more predictable ablation zone, a larger ablation volume in a shorter procedure time. However, MWA antenna has some problems; it is difficult to insert into the liver. It cannot be seen clearly by US. It is easily broken. Further studies are needed from viewpoints of adverse events and long-term survival.

Incidentally, ablation is highly operator-dependent. Its skills and outcomes are very different from operator to operator. In order to disseminate skills and know-hows for ablation, we have held domestic training programs 12 times, with a total of 201 participants. We also have held international training programs six times, which were successfully completed with 91 participants in total. Programs are composed of comprehensive lectures, live demonstrations and case studies. Content of the lectures are overview of RFA, RFA devices, ultrasonography, and others. In the live demonstrations, RFA and new-generation MWA are performed on a wide variety of cases: cases of newly diagnosed cancer not difficult to ablate, tumors below the diaphragm requiring artificial ascites, in the caudate lobe, adjacent to the heart, a portal vein or hepatic vein, over 5 cm, more than five tumors, hepatic metastasis, etc. We demonstrate the importance of having appropriate patient posture, the usefulness of our original dedicated US transducer for interventional procedures and our dedicated procedure bed US-guided ablation, as well as ways to perform ablation under contrast-enhanced US guidance and with multimodality fusion imaging. In the case studies, difficult to ablate cases from participants’ hospitals are presented and discussed. Many participants remarked on the benefit of being directly trained in an academic environment. Questionnaire surveys revealed overwhelmingly positive feedback from the participants. Our programs may be useful to provide opportunities to understand basic concepts and learn essential technical tips in ablation.

Sophisticated ablation, which is potentially curative, minimally invasive and easily repeatable for recurrence, would be superior to conventional surgery in some selected cases.
New Insight for Lower Abdomen and Kidney USG

Seong Sook Hong
Soonchunhyang University Seoul Hospital, Korea

From Jan.1 2019, national health insurance was applied to the lower abdomen USG (appendix, small intestine, rectum, perineal area, inguinal area) and urinary USG (kidney, bladder, adrenal gland). Now we will discuss to these new issues about new applications and essential standard images about lower abdominal USG and urinary USG. The doctors who will perform ultrasonography have to obtain standard images and have to store the reading results of lower abdominal and urinary USG.

Keywords: Ultrasonography, Appendix, Intestine, Kidney urinary bladder

서 론

2019.2.1부터 하복부 초음파(충수,소장,대장,서혜부,직장,항문) 및 비뇨기(신장, 부산,방광) 초음파 요양급여 적용이 고시되었다. 진료의사의 의학적 판단에 따라 하복부나 비뇨기계에 질환이 의심되어 해부학적 이상을 진단하거나 정기적 관찰이 행해질 경우 진료보험 적용이 된다. 하복부 초음파는 급성 충수염을 포함한 장초음파와 신장 초음파, 골반 초음파를 일반적으로 통칭하나 이번 강의에서는 소장, 대장 충수의 초음파 소견과 신장 및 방광 초음파에 대하여 다루도록 한다. 장초음파는 통상 간이나 췌장 등과 비교할 때 소화관은 판내에 존재하는 공기에 의한 반향(reverberation)과 길이가 매우 길고 구불구불하게 이어져 있어서 초음파 검사가 좀 더 어려운 부위이다. 그러나 급성 우하복부 통증을 호소하는 환자에서는 일차적으로 별다른 전처리 없이도 비교적 유용하게 이용할 수 있는 영상기법이기도 하다. 특히 초음파 검사는 급성 충수돌기염(acute appendicitis)의 진단과 다른 질환과의 감별 진단에 매우 유용하다.

신장 초음파역시도 신장염이나 신장질의 같은 급성 질환이나 암검진 등의 목적으로 다양하게 사용되고 있다.

I. 하복부 초음파 보험

1. 산정요건
   획득해야 하는 표준 영상을 획득하고 검사의가 판독소견서를 작성하고 보관하여야 함. 단 제한초음파는 문제되는 부위 주변의 영상을 획득하고 판독소견서를 작성,보관하여야 함.

2. 표준영상
   가) 충수: 상행결장 횡스캔, 상행결장 종스캔, 충수의 장축스캔, 충수의 횡축스캔 (충수가 안보일 경우 맹장 말단부 스캔)
   나) 소장, 대장: 장간막동맥을 포함한 장간막 스캔, 회행판 스캔, 복부의 사분면인 우상부, 우하부, 좌하부의 장이 각각 포함되는 스캔
   다) 서혜부: 좌,우측 각각의 서혜부 횡스캔 좌,우 측 각각의 서혜부 종스캔
   라) 직장: 항문: 직장벽 5층이 포함되는 스캔, 항문의 하부스캔, 항문의 중부스캔, 항문의 상부스캔
3. 판독소견서
가) 등록번호, 성명, 생년월일 또는 나이, 성별, 검사명, 검사일시, 판독일시, 검사와 판독한 의사 (면허번호), 
검사소견, 결론, 의료기관명
나) 충수; 충수 관찰 여부, 충수가 관찰된 경우 직경, 장벽의 비후 여부, 복수 유무, 충수시 유무, 농양 또는 액체저류 유무
다) 서해부; 방장 유무, 종괴 유무, 림프절 비대 여부
라) 서혜부; 탈장 유무, 종괴 유무, 림프절 비대 여부
마) 항문; 치루 유무, 누관의 경로, 농양 유무, 종양 유무.

II. 장초음파
1. 정상 장의 해부학
상행결장은 후복막에 고정되어 있고 거의 일정한 위치에 있으나 병명을 사람에 따라 위치가 다양하게 위치 
해 골반강 내 혹은 상당히 상복부로 이동하여 위치하는 경우가 있어 주의를 요한다. 충수돌기는 횡막관의 약 
1-2 cm 하방, 즉 맹장의 후방중앙으로 주행하는 경우가 가장 흔하다. 6-7 cm 정도로 주행하는 연동운동이 없는 
끝이 막힌 관형구조물이다.
2. 장초음파감사법
A. 정상 소화관의 초음파상
정상 소화관은 초음파상으로 5층으로 분리되어 보인다. 정상 장관 두께는 3~5mm이고 특정적인 소견과 연동운 
동 등으로 부위를 구분할 수 있다.
대장은 분변이 차 있어 더 복잡한 초음파음향을 보인다. 대장의 내용물은 분변과 기포 및 공기 층이 혼재된 음 
영과 반향을 보며 정상의 경우에서 장벽이 잘 구분되어 보이지 않을 수도 있다. 분변은 내부에 미세 기포가 포 
함되어 있기 때문에 고에코로 보이지만 가스와는 달리 지저분한 후방음향을 동반하지 않는다. 분변과 가스 
음영 사이에 불규칙한 장관 내관으로 보이는 장의 특징적인 구조물은 결장팽기(haustra)가 보인다. 충수돌기 
는 회장 말단과는 달리 연동운동이 없다.
3. 충수돌기 스캔법
위에 언급한 방법대로 상행결장을 찾은 다음 횡스캔을 이용하여 화향관을 찾은 후 좀 더 하방의 충수돌기 시 
작부위를 찾는다. 대장의 분변이 많거나 가스가 많아 영상이 혼란될 때는 압박을 좀 더 하거나 후방 압박법, 체 
위변환 등의 방법을 사용해 본다. 점진적인 압박법 (graded compression technique)을 시행하여 장관과 지방 
층을 강압적으로 이동시키거나 압박하여 장관과의 거리를 줄여 주는 것이 해상도를 높여준다.
 후방압박법을 시행하면 장관과의 거리를 줄일 수 있고, 좌측누운위치 (left lateral decubitus 혹은 oblique position)을 취하게 되면 가스가 모여서 영상의 질을 좀 더 향상 시 
킬 수 있으나 환자가 피하지방이 많거나 충수가 깊게 위치한 경우에는 낮은 주파(low frequency)의 탐촉자로 바 
꾸어 주는 것이 좋다.
또한 이 방법은 환자가 가장 pain을 호소하는 Maximum tender point를 손가락으로 지적하게 한 후 그 
부위에 염증이 있는 appendix를 먼저 찾은 후, 맹장과 연결되어 있는 끝을 가진 맹관 인지를 확인 하고, 맹장과 
연결된 base를 확인하고, 그 상부의 IC Valve를 확인하는 방법이 있다.

III. 신장 초음파
1. 비뇨기 초음파
  1) 신장-부신: 신문(renal hilum)을 포함하는 좌·우신 각각의 관상면 스캔, 좌·우신 각각의 상부 횡스캔, 좌·우신 각각의 중간부 횡스캔, 좌·우신 각각의 하부 횡스캔.
※ 부산 종괴가 있는 경우 종괴를 포함한 스탠
2) 방광: 방광 상부 횡스캔, 방광 중간부 횡스캔, 방광 경부 횡스캔, 방광 중간부 시상면 스탠
3) 판독내용
가) 신장·부신: 신장 실질의 에코, 신장의 크기, 신장의 국소병변(낭종, 고형종괴 등) 유무, 수신증 유무, 부신 이상 유무
나) 방광: 방광벽 비후 여부, 방광 종괴 유무, 방광 결석 유무

2. 신장 초음파의 해부학

신장은 후복강의 장기로 신실파드와 신수질로 이루어진 신실질과 신배(calyx), 신우(pelvis), 신혈관과 결합조직 및 지방조직으로 구성된 신동(renal sinus)로 나뉘어 진다.

3. 신장의 스탠 방법

신장의 검사를 위해서는 특별한 전처치는 필요하지 않다. 다만 후복강내의 장기이기 때문에 앞쪽의 대장이나 위장관내의 의한 공기 음창의 방해를 받지 않도록 주의해야 한다. 그러므로 6-8시간의 금식을 권하며 후좌위 (supine position)가 기준 자세이고 경우에 따라 좌우위나 보성위를 시행하기도 한다. 한 환자에서 양쪽위, 왼위, 전위, 좌오위 등 다양한 자세로 바꾸어 검사하기도 한다. 같은 날 상부위장관 촬영이나 내시경 검사를 시행하는 경우는 초음파를 먼저 시행하는 것이 좋다. 우측 신장은 간의 우엽을 음창으로 사용하면 간실질의 에코와 간실질의 에코 차이를 비교하기 쉽다. 좌측 신장의 경우는 측우위 자세로 시행하는 것이 짧아 위해 가려진 좌측의 신장을 잘 관찰할 수 있다. 자세가 힘든 환자에서는 좌측 양구리에 베개를 넣는 방법도 많이 이용된다.

신장 초음파 검사의 일반적인 적응증은 신장 크기의 측정, 요관 막힘의 진단, 신장 종괴의 유무 및 감별진단, 신실질의 해부학적 변화가 의심되는 경우, 신혈관을 평가하고자 할 때이고 진동적인 급기증은 거의 없는 장점이 있다.

신장 질환에서 초음파의 진단 정확도는 76-98%로 보고되고 있으며, 사용하기 편하여 환자의 순응도가 높고, 비침습적이며 방사선 해가 없으며, 실시간 영상을 얻을 수 있다는 장점과 높은 적응증으로 비교적 많이 쓰이는 진단modality이란 연조직과의 구분이 다른 modalities에 비하여 낮고 비특이적이며, 시야가 좁고, 시술자 의존적이며, 환자의 체형에 영향을 받는다는 단점이 있다.

성인에서 주로 3-5 MHz 수평형(convex) 탐촉자를 이용하여 좌우 신문부(renal hilum)가 포함되도록 신장의 장축 방향으로 시상면 스탠하여 최대 장경의 신장크기를 측정하고 탐촉자를 평행하게 움직여 앞쪽에서 뒤쪽으로 수직 장경의 단면을 얻는다. 이때 수신증의 동반여부나 신장 실질 뒤쪽의 근위 요관(proximal ureter)도 관찰해야 한다. 신문부가 포함된 장축 중심에서 탐촉자를 수직으로 돌려 평행하게 신장의 상극(upper pole)에서 하극(lower pole)까지 스탠하여 좌측 단면 영상을 얻는다.

회색 초음파와 같은 순서로 석도플러 초음파를 시행하고 신혈관을 관찰한다. 신장이 보이는 시상면 석도플러 영상에서 엽관동맥(interlobar vessel)의 도플러 파형을 2회 이상 추출하여 저항지수(Resistive index;RI)를 측정한다.

방광 초음파는 소변을 참게 하거나 도뇨관을 통해 수액을 주입하여 방광을 확장 시킨 후에 시행해야 한다. 경계로 방광 전장부에서 방광 경부까지 관찰하고, 시상면에서 좌우 스캔하여 방광벽과 내부를 관찰한다. 잔뇨 검사 및 배뇨 후 전후 변이를 보기 위해 배뇨 후 영상을 추가하여 얻기도 한다. 이제 액체로 차 있는 방광은 artifact를 줄이기 위해 하모닉 영상을 추가하면 좋다.

4. 정상 신장 초음파 소견

초음파 검사에서 신실파드의 에코는 간이나 비장의 에코보다 약간 낮거나 거의 비슷한 정도로 보인다. 지방간이 있는 환자에서 만성 신질환이 동반되어 있을 경우, 정상처럼 보일 수도 있어 주의를 요한다. 신수질은 정상적으로 신실파드와 비교하여 약간 낮은 에코로 구분되어 보인다. 정상 성인에서 대략 반반의 두께를 차지한다. 신수질-피
질의 구별은 환자의 체형, 초음파 탐촉자의 주파수, 그리고 환자의 수분 공급상태에 따라 다르게 나타난다. 신동(renal sinus)는 신장 중앙에서 지방조직으로 인해 고에코로 보이며 종단 스캔에서는 난원형으로 횡단 스캔에서는 원형으로 보인다. 이를 중심에코복합체(central echo complex)라고 부른다. 복합신배의 영향으로 양측 극부위는 저에코로 보이게 되어 종괴로 오인되기도 한다. 피질-수질 경계부를 따라 가는 근마방(archeate artery)은 밝은 에코를 보인다. 소신배는 정상적으로 잘 구분이 어려우나 대신배와 신우는 얇은 벽을 가진 무에코의 낭성 구조로 보인다.

초음파에서 신장의 크기는 일반적으로 종축의 길이가 9-12 cm, 횡축의 길이가 4-5 cm 정도이다 양측 신장의 크기 차이는 1.5-2 cm이내이다. 신장의 크기를 측정할 때 조심해야 하는 것은 신장의 가장 장축을 측정해야 하는 것이다 신장은 축에 다양한 변이가 있어 탐촉자의 방향을 적절히 기울여 신장의 가장 장축을 찾는 것이 중요하다.

5. 신장초음파의 한계점

양측 극(pole)에 RCC가 있을 경우 종괴가 저에코로 보여 진단이 어렵고, 소량의 지방을 함유한 Angiomyolipoma의 경우도 RCC와 감별이 어렵다. 또한 신실질 질환을 감별하는 데도 어려움이 있고 신기능을 평가하기도 어렵다. 초음파만으로는 특이도와 민감도에 한계가 있다.

References
1. 최병인. 복부 초음파 진단학 입문 2006. 228-238.
Present and Future of National Health Insurance System for USG: What Do We Need to Prepare for?

Hong Soo Kim

Department of Internal Medicine, Soonchunhyang University, Chonan, Korea

In the past, the national insurance coverage of ultrasound examinations in South Korea was limited to cancer, heart and cerebrovascular diseases and rare incurable diseases.

As a Moon Jae-in Care, national medical insurance plan covered costs of abdomen ultrasonography in April, 2018.

Currently, the abdominal ultrasound starts with a budget of 250 billion won per year, and about 150,000 number of USG are made every month.

In the process of negotiations with the government, it is estimated that the medical system will cost at least 2 trillion won for financial estimation after the classification of the behavior of the ultrasound.

Accordingly, the definition and number of actions of abdominal ultrasound were newly determined through reclassification to 52 division, But it seem to be very complex and unclear.

The Korean association for the study of the liver should be recommends that accurate guidelines and set up to negotiate with the government, about the heath insurance review and assessment of abdominal ultrasonogram.

The aim of this presentation is to review the current changes of the present and anticipate the future of national health insurance system policy of abdominal ultrasound and think about what do we need to prepare for?
USG Trainee Session (*K)

Chair:
Young Seok Kim (Soonchunhyang Univ.)
How to Utilize the Various Functions of USG Machine

Moon Young Kim
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

Various Function of USG

- Doppler US
- CEUS
- Liver Package

Doppler US

- Blood velocity
- Blood flow
- Vein waveform
- Arterial resistance

Doppler US

Baik SK. LI 2010

Doppler effect

Christian Andreas Doppler
Doppler US

- Color Doppler
- Pulsed wave Doppler
- Continuous wave Doppler
- Power Doppler
- Spectral Doppler
- Duplex Doppler ultrasonography

CDUS for PHT in CLD

- Porto-systemic abdominal collaterals
- Splenomegaly
- Portal vein, splenic vein and mesenteric vein dilatation
- Reduction of the respiratory variations of splenic and mesenteric vein diameters
- Hepatofugal flow (reversal of flow) in the portal vein system
- Reduction of portal vein blood velocity
- Subclinical ascites
- Congestion index of the portal vein
- Flattening of Doppler hepatic vein waveform
- Eenal, splenic and SMA Doppler arterial impedance indexes

Porto-systemic abdominal collaterals

Reverse portal flow

- Hepatofugal portal blood flow has been observed in 3 = 15%
- In 228 pts with cirrhosis and PHT
- Child’s C (15.4%) and B (12.5%) vs. Child’s A (2.7%) (P < 0.02)
- Higher frequency of hepatic encephalopathy (21% vs. 7.2%; P < 0.05)
- Increase in variceal hemmorhage in 12-18 months follow up (P < 0.02)


Pulsed wave Doppler US - Vein

Blood velocity and flow

Portal vein
Splenic vein
**Portal & Splenic vein velocity & flow**

- PVV ↓, PVV < 15cm/s, ST 88% & SP 96% for PH
- PPF ↑
- SVV ↑
- SVF ↑

**Damping Index: Quantification of HVW**

**Doppler Hepatic Vein Waveform**

- Mono-phasic HV for severe portal hypertension (HVPG>15mmHg)
  - Odds ratio 28.8, sensitivity 74%, specificity 95%

**Pulsed wave Doppler US - Artery**

- Hepatic artery, splenic artery, renal artery
  - Resistive Index (RI)
  - Pulsatility Index (PI)

**superior mesenteric artery**

**Doppler US**

- Normal and abnormal resistance by RI and PI
HVW represents hemodynamic change by vasoactive agent

Terlipressin 2mg IV
Propranolol for 3m
HVPG: 18 mmHg
HVPG: 9 mmHg
HVPG: 16 mmHg
HVPG: 11 mmHg


What is CEUS?

US Contrast Agent(UCA)

FREE GAS BUBBLES
Free gas bubble 용어로 불리는 움직임을 응용할 수 있는 주기의 가스 자외선의 가스로 더욱 손해 버릴 것이다.

ENCAPSULATED AIR BUBBLES
Levovist
LOW SOLUBILITY GAS BUBBLES
Low solubility gas bubble 용어로 불리는 움직임을 응용할 수 있는 주기의 가스로, 스파이의 관점을 가질 수 있다.

US Contrast Agent(UCA)

Microbubble (⌀2-8μm)
- Small sphere of gas
- 2μm: Phospholipid layer for stabilization in blood
- Low MI imaging: stability, solubility

Structure of 2nd UCA

Phospholipid layer

Margaret A et al. Ultrasound 2016
**Mechanism of CEUS imaging**

- **3MHz US beam**
- **Non-linear harmonic**
- **500μm**
- **Non-linear harmonic**
- **Non-linear harmonic**
- **Non-linear harmonic**
- **Non-linear harmonic**

**Pulse Inversion Harmonic**

- **Basic principle: Detection of USCA**
- **Non-linear harmonic**
- **Non-linear harmonic**
- **Background: “ZERO”**

**UCAs – Mechanical index (MI)**

<table>
<thead>
<tr>
<th>MI value</th>
<th>Levovist</th>
<th>Sonazoid</th>
<th>SonoVue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **1st generation USCA**
  - **Levovist®**
  - **Bayer (Schering)**
  - **Air**
  - **Bubbles stick to galactose & thin palmitic acid shell**
  - **2-3 μm**

- **2nd generation USCA**
  - **SonoVue®**
  - **Bracco**
  - **Sulfur hexafluoride**
  - **Phospholipid**
  - **2.5 μm**

- **Sonazoid®**
  - **GE (Amersham)**
  - **Undisclosed perfluorcarbon**
  - **Lipid**
  - **3.0 μm**

**Contrast enhanced US(CEUS)**

- **2nd generation vs. 1st generation UCA**
  - **Low MI**
  - **High MI**
  - **Disappearance**
  - **Resonance**
  - **Harmonic Mode**
  - **Imaging method**
  - **Doppler Mode**
  - **Low MI**
  - **High MI**
  - **As CE disappears shortly;**
  - **High Real-time imaging**
  - **Observe organ continuously**
  - **Higher resolution**
  - **Insensitive to other mobilizing organs (eg, Heart)**
  - **Sensitive to mobilizing organs**
  - **Low resolution**

**Various UCAs**

<table>
<thead>
<tr>
<th>Products</th>
<th>Manufacturer</th>
<th>Inner gas</th>
<th>Outer shell</th>
<th>Mean size (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st generation USCA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levovist®</td>
<td>Bayer (Schering)</td>
<td>Air</td>
<td>Bubbles stick to galactose &amp; thin palmitic acid shell</td>
<td>2-3</td>
</tr>
<tr>
<td>2nd generation USCA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SonoVue®</td>
<td>Bracco</td>
<td>Sulfur hexafluoride</td>
<td>Phospholipid</td>
<td>2.5</td>
</tr>
<tr>
<td>Sonazoid®</td>
<td>GE (Amersham)</td>
<td>Undisclosed perfluorcarbon</td>
<td>Lipid</td>
<td>3.0</td>
</tr>
</tbody>
</table>
**SonoVue®**

- 2nd generation ultrasound contrast agent, Bracco, 2001
- made of sulfur hexafluoride and phospholipids
- Characterized by a microbubble structure consisting of gas bubbles stabilized by a shell
- SonoVue® microbubbles (2.5 microns) cross the pulmonary barrier and circulate within the blood vessels.

**Sonazoid®**

- perfluorbutane microbubbles suspended with 2 mL of attached water for injection.
- Usually, once for an adult, 0.015 mL/kg as suspension is administered intravenously.
- At late phase, phagocytosis by Kupffer cell – Kupffer image
- for Focal Liver Lesions in Ultrasonography

**UCAs hemodynamic in Liver**

- Early/Late vascular phase
- Parenchyma phase
- SonoVue
- Levovist
- Sonazoid

**Mass contrast enhanced US (Sonazoid)**

**HCC-sonazoid**
**Diagnosis - comparison with CT scan -**

- CEUS now almost equals CECT
  (in some instances, CEUS exceeds CT in accuracy)

- **Real time nature** of CEUS: reveals important rapid flow phenomena
  (CT, with its intermittent imaging, sometimes misses these)

- Partly, also the persistence of microbubbles beyond the large vessel enhancement period (the late phase) provides a marker for the sinusoidal space; lesions that lack this vascular space, notably metastases, appear as late phase defects (sinusoidal phase)

- The origin of this late phase suggests mechanisms include sinusoid pooling and RES/Kupffer cells uptake

---

**2nd UCA’s Safety**

- **Not nephrotoxic** and do not interact with the thyroid

- **Not necessary of renal function test before administration**

- Very safe with a low incidence of side effects

---

**Hemodynamic in cirrhosis**

- Hepatic Vein Arrival Time (HVAT) (sec)
  - Time until microbubble contrast arrive at hepatic vein after injection of microbubble contrast
  - Shortening in advanced fibrosis and cirrhosis due to abundant shunts formation

---

**Hepatic Vein Arrival Time (HVAT) (sec)**

- Shortening of HVAT – formation of collaterals and shunts
  - Intrahepatic sinusoidal remodeling
    - Capillarization and arterIALIZATION
  - New angiogenesis
    - Vascular endothelial growth factor (VEGF)
    - Platelet derived growth factor (PDGF)
    - Placental growth factor (PIGF)
  - Opening of pre-existing vessels
Liver Package for Diffuse Liver Disease

- Shear Wave Elastography
- Shear Wave Dispersion
- Attenuation Image

Shear Wave Elastography

- Deformation of tissue through strong push pulse, shear wave is generated.
- Shear wave propagates faster in stiffer tissue.
- Shear wave propagation (phase velocity) is traced.
- Plotting shear wave propagation with same interval.
- Elasticity (kPa) can be calculated through shear wave speed (m/s)

Liver Package

Liver Assessment
- Fibrosis ➔ Elastography
- Steatosis ➔ MRI or Biopsy
- Inflammation ➔ Biopsy

Shear Wave quantifies tissue stiffness that is correlated with fibrosis.
- Attenuation Imaging quantifies tissue attenuation that is correlated with fat infiltration.
- Dispersion Imaging quantifies frequency dispersion that is correlated with viscosity related to necro-inflammation.

Commercialized Abdominal Elastography Equipment

- Non invasive method
- Imaging depth affects global look at tissue
- Fat quantification
- Expensive
- Long exam time

- Non invasive method and cost effective
- 2D image + liver stiffness measurement
- Easy & short exam time
- Better spatial resolution

Liver Package for Diffuse Liver Disease

Shear Wave Elastography
Shear Wave Dispersion

- Visualizing and measuring frequency dispersion of shear wave propagation.
- Viscosity (inflammation, steatosis, circulation disorder etc), Dispersion
- Quantification of Dispersion \([\text{m/s/kHz}]\) allows estimation of liver viscosity.

Liver Package for Diffuse Liver Disease

Preliminary Clinical Evaluation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Viscosity</th>
<th>Elasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hepatitis</td>
<td>&gt;</td>
<td>&gt;</td>
</tr>
<tr>
<td>Cirrhosis model</td>
<td>&lt;</td>
<td>&gt;</td>
</tr>
</tbody>
</table>

- Elasticity → Fibrosis
- Viscosity → Necrosis & Inflammation of hepatocyte

Attenuation Imaging

- Quantify degree of attenuation by attenuation coefficient (dB/cm/MHz)
- Potential clinical benefit as an indicator of liver steatosis.

Attenuation Imaging

- The ultrasound waves in the body are attenuated by acoustic scattering, reflection, and absorption (heat).
- Attenuation is frequency-dependent.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Attenuation Coefficient (dB/cm/MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>0.00 - 0.06</td>
</tr>
<tr>
<td>Liver</td>
<td>0.10 - 0.30</td>
</tr>
<tr>
<td>Fat</td>
<td>0.10 - 0.30</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.37 - 0.55</td>
</tr>
</tbody>
</table>

ATI – Hepatic steatosis

ATI study with CAP

Dr. Hiroko Iijima
Department of Hepatobiliary and Pancreatic Disease
Hyogo College of Medicine, Japan
JSUM 2017
Summary

- US has some limitations in accuracy so it has been mainly applied as screening test in the past.
- However, US is one of the most promising non-invasive diagnostic tool for the detection of cirrhosis/portal hypertension and malignancy.
- Various new technology of US is upcoming beyond Doppler US including elastography, attenuation image, viscosity, contrast US.
- New horizon of Image biomarkers.
- Early try, early adapt, early research.
Basic Liver Scanning and Key Findings

Jeong Eun Song
Department of Internal Medicine, Daegu Catholic University School of Medicine, Daegu, Korea

Contents

• Liver Anatomy
  • Basic Liver scanning
  • Key Findings in USG

Liver anatomy – Couinaud segmentation

• Hepatic veins: 腹部の経路を取る
• Portal veins: 腹部の経路を取る

초음파 화면의 이해 : 3차원적 구조의 2차원적 이미지화

横向扫描 (Transverse scan)
초음파 화면의 이해 : 3차원적 구조의 2차원적 이미지화

초음파 화면의 이해: 3차원적 구조의 2차원적 이미지화

간구역구분의 Landmark

Contents

• Liver Anatomy

• Basic Liver scanning

• Key Findings in USG

탐측자 스캔 조작 방법

• 탐측자 위치

• 탐측자 움직임

일정한 순서로, 다양한 스캔법을 이용

환자의 머리쪽 구조가 화면의 왼쪽, 환자의 다리쪽 구조가 화면의 오른쪽에 위치합니다.

탐측자 위치

• Lt. lobe

• Rt. lobe

탐측자 움직임

• Longitudinal

• Transverse

• Subcostal

• Intercostal

Contents

• Liver Anatomy

• Basic Liver scanning

• Key Findings in USG
상복부 초음파 표준영상
보건복지부 고시 제2018-66호

1) 간좌엽의 종스캔
2) 간좌엽의 횡스캔
3) 간정맥의 늑간하스캔
4) 좌우간문맥 분기점의 횡스캔 (정밀)
5) 간우엽의 상부
6) 간우엽의 횡스캔
7) 우간문맥을 포함한 간우엽의 늑간스캔 (정밀)
8) 우간문맥을 포함한 간우엽의 늑간스캔 (정밀)
9) 우간하부와 우측신장피질의 늑간면 스캔

표준영상은 기본으로 조영과 이미지를 함께 결과로 남겨야 하지만, 초음파 검사의 기본적인 성격은, Live !
7. 우간문맥을 포함한 간우엽의 늑간스캔

8. 우간정맥을 포함한 간우엽의 늑간스캔

9. 우간하부와 우측신장피질의 관상면 스캔

Contents

- Liver Anatomy
- Basic Liver scanning
- Key Findings in USG
  - Diffuse liver disease
  - Focal liver lesions

Diffuse Liver Disease

- Fatty liver
- Chronic liver disease – Liver cirrhosis

Fatty liver

- Bright Liver
  - 신장 (hepatorenal contrast) 및 비장 (hepatosplenic contrast)에 비해 간실질의 에코가 높아짐
- Vessel blurring
  - 간실질 에코의 증가로 인해 간문맥의 벽에코가 보이지 않음
- Deep attenuation
  - 음향 감쇠의 증가로 인해 탄성질의 벽에코가 보이지 않거나 희미하게 보임
Fatty liver

- Echo pattern of liver parenchyme
  - coarse ~ meshwork pattern
  - fatty fibrotic pattern
- Liver surface irregularity
  - slightly irregular ~ nodular
- Change of liver contour
  - 간엽 끝이 둔화
  - 간좌엽 및 caudate lobe 비대
- Extrahepatic change (Liver cirrhosis)
  - Splenomegaly, ascites, GB wall edema, collateral circulation

Focal lesion in Fatty liver

- Focal fat sparing
- Focal fat deposition

Chronic liver disease – Liver cirrhosis

- Echo pattern of liver parenchyme
  - coarse ~ meshwork pattern
- Fatty liver cirrhosis
- Liver surface irregularity
  - 간엽 끝이 둔화
- 간좌엽 및 caudate lobe 비대
- Change of liver contour
- Extrahepatic change (Liver cirrhosis)
  - Splenomegaly, ascites, GB wall edema, collateral circulation

Focal liver lesions

- Liver cyst
- Hemangioma
- Hepatocellular carcinoma

Liver cyst

- Anechogenicity (무에코)
- Well-defined capsule (경계가 명확한 편막)
- Posterior enhancement (후방음영증가)
Hemangioma

- 전형적인 초음파 소견
  - 분명한 경계와 균일한 고에코
  - 간외 부방음향증강 소견이 동반

- 비전형적인 초음파 소견
  - 불규칙한 종괴 내부 에코
  - 고에코의 헤두리 (hyperechoic rim)가 동반
  - 지방간에서는 피로의 영향으로 보이기도 함

*비전형적인 초음파 소견은 지방간이나 만성 간염, 간경변증 등 주위 간실질 에코가 증가하는 경우에 흔히 관찰됨.
악성 간종양과의 감별이 어려운 경우가 흔함.

Hepatocellular carcinoma

- 동반점암 유무 확인 (만성 B형 간염, 만성 C형 간염, 간경변증 등)

- 다양화 초음파 소견
  - 내부 에코: 저에코, 고에코, 모자이크 양상 (> 4cm)
  - 변연저음영 (Halo sign)
  - 빈혈음영
    - Hump sign

- 형태에 따른 분류
  - 결절형 (nodular)
  - 고양형 (massive)
  - 미만형 (diffuse infiltrative)

Massive type HCC

Diffuse infiltrative type HCC
Pancreatobiliary USG Scanning Made Easy

Soon Sun Kim
Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Location of GB

- Main interlobar fissure
  (GB fossa between right & left lobe)

Normal GB

- 장경 10 cm 이하, 단경 5 cm 이하, 용적 100-160 ml
- 담낭두께: 공복시 2-3 mm, 식후 4-7 mm
Artifacts of GB

- Reverberation artifact
- Side lobe artifact
- Slice thickness artifact

Side lobe artifact

Slice thickness artifact

Portal vein and intrahepatic bile duct
Normal anatomy of IHD

2 or 3° IHD: < 1 mm

Main IHD: < 2 mm

Normal Anatomy of EHD

< 5 mm

< 6 mm

Rt. intercostal scan

Rt. longitudinal scan

Transverse scan

*Lt. decubitus position을 하면서 distal CBD까지 관찰 가능

한정 초음파 스캔
Normal ultrasonic anatomy

Ultrasonic Anatomy of the Pancreas

Scanning methods of the pancreas

Transverse or Oblique  Longitudinal  Lt intercostal trans-splenic

Transverse scanning

Oblique scanning
Transverse or Oblique Scanning

- Horizontal type
- Ascending type
- Sigmoid/Descending type

Rt. oblique scan in descending type

Longitudinal scan

- Pancreas head
- Pancreas neck
- Pancreas body

Trans-splenic view

Areas of the pancreas prone to miss

Holizontal Ascending Sigmoid/Descending
Disturbing factors for pancreas scan

- Mechanical compression
- Acoustic window (liver, spleen)
- Position change (sitting position)
- Fluid filled stomach

- Hyperechoic mass
- Dilated pancreatic duct
- Posterior wall of stomach

Water filling Method

Trans-splenic view

Sitting position

Pancreatic duct dilation vs. Splenic artery

췌담도 표준 영상

1. 간자회화의 응호선
2. 간자회화의 양호선
3. 간자회화의 통호선
4. 간자회화의 양호선
5. 간자회화의 응호선
6. 간자회화의 양호선
7. 간자회화의 통호선
8. 간자회화의 응호선
9. 간자회화의 양호선
10. 간자회화의 통호선
11. 간자회화의 응호선
12. 간자회화의 양호선
13. 간자회화의 통호선
14. 간자회화의 응호선

Pancreatic duct dilation vs. Splenic artery
췌담도의 초음파검사
✓ 초음파의 기본 원리를 숙지
✓ 충분한 시간동안 세밀하게 다양한 스캔법으로 검사
✓ 환자의 자세를 바꾸어 검사
✓ 다른 영상소견 및 Clinical finding과 연동하여 검토
✓ 의심시에는 반복검사 및 추적검사
✓ 필요시에는 추가 검사: CT, ERCP, MRCP
Plenary Session 1

Chairs: Joung Il Lee (Kyung Hee Univ.)
       Hee Jung Wang (Ajou Univ.)
       Jung-Hwan Yoon (Seoul National Univ.)

DAY 2: June 21, 2019, 10:10-11:10
The Discontinuation of Nucleos(t)ide Analogue Treatment Is Not Associated with Higher Risk of HBsAg-Seroreversion after Antiviral-Induced HBsAg-Seroclearance: A Multicenter Cohort Study

Minseok Albert Kim,1 Jeong-Hoon Lee,1 Young-Suk Lim,2 Dong Hyun Sina1, Yewon Park1, Seung Up Kim,3 Sang Gyune Kim,4 Yang Hyun Baek,5 Jae-Jun Shin,6 Heejooon Kang,7 Sun Woong Kim1, Cheol-Hyung Lee1, Yun Bin Lee1, Eun Ju Cho1, Su Jong Yu,7 Yoon Jun Kim1, Jung-Hwan Yoon1

1Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; 2Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 3Division of Gastroenterology and Hepatology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 4Department of Internal Medicine and Yonsei Liver Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; 5Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea; 6Department of Internal Medicine, Dong-A University College of Medicine, Busan, Korea; 7Department of Internal Medicine, Kyung Hee University School of Medicine, Seoul, Korea.

Aims: The discontinuation of nucleos(t)ide analogues (NAs) is recommended when HBsAg-seroclearance is achieved during NA treatment in patients with chronic hepatitis B, although the level of evidence is not high. We aimed to evaluate whether the discontinuation of NA treatment was as safe as continuation after NA-induced HBsAg-seroclearance.

Methods: This multicenter study included 318 patients who achieved HBsAg-seroclearance during NA treatment from 7 hospitals: 159 (53.7%) stopped NA treatment within 2 months after HBsAg-seroclearance (the NA-discontinuation group) and 137 (46.3%) continued NA treatment (the NA-continuation group). Primary endpoint was HBsAg reappearance and secondary endpoints included the development of HCC.

Results: During follow-up (median=32.3 months, interquartile range=0.9–124.1 months), 27 patients (8.5%) experienced HBsAg-reappearance and 7 (2.2%) developed HCC. The discontinuation of NA treatment was not an independent risk factor of HBsAg reversion (vs. continuation: hazard ratio [HR]=0.66, 95% confidence interval [CI]=0.30–1.44, P=0.30), whereas aminotransferase level of > 40 IU/L at the time of HBsAg-seroclearance (HR=2.61, 95% CI=1.11–6.13, P=0.03) and previous experience of ≥2 NA treatment regimens (HR=2.38, 95% CI=1.10–5.15, P=0.03) were independent risk factors (Table 1). The cumulative probabilities of HBsAg-reappearance at years 1, 3, and 5 were 4.5%, 7.9%, and 7.9% in the NA-discontinuation group; and 12.8% and 12.8% in the NA-continuation group, respectively. The NA-discontinuation was not independently associated with higher risk factor of HCC development (HR=0.45, 95% CI=0.05–4.33, P=0.49), either. Interestingly, HBsAg-seroreversion was an independent risk factor of HCC development (HR=9.01, 95% CI=1.86–43.82, P=0.01) (Table 2).

Conclusions: The discontinuation of NA was not associated with higher risk of either HBsAg-reappearance or HCC development among patients achieving NA-induced HBsAg-seroclearance. HBsAg-reappearance was independently associated with higher risk of HCC development.

Table 1. Cox regression analyses for HBsAg reversion

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60 yr</td>
<td>1.41 (0.63–3.13)</td>
<td>0.66 (0.30–1.44)</td>
</tr>
<tr>
<td>Male</td>
<td>2.31 (0.80–5.58)</td>
<td>2.61 (1.11–6.13)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1.95 (0.90–4.22)</td>
<td>3.16 (1.33–7.77)</td>
</tr>
<tr>
<td>ALT &gt; 40 IU/L</td>
<td>3.16 (1.33–7.77)</td>
<td>3.16 (1.33–7.77)</td>
</tr>
<tr>
<td>Exposure to ≥ 2 NAs</td>
<td>2.38 (1.10–5.14)</td>
<td>2.38 (1.10–5.14)</td>
</tr>
<tr>
<td>NA-discontinuation</td>
<td>0.57 (0.26–1.22)</td>
<td>0.57 (0.26–1.22)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, ALT >40 IU/L, and NAs ≥2.

Table 2. Cox regression analyses for HCC development

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60 yr</td>
<td>3.81 (0.87–17.05)</td>
<td>6.03 (1.35–31.55)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>9.65 (1.16–80.21)</td>
<td>5.23 (0.47–57.99)</td>
</tr>
<tr>
<td>ALT &gt; 40 IU/L</td>
<td>9.00 (2.21–44.3)</td>
<td>3.71 (0.67–20.71)</td>
</tr>
<tr>
<td>Exposure to ≥ 2 NAs</td>
<td>2.46 (0.95–11.02)</td>
<td>2.46 (0.95–11.02)</td>
</tr>
<tr>
<td>HBsAg reversion</td>
<td>13.29 (2.97–59.38)</td>
<td>9.01 (1.86–43.82)</td>
</tr>
<tr>
<td>HIV DNA re duplication</td>
<td>1.63 (0.20–13.60)</td>
<td>1.63 (0.20–13.60)</td>
</tr>
<tr>
<td>NA-discontinuation</td>
<td>0.34 (0.02–1.30)</td>
<td>0.45 (0.05–4.33)</td>
</tr>
</tbody>
</table>

*Adjusted for age, cirrhosis, ALT >40 IU/L, and HBsAg reversion.

Keywords: Chronic hepatitis B, HBsAg-seroclearance, Nucleos(t)ide analogue, Hepatocellular carcinoma

Gender Differences in the Association of Adipose Tissue and Sarcopenia in Patients with Cirrhosis

Seong Hee Kang,1 Soon Koo Baik,2 Moon Young Kim

1Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, 2Regeneration Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea

Background and Aims: We investigated the independent prognostic significance of visceral and subcutaneous adiposity in predicting mortality in cirrhosis.

Method: The skeletal muscle (SM) and adipose tissue markers, including the visceral adipose tissue index (VATI, cm²/m²) and the subcutaneous adipose tissue index (SATI, cm²/m²) were esti-
Plenary Session 1

**Ephrin-A3 (EFNA3) Is a Key Player in Hypoxic Microenvironment of Hepatocellular Carcinoma**

Abdullah Husain, Elley Yung-Tuen Chiu, Daniel Wai-Hung Ho, Karen Man-Fong Sze, Lo-Kong Chan, Yu-Man Tsui, Carmen Chak-Lui Wong, and Irene Oi-Lin Ng

**Aims:** Intra-tumoral hypoxia is a critical driver of disease progression in hepatocellular carcinoma (HCC). However, mechanistic understanding of this phenomena is still lacking.

**Methods:** Integrative analysis of multiple transcriptomic profiles was performed to identify clinically relevant genes upregulated by hypoxia in HCC. EFNA3 knockdown cell models were generated to evaluate its functional role and determine the corresponding Eph receptor activity using human RTK phosphorylation antibody array. Cancer stemness marker based sorted cells from PDTX models and patients were analysed for expression of EFNA3.

**Results:** Our integrative analysis identified Ephrin-A3 (EFNA3) as a potential hypoxia-regulated gene target related to disease progression in HCC. EFNA3 encodes Ephrin-A3, a membrane bound ligand for multiple members of the Eph receptor family. EFNA3 was found to be significantly overexpressed in human HCC samples (n=97, p<0.0001). Clinicopathological correlation analysis revealed significant association of EFNA3 overexpression with advanced tumor stage and presence of venous invasion. Functionally, EFNA3 was upregulated in multiple HCC cell lines upon hypoxia treatment, and this upregulation was abolished upon knockdown of HIF-1α or HIF-2α. Knockdown of EFNA3 significantly reduced proliferative, migratory and self-renewal ability of HCC cells in normoxia and hypoxia in vitro, and resulted in lower tumor incidence rate, smaller primary tumor size and fewer lung metastases in vivo. HCC PDTX model sorted for multiple liver cancer stemness markers population demonstrated higher EFNA3 expression. Human HCC samples enriched for CD47 showed higher expression of EFNA3 (n=15). Moreover, EFNA3 knockdown reduced expression of CD47. Mechanistically, evaluation of relative phosphorylation levels of Eph receptors upon EFNA3 knockdown in various HCC cell lines revealed consistent inactivation of multiple candidate Eph receptors, hinting at their critical role in HCC.

**Conclusions:** EFNA3 was identified as a frequently overexpressed hypoxia-inducible gene in human HCC. Our findings suggests it may play a critical role in hypoxia driven disease progression of HCC.

**Keywords:** Hepatocellular Carcinoma, Hypoxia, Cancer stemness, Ephrin
tial after liver transplantation (LT) in HBV-associated recipients. This study established an individualized HBV prophylaxis protocol, through optimization of hepatitis B immunoglobulin (HBIG) administration, with application of simulative half-life (SHL).

Methods: This study involved five parts: Part 1 developed the SHL estimation method with 20 patients; Parts 2 and 3 assessed the SHL variability and developed a simulation model to apply SHL in 100 patients; Part 4 validated the simulation model in 114 patients, and Part 5 was a cross-sectional study on current status of HBIG infusion intervals in 660 patients.

Results: In Part 1, infusion of 10,000 IU HBIG induced add-on rise anti-HBs titer of 5252.5±873.7 IU/L, and mean SHL of 20.0±3.7 days were 4.4% lower and 2.2% longer than the actual measurements, respectively. In Part 2, the medians of the intra- and inter-individual coefficient of variation in SHL were 13.5% and 18.5%, respectively. Pretransplant HBV DNA load and posttransplant antiviral therapy did not affect SHL. In Part 3, a simulation model was developed to determine the interval of HBIG infusion, by using SHL. In Part 4, all 114 patients were successfully managed with regular HBIG infusion intervals of ≥8 weeks, and the interval was prolonged to ≥12 weeks in 89.4%, with a target trough anti-HBs titer ≥200 IU/L. In Part 5, 47.4% of our patients received HBIG excessively, at a target trough titer of 500 IU/L.

Conclusions: SHL estimation using only clinically available parameters seems to be reliably accurate when compared with actual measurements. We believe that SHL estimation is helpful to establish a personalized HBV prophylaxis protocol for optimizing HBIG administration.

Keywords: HBIG, Recurrence, Prophylaxis, Hepatitis B virus
Plenary Session 2

Chairs:  Joong-Won Park (National Cancer Center)
        Han Chu Lee (Univ. of Ulsan)
        Myung-Hee Yoon (Pusan National Univ.)

DAY 3: June 22, 2019, 11:20-12:20
PS 2-1

Novel SNPs for Screening of Nonalcoholic Fatty Liver Disease: A Korean Population-Based Study

Min-Su Park
Department of Surgery, Kyung Hee University, Korea

Aims: Genetic susceptibility plays a key role in the development of nonalcoholic fatty liver disease (NAFLD). The fatty liver index (FLI) is a simple and accurate noninvasive method for predicting NAFLD. The aim of this study was to identify novel susceptibility genes associated with NAFLD as assessed by the FLI by performing a genome-wide association study (GWAS).

Methods: A prospective cohort study of 52510 adults (25840 men and 26670 women) aged 40–70 years was examined. Patients were classified into three groups by FLI (FLI <30, no NAFLD; FLI ≥60, NAFLD; and 30 ≤ FLI <60, intermediate FLI). To investigate the severity of fibrosis, NAFLD patients were stratified into three groups based on their NAFLD scores (NAFLD score <1.455, low fibrosis; NAFLD score > 0.676, advanced fibrosis; and -1.455 ≤ NAFLD score ≤ 0.676, intermediate fibrosis). We investigated single-nucleotide polymorphisms (SNPs) related to NAFLD.

Results: After adjusting for age, sex, and body mass index, 20 SNPs in 12 genes (rs10790162, rs9326246, rs2075290, rs2266788, rs964184, rs7350481, rs780093, rs780094, rs1260326, rs10401969, rs671, rs11066280, rs11066015, rs150401869, rs1109501, rs3782886, rs76178990, rs61737409, rs201338826, and rs1448349) showed significant associations with the susceptibility to NAFLD (P<0.0001). Five genes (BUD13, GCKR, KCNQ2, MUC7, and C12orf51) of 12 genes were duplicated and meaningful. Seven SNPs in 3 genes (rs780093, rs1260326, rs1109501, rs1448349, rs780092, rs780094, and rs11249502) showed significant associations with the severity of liver fibrosis based on the NAFLD fibrosis scores.

Conclusions: We demonstrated that 20 SNPs in 12 genes are significantly associated with the presence of NAFLD in a Korean population. These findings suggest the value of genetic factors in the pathogenesis of NAFLD.

Keywords: NAFLD, Fatty liver index, GWAS

PS 2-2

Statin Use and the Risk of Hepatocellular Carcinoma in Patients with Chronic Hepatitis B

Myung Ji Goh, Dong Hyun Sinn, Wonseok Kang, Geum-Youn Gwak, Yong-Han Paik, Moon Seok Choi, Joon Hyeok Lee, Kwang Cheol Koh, Seung Woon Paik
Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: Statins have pleiotropic effects which may include chemoprevention. Several observational studies have suggested that statins may prevent hepatocellular carcinoma (HCC) but they have not yet been fully studied in patients with chronic hepatitis B virus (HBV) infections.

Methods: A hospital-based retrospective cohort of 7,713 chronic HBV-infected individuals between January 2008 and December 2012 were analyzed. The primary outcome was the development of HCC. Patients who used statins for at least 28 cumulative defined daily doses (cDDD) during the follow-up period were defined as statin users (n = 713). The association between the use of statins and the incidence of HCC was analyzed using the multivariable Cox proportional hazards model with time-dependent covariates.
Results: During a median follow-up of 7.2 years (min-max: 0.5-9.7), HCC newly-developed in 702 patients (9.1%). Statin use was associated with a lower risk of HCC (adjusted hazard ratio (HR)= 0.36, 95% confidence interval (CI): 0.19-0.68, adjusted for age, sex, cirrhosis, diabetes, hypertension, serum alanine aminotransferase, cholesterol, HBV DNA level, antiviral treatment, and antiplatelet therapy). The observed benefit of the statin was the greatest in the highest cumulative-dose group with more than 1095 cDDDds of statin (adjusted HR= 0.63, 95% CI: 0.31-1.28; HR= 0.51, 95% CI: 0.21-1.25, HR= 0.32, 95% CI: 0.07-1.35, and HR= 0.17, 95% CI: 0.06-0.48 for patients with statin use of 28-365, 366-730, 731-1095, and more than 1095 cDDDds, respectively). In subgroup analysis, the association between statin use and reduced HCC risk was significantly or marginally significantly observed regardless of status of liver cirrhosis and presence of diabetes.

Conclusions: Statin use was associated with a reduced risk of HCC development in chronic HBV-infected patients after adjustment for important confounders in a dose-dependent manner. These findings warrant a prospective evaluation.

Keywords: Statin, HCC, Liver cirrhosis, Chronic hepatitis B

Robotic Major Liver Resections: Surgical Outcomes Compared with Open Major Liver Resections
Hye Yeon Yang, Seoung Yoon Rho, Dai Hoon Han, Jin Sub Choi, Gi Hong Choi
Division of Hepatobiliary and Pancreas, Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

Background: Laparoscopic liver resection has been rapidly developed, laparoscopic major liver resections are still considered innovative procedures according to the second international consensus conference. Robotic surgery overcomes the limitations of laparoscopic techniques and is gaining popularity in many centers. In this study, we investigated surgical outcomes after robotic major liver resections.

Method and materials: From January 2009 to October 2018, 70 patients underwent robotic major liver resections, which included conventional major liver resections and sectionectomy of the right liver. Short-term and long-term outcomes were compared with 252 open major liver resections, which were performed during the same period.

Results: Hepatocellular carcinoma (HCC) was the most common diagnosis in robotic (n=41) and open group (n=170). Operative time was longer in robotic group (472 min vs 349 min, p<0.001), however estimated blood loss was lower in robotic group than open group (269 mL vs 548 mL, p=0.009). Postoperative complication rate of robotic group was lower than the open resection (p<0.001). Hospital stay was shorter in robotic group (9.5 days vs 15.1 days, p=0.006). There were no significant differences in overall (p=0.22,) and disease free survival (p=0.19) between the two groups in HCC. In the propensity score matching in 27 pairs with similar baseline characteristics, operative time was longer in robotic group than open group (482 min vs.374 min, p=0.04) but hospital stay was shorter in robotic group (8.9 days vs 14.4 days, p=0.001). However, there was no difference in complication rates (p=0.084) and estimated blood loss (p=0.107) between two paired group. Overall survival and disease free survival showed no difference between paired HCC groups after PSM.

Conclusion: Robotic major liver resections showed improved perioperative outcomes and comparable long-term oncologic outcome compared with open resections. Therefore, robotic surgery should be considered one of the options for minimally invasive major liver resections.

Table 1. Patient characteristics of cohort

<table>
<thead>
<tr>
<th>Variables (Mean ± SD)</th>
<th>Robotic resection (N=70)</th>
<th>Open resection (N=252)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.6 ± 11.36</td>
<td>59.3 ± 10.1</td>
<td>0.797</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.044</td>
</tr>
<tr>
<td>Male</td>
<td>44 (62.9%)</td>
<td>189 (75.0%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 (29.2%)</td>
<td>63 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 3.2</td>
<td>23.7 ± 3.6</td>
<td>0.593</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td></td>
<td></td>
<td>0.561</td>
</tr>
<tr>
<td>None</td>
<td>31 (44.3%)</td>
<td>104 (41.3%)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>38 (54.3%)</td>
<td>138 (54.8%)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1 (1.4%)</td>
<td>10 (4.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Perioperative outcomes of liver resection

<table>
<thead>
<tr>
<th>Variables (Mean ± SD)</th>
<th>Robotic resection (N=70)</th>
<th>Open resection (N=252)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right hemihepatectomy</td>
<td>17 (24.3%)</td>
<td>120 (47.6%)</td>
<td></td>
</tr>
<tr>
<td>Left hemihepatectomy</td>
<td>37 (52.9%)</td>
<td>56 (22.2%)</td>
<td></td>
</tr>
<tr>
<td>Central bisectionectomy</td>
<td>2 (2.9%)</td>
<td>26 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Right posterior sectionectomy</td>
<td>11 (15.7%)</td>
<td>37 (14.7%)</td>
<td></td>
</tr>
<tr>
<td>Right anterior sectionectomy</td>
<td>3 (4.3%)</td>
<td>13 (5.2%)</td>
<td></td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>472.0 ± 202.7</td>
<td>349.0 ± 144.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative complication (Clavien-Dindo )</td>
<td>269.9 ± 353.8</td>
<td>548.5 ± 536.7</td>
<td>0.009</td>
</tr>
<tr>
<td>No</td>
<td>48 (68.6%)</td>
<td>105 (41.7%)</td>
<td></td>
</tr>
<tr>
<td>I, II</td>
<td>20 (28.6%)</td>
<td>126 (50%)</td>
<td></td>
</tr>
<tr>
<td>III, IV</td>
<td>2 (2.9%)</td>
<td>207 (79.9%)</td>
<td></td>
</tr>
<tr>
<td>V (death)</td>
<td>0 (0%)</td>
<td>10 (4.0%)</td>
<td></td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>9.5± 6.3</td>
<td>15.1± 8.2</td>
<td>0.006</td>
</tr>
</tbody>
</table>
The Liver Week 2019

(a) Overall survival

(b) Disease free survival

Figure 1. Survival analysis of hepatocellular carcinoma

(a) Overall survival

(b) Disease free survival

Figure 2. Survival analysis of liver metastasis

Figure 3. Survival analysis of cholangiocarcinoma

Table 3. Patient characteristics between robotic anatomical resection and open resection after propensity score matching

<table>
<thead>
<tr>
<th>Variables (Mean ± SD)</th>
<th>Open resection (N=27)</th>
<th>Robotic resection (N=27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.1 ± 9.6</td>
<td>58.4 ± 9.1</td>
<td>0.377</td>
</tr>
<tr>
<td>Sex</td>
<td>0.499</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23 (85.2%)</td>
<td>20 (74.1%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (14.8%)</td>
<td>7 (25.9%)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.9 ± 4.8</td>
<td>23.9 ± 2.7</td>
<td>0.348</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0.736</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7 (25.9%)</td>
<td>9 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>18 (66.7%)</td>
<td>17 (63.0%)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>2 (7.4%)</td>
<td>1 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>3.2 ± 1.2</td>
<td>3.2 ± 1.6</td>
<td>0.850</td>
</tr>
</tbody>
</table>

Table 4. Perioperative outcomes between robotic anatomical resection and open resection after propensity score matching

<table>
<thead>
<tr>
<th>Variables (Mean ± SD)</th>
<th>Open resection (N=27)</th>
<th>Robotic resection (N=27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation</td>
<td>0.019</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right hemihepatectomy</td>
<td>15 (55.6%)</td>
<td>9 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Left hemihepatectomy</td>
<td>4 (14.8%)</td>
<td>13 (48.1%)</td>
<td></td>
</tr>
<tr>
<td>Central bisectionectomy</td>
<td>4 (14.8%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Right posterior sectionectomy</td>
<td>3 (11.1%)</td>
<td>5 (18.5%)</td>
<td></td>
</tr>
<tr>
<td>Right anterior sectionectomy</td>
<td>1 (3.7%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Length of stay (months)</td>
<td>14.4 ± 6.9</td>
<td>8.9 ± 3.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>374.4 ± 165.8</td>
<td>482.3 ± 215.1</td>
<td>0.044</td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>511.5 ± 423.9</td>
<td>336.1 ± 359.9</td>
<td>0.107</td>
</tr>
<tr>
<td>Postoperative complication (Clavien-Dindo)</td>
<td>0.084</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No</td>
<td>9 (33.3%)</td>
<td>17 (63.0%)</td>
<td></td>
</tr>
<tr>
<td>- I/II</td>
<td>15 (55.6%)</td>
<td>9 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>- III, IV</td>
<td>3 (11.1%)</td>
<td>1 (3.7%)</td>
<td></td>
</tr>
</tbody>
</table>
Early Reduction of Regulatory T Cells by Calcineurin Inhibitor Is Associated with Acute Rejection in Liver Transplantation

Ji Won Han1,2, Dong Jin Joo3,4, Jong Hoon Kim1,2, Min-Seok Rha1, June Young Koh1, Hye Jung Park1,4, Jae Geun Lee1, Myoung Soo Kim2, Soon Il Kim2, Eui-Cheol Shin1, Jun Yong Park1,*, Su-Hyung Park1,*

1Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Republic of Korea; 2Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea; 3Department of Dermatology, Cutaneous Biology Research Institute, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 4Department of Internal Medicine, Yonsei University College of Medicine, Yonsei Liver Center, Severance Hospital, Seoul, Republic of Korea; *These authors contributed equally to this work.

Aims: Regulatory T (Treg) cells are important in preventing acute rejection in solid organ transplantation, but the clinical relevance of the different kinetics after liver transplantation (LT) in acute rejectors and non-rejectors is unclear.

Methods: We analyzed peripheral blood samples of LT recipient receiving tacrolimus-based immunosuppression from a discovery cohort from 2013 to 2016 (n=64) and a validation cohort from 2017 to 2018 (n=64). Samples were obtained at pre-transplantation, D7, and D30 after LT. Treg frequency was analyzed by flow cytometry. MLR assay was performed using recipient PBMCs (pre-transplantation) and matched irradiated donor PBMCs. Apoptosis and IL-2 signaling by Tregs from recipients were investigated. The predictive value of Treg frequency at D7 was assessed in the discovery cohort and was validated in the validation cohort.

Results: We found that the frequencies of total and activated Tregs at D7 were significantly lower in recipients with acute rejectors (n=12) than non-rejectors (n=52). Tacrolimus-induced Treg suppression was predominant in rejectors. Moreover, an early reduction of Treg frequency in rejectors was associated with a greater increase in Treg apoptosis and further attenuated IL-2 signaling. In multivariate analysis, Treg frequency at D7 was an independent risk factor of acute rejection (AR) and significantly predicted AR, which was subsequently validated in the validation cohort (n=64).

Conclusions: Our results suggest that first-week blood Treg frequency after LT may be a useful biomarker for predicting AR in transplant recipients under conventional immunosuppression, which may contribute to improving long-term outcomes of LT by pre-identifying recipients at risk for AR.

Keywords: Liver transplantation, Acute rejection, Regulatory T cell, Calcineurin inhibitor
Free Paper Session

O-001~O-006  HBV
O-007~O-012  ALD & NAFLD
O-013~O-018  Liver Cancer, Basic
O-019~O-024  Cirrhosis & Liver Failure
O-025~O-030  HCV
O-031~O-036  Liver Cancer
O-037~O-044  Surgery, Biliary
O-045~O-052  Surgery, Technical Issues
O-053~O-060  ALD & NAFLD
O-061~O-066  Liver Transplantation
O-067~O-072  HBV
O-073~O-078  Liver Cancer, Clinical
O-079~O-084  Cirrhosis & Liver Failure
O-085~O-090  Liver Cancer, Clinical
O-091~O-096  Liver Cancer, Clinical
O-097~O-102  Basic & Others
1. HBV

June 21, 2019

Regular Follow-Up and Mortality in Patients with Chronic Hepatitis B: A National Health Insurance Cohort Study

Jae-Jun Shim1, Gi-Ae Kim1, Eunhye Kang1, Jisun Myung1, In-Hwan Oh2, Byung-Ho Kim3

1Department of Internal Medicine, 2Departments of Preventive Medicine, School of Medicine, Kyung Hee University, Seoul, Korea

Aims: Chronic hepatitis B (CHB) is a major cause of liver-related mortality in Asian countries. Regular medical follow-up can be highly necessary for patients with CHB as it can increase the likelihood of treatment and surveillance testing and ultimately reduce liver-related mortality. In this large cohort study, we aimed to investigate whether regular follow-up can reduce overall or liver-cancer mortality in patients with CHB.

Methods: CHB patients who were newly diagnosed between 2007 and 2013 were collected from customized health data of Nation Health Insurance Service in Korea. The patients who developed liver cancer or died from any diseases within 2 years were excluded. Follow-up was defined when the patients were cared in clinics or hospitals under diagnosis of CHB (B180 or B181). The number of follow-up for CHB was counted every 3-month interval during 2 years after the first diagnosis. The number 0, 1 to 3, and 4 to 8 were classified as none, irregular, and regular follow-up group, respectively. Liver cancer incidence and its mortality after 2 years of diagnosis was investigated among groups.

Results: Of 414,074 patients with CHB, regular follow-up rate was 22.9%. Cirrhotic patients had more regular follow-up than non-cirrhotic patients (60.9% vs. 20.3%, P<0.0001). Although more liver cancers were diagnosed in regular follow-up group than in none follow-up group (Hazard ratio [HR], 1.538; 95% confidence interval [95% CI], 1.436–1.647; P<0.0001), liver-cancer mortality was significantly lower in regular follow-up group than in none follow-up group (HR, 0.597; 95% CI, 0.569–0.625; P<0.0001). The favorable effects of regular follow-up was consistently observed in both cirrhotic and non-cirrhotic patients. The best follow-up number associated with the lowest overall mortality was eight (follow-up every 3 months).

Conclusions: Regular follow-up at least twice a year can significantly reduce liver-cancer and overall mortality in patients with CHB.

Keywords: Hepatitis B, Chronic, Mortality, Office visits, Liver neoplasms

O-002

Bone and Renal Safety Improvements in CHB Patients Switched to Tenofovir Alafenamide (TAF) after Tenofovir Disoproxil Fumarate (TDF) Treatment

Wai Kay Walter Seto1, Maria Buti2, Namiki Izumi3, Young-Suk Lim4, Jia-Horng Kao5, Adrian Streinu-Cercel6, Elena Nurmulhametova7, Xiaoli Ma8, Fehmi Tahak9, Maciej Jablonski10, Vithika Suri11, John F. Flaherty11, Audrey H. La12, Anuj Gaggar13, Shuyuan Mo14, Abhijit Chowdhury12, Scott K. Fung13, Wan-LONG Chiang14, Edward J. Gane15

1Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong; 2Hospital Universitari Vall d’Hebron, Barcelona, Spain; 3Department of Gastroenterology and Hepatology, Japan Red Cross Musashino Hospital, Tokyo, Japan; 4Department of Gastroenterology, Assan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 5Department of Internal Medicine, Division of Gastroenterology and Hepatology, National Taiwan University Hospital, Taipei, Taiwan; 6National Institute for Infectious Diseases Matei Bals, Bucharest, Romania; 7Infectious Clinical Hospital #1 of Moscow Healthcare Department, Moscow, Russian Federation; 8Xiaoli Ma, PC, Bryn Mawr, PA, United States; 9Infectious Diseases, Istanbul Universitesi Cerrahpaşa Tip Fakultesi Hastanesi, Istanbul, Turkey; 10Oddziak Obserwacyjno-Zakazny Poland; 11Gilead Sciences, Inc, Foster City, California, USA; 12Department of Hepatology, School of Digestive & Liver Diseases, Instituto of Post Graduate Medical Education and Research,Kolkata, India; 13University of Toronto, Toronto, on, Canada; 14Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; 15Auckland Clinical Studies, Auckland, New Zealand

Aims: As part of a protocol amendment to extend double blind (DB) treatment for 1 additional year (96w to 144w), only ~50% consented in time for this change; the remainder had already been receiving open-label (OL) TAF after 96w. Here, we evaluate the 4 years (192w) safety and efficacy of switching to OL TAF in patients who had received DB TDF treatment for either 2 or 3 years.

Methods: In 2 identically-designed studies, 1298 HBeAg-negative and HBeAg-positive CHB patients (873 TAF, 425 TDF) were randomized and treated with either TAF or TDF. In the TDF group, 180 patients were switched to OL TAF at 96w, while 202 patients switched at 144w. Viral suppression, biochemical responses and safety improvements were assessed at 192w using the time of rollover to TAF as the respective OL baseline (BL). Within group changes in bone and renal parameters were assessed by paired t test or Wilcoxon signed rank test.

Results: Patient characteristics were similar for those receiving OL TAF for 1 or 2 years following DB TDF treatment. Significant increases in eGFRc0 from OL BL were observed within each group at Week 192 (Table). Significant increases in hip and spine BMD from OL BL occurred within each group. Within each group, virologic suppression (HBV DNA <29 IU/mL) was maintained from OL BL to 192w in patients who remained on TAF treatment (OL TAF 96w group: 88% and 88%; OL TAF 48w
A Phase 3, Stable Switching from Tenofovir Disoproxil Fumarate (TDF) to Tenofovir Alafenamide (TAF) in Chronic Hepatitis B (CHB) Patients: 48w Results

Sang Hoon Ahn1, Won Young Tak2, Seung-Kew Yoon3, Young-Suk Lim4, Kwan Soo Byun5, June Sung Lee6, Yoon Jun Kim6, Hyung Joon Kim6, Seung Woon Paik7, Henry LY Chan10

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Korea; 3Department of Internal Medicine, Seoul St. Mary’s Hospital, The Catholic University Liver Research Center, The Catholic University of Korea, Seoul, Korea; 4Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 5Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea; 6Department of Internal Medicine, Inje University College of Medicine, Goyang, Korea; 7Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 8Department of Internal Medicine, College of Medicine, Chung-Ang University College of Medicine, Seoul, Korea; 9Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 10Institute of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Background and Aims: TAF, a novel prodrug of tenofovir (TFV), has greater plasma stability and reduced circulating levels of TFV compared to TDF at approved doses. TAF has shown efficacy non-inferior to TDF with improved renal and bone safety in viremic CHB patients. We evaluated efficacy and safety in stable, virally-suppressed patients who were switched from TDF to TAF vs. continued TDF for an additional year.

Methods: In this Phase 3 study (NCT02979613), CHB patients on TDF for ≥48w with HBV DNA <LLOQ (local laboratory) for ≥12w and <20 IU/mL at screening were randomized (1:1) to TAF 25 mg QD or TDF 300 mg QD, each with matching placebo, and treated for 48w. After this, all patients received open-label TAF for an additional 48w. The primary efficacy analysis was the proportion of patients with HBV DNA ≥20 IU/mL at 48w based on the modified US FDA-defined Snapshot algorithm. Key pre-specified secondary safety endpoints were changes in hip and spine bone mineral density (BMD), and changes in eGFR (mL/min/1.73 m²).

Results: 488 patients were randomized and treated at 42 sites in 8 countries. At baseline the groups were similar: median age 52y (22% ≥60y), 71% male, 82% Asian, 68% HBeAg-negative, and median ALT 23 U/L. Median eGFR was 90.5 mL/min; 45% and 50% had low BMD by T scores at hip and spine, respectively. Median (Q1, Q3) duration of prior TDF was 222 (145, 305) weeks. Key efficacy/safety results are summarized in the Table. TAF demonstrated non-inferior efficacy to TDF and TAF treatment resulted in increases in hip/spine BMD with less impact on bone turnover makers; switching from TDF to TAF also resulted in increased eGFR back to baseline.

Table

<table>
<thead>
<tr>
<th></th>
<th>N/N (%) TAF (N=243)</th>
<th>TDF (N=245)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV DNA ≥20 IU/mL 2</td>
<td>1/243 (0.4)</td>
<td>1/245 (0.4)</td>
<td>0.95</td>
</tr>
<tr>
<td>HBV DNA &lt;20 IU/mL 2</td>
<td>234/243 (96.3)</td>
<td>236/245 (96.3)</td>
<td>0.98</td>
</tr>
<tr>
<td>No virologic data in Week 48 window</td>
<td>8/243 (3.3)</td>
<td>8/245 (3.3)</td>
<td>-</td>
</tr>
<tr>
<td>ALT normal (2018 AASLD criteria)</td>
<td>192/243 (79)</td>
<td>184/245 (75.1)</td>
<td>0.31</td>
</tr>
<tr>
<td>HBeAg seroconversion 3</td>
<td>2/78 (2.6)</td>
<td>0</td>
<td>0.13</td>
</tr>
<tr>
<td>HBsAg seroconversion 3</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><strong>Bone safety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip BMD, mean (SD) % change</td>
<td>+6.6 (2.08)</td>
<td>-0.51 (2.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spine BMD, mean (SD) % change</td>
<td>+1.74 (3.46)</td>
<td>-0.11 (3.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTX, median (Q1, Q3) % change (ng/mL) 4</td>
<td>794 (44.2, 143.4)</td>
<td>797.1 (148.3, 32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P1NP, median (Q1, Q3) % change (ng/mL) 4</td>
<td>-18.4 (-32.2, -7.5)</td>
<td>+1.70 (-12.5, 17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Renal safety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR&lt;10, median (Q1, Q3) change (mL/min) 4</td>
<td>-0.99 (-4.47, 6.35)</td>
<td>-2.74 (-7.87, 1.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RBPC, median (Q1, Q3) % change 5</td>
<td>-17.7 (-41.3, 17.2)</td>
<td>+18.6 (-15.3, 67.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>j2MG/Cr, median (Q1, Q3) % change 5</td>
<td>-36.0 (-61.9, 11.5)</td>
<td>+10.7 (31.9, 90.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

4HBV DNA results by modified US FDA Snapshot algorithm; other efficacy data are missing=failure. 5Stratified Cochran-Mantel-Haenszel test. 6ALT normal is the proportion with ALT ≤ULN at Week 48, regardless of baseline status. 7ULN 35 IU/L males, 25 IU/L females; HBeAg-positive at baseline. 8Bone-specific collagen (bone resorption marker); 9Procollagen type I N-terminal propeptide (bone formation marker).
Conclusion: Virologically-suppressed CHB patients who were switched to TAF demonstrated noninferior efficacy to continued TDF with improved bone and renal safety.

Keywords: TAF, Stable switch, TDF, Switch

---

O-004

**Tenoforv Disopropix Fumarate Directly Regresses Liver Fibrosis by Inducing Hepatic Stellate Cell Apoptosis**

Sung Won Lee, Sung Min Kim, Byung-Yoon Kang, Wonhee Hur, Hee Chul Nam, Jeong Won Jang, Seung Kew Yoon

Division of Hepatology Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea; The Catholic University Liver Research Center

Aims: The treatment with tenoforv disopropix fumarate (TDF) results in the regression of liver fibrosis but its underlying mechanism has not been clarified thus far. We aimed to evaluate the direct association between TDF treatment and the activated hepatic stellate cells (HSCs) which are major sources of fibrogenic liver cells.

Methods: - In vitro experiment: Activated hepatic stellate cell lines, LX2 and HSC-T6 were used to evaluate the effect of antiviral agents entecavir (ETV), lamivudine (LAM) and TDF on HSCs. After treatment with each antiviral agent, cell viabilities were detected using the MTT assay, apoptotic features were quantified by Annexin V assay and the apoptosis signaling pathways were determined by western blot. Apoptotic nuclei were visualized using Tunel staining.
- In vivo experiment: In mouse liver fibrosis models induced by thioacetamide (TAA), ETV, LAM and TDF were given by oral gavage every day for 10 weeks. After sacrificing the mouse, the collagen deposition in the liver was assessed by Sirius red staining and quantified. a-SMA and TIMP-1, serum ALT and creatinine were measured. Apoptotic nuclei were visualized using Tunel staining.

Results: The cell viabilities of LX2 and HSC-T6 cells decreased after TDF treatment but not after ETV or LAM. TDF-treated cells showed morphological changes compatible with apoptosis. Annexin-V assay demonstrated that TDF-induced HSC death was due to apoptosis and after Tunel staining, TDF-treated HSCs showed increased apoptotic features. Regarding the apoptosis signaling pathways, PARP and Caspase-3 were cleaved with inhibition of the anti-apoptotic gene, Bcl-xl following TDF treatment.

In TAA-induced liver fibrosis mouse model, significantly decreased fibrotic areas were observed in the TDF group compared to ETV and LAM. Also, a-SMA and TIMP-1 were significantly decreased in the TDF group. Tunel staining demonstrated that the apoptotic nuclei were concentrated surrounding the portal vein tract merging on a-SMA stains which indicated the apoptosis of HSCs. In terms of toxicity, serum ALT and creatinine were not significantly elevated after TDF.

Conclusions: Our experiment has demonstrated, for the first time, that TDF directly regresses liver fibrosis by inducing HSC apoptosis. Anti-fibrotic effects of TDF may be taken into account as a factor in the selection of antiviral drug for CHB patients and TDF may be considered as a therapeutic agent for the treatment of liver fibrosis.

---

O-005

**Risk of Hepatocellular Carcinoma in Patients with Immune-Tolerant Chronic Hepatitis B**

Gyeol Seong, Dong Hyun Sinn, Wonseok Kang, Geum-Youn Gwak, Moon Seok Choi, Joon Hyek Lee, Kwang Cheol Koh, Seung Woon Paik, Yong-Han Paik

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: Recent studies have suggested that patients with immune-tolerant chronic hepatitis B (CHB), characterized by hepatitis B e antigen (HBeAg) positive patients with high serum hepatitis B virus (HBV) DNA but normal alanine aminotransferase (ALT), may develop hepatocellular carcinoma (HCC). However, it is unclear how to stratify HCC risk in these patients.

Methods: A retrospective cohort of 651 HBeAg positive, adult patients with high serum HBV DNA levels (>7 log IU/mL) but normal or mildly elevated ALT levels (<80 U/L) were analyzed. Age and RB-4 index were used to categorize patients, and assessed actual HCC incidence rate in each subgroups. Normal ALT was defined as <35 U/L for males and <25 U/L for females.

Results: During a median 5.2 years of follow-up (range: 1.0-17.8 years), 24 (3.7%) patients developed HCC. Age and RB-4 index were independent factors associated with HCC development. When stratified, 5 and 10-year cumulative HCC incidence rates were 0% and 2.0% for patients aged <40 years plus FIB-4 index <1.45, and were 5.9% and 32.7% for patients aged ≥40 years plus FIB-4 index ≥1.45, respectively (P<0.001). When analysis was limited to patients with normal ALT levels (n = 301), 10-year HCC incidence rate was 0% for patients aged <40 years plus FIB-4 index <1.45, while 5 and 10-years HCC incidence rate was 4.5% and 27.1% for patients aged ≥40 years plus FIB-4 index ≥1.45, respectively (P<0.001).

Conclusions: In patients with immune-tolerant CHB, HCC risk was considerably high for aged patients with elevated FIB-4 index while HCC risk was very low for young patients with low FIB-4 index. These two factors could effectively stratify HCC risk, indicating that they may guide management plan for this
Keywords: Hepatitis B virus infection, Age, Fibrosis-4, Antiviral treatment

O-006 Detection of HBV Integration in the Human Genome Using High-Throughput Targeted Sequencing

Jeong Won Jang1,2*, Jin Seoub Kim1,2, Hye Seon Kim1,2, Hee Chul Nam1,2, Pill Soo Sung1,2, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,2

1Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2The Catholic University of Korea, Seoul, Republic of Korea.

Aims: While it has long been known that hepatitis B virus (HBV) integrates into the host genome, the biological role of the integrated HBV DNA in hepatocarcinogenesis still remains uncertain. The study aimed to localize HBV integrants throughout the host genome by high-throughput sequencing method.

Methods: Next-generation sequencing (NGS)-based target enrichment sequencing was performed to detect HBV integration in paired tumor/non-tumor tissues from 33 hepatocellular carcinoma (HCC) patients. The Illumina NGS workflow was conducted in the following steps: gDNA sonication to generate DNA libraries, HBV sequence capture using HBV probes, followed by high-throughput sequencing. Chimeric Count >10 and AVG_MQ >20 was regarded as true signal. Sanger sequencing was done to verify the HBV-integrated breakpoints.

Results: HBV integration was identified in all (25/25, 100%) HBsAg-positive and 2 (2/8, 25%) HBsAg-negative patients with HCC. Two patients who lost HBsAg before HCC development also harbored HBV integration in both tumor and non-tumor tissues. The average number of integration sites in HBV-related HCC and adjacent non-tumor tissues was 12.45 and 24.04 per sample, respectively. HBV integration most frequently occurred in chromosomes 5 and 10. Recurrent target genes for HBV integration included TERT, MLL4, and PREX2 for tumor and FN1 for non-tumor. The major hotspot breakpoints of host and HBV genomes were located at upstream of hTERT gene and nt 1600-1800 of HBV genome, respectively. Integrations in tumor were over-presented in promoter or exon and less presented in intergenic region. Gene-annotation analysis indicated that the recurrent HBV integrations are enriched in cancer-associated genes. HBV integration breakpoints were validated by Sanger sequencing in six randomly selected tumor tissues.

Conclusions: Our study reports a new high-throughput targeted sequencing using NGS method with high detection ability to identify HBV integration in the human genome. This cost-effective method facilitates a survey of HBV integration in a large number of samples in an unbiased way.

Keywords: Hepatitis B virus, Integration, Carcinogenesis, Sequencing

O-007 Incidence and Risk Factors Analysis of Liver Cancer in Patients with Alcoholic Liver Disease: Retrospective Cohort Analysis of 5,160 Patients

Kyunghan Lee1, Jin-Wook Kim1,2, Si Ho Kim1, Boo-Ok Jang1, Jae Kyun Choi1, Gwang Hyeon Choi1, Eun Sun Jang1, Sook-Hyang Jeong1,2

Aims: To evaluate the incidence of liver cancer in patients with alcoholic liver disease (ALD) and to identify risk factors for liver cancer development.

Methods: A retrospective cohort analysis was conducted on 5,160 patients with ALD, who had been followed up at the Liver Research Center of our hospital from 2000 to 2018. Liver cancer was diagnosed using the World Health Organization criteria. Cox proportional hazards regression analysis was performed to identify risk factors for liver cancer.

Results: During the follow-up period of 8 years, 33 liver cancers were diagnosed. The incidence rate of liver cancer was 6.5 per 1,000 person-years. Significant risk factors for liver cancer were age, alcohol consumption, and duration of ALD. The adjusted hazard ratio for each risk factor was as follows: age (1.04, 95% CI: 1.03-1.05), alcohol consumption (1.02, 95% CI: 1.01-1.03), and duration of ALD (1.00, 95% CI: 1.00-1.01).

Conclusions: Our study indicates that age, alcohol consumption, and duration of ALD are significant risk factors for liver cancer in patients with ALD. Early intervention and close monitoring of these risk factors may help prevent liver cancer development.

Keywords: Liver cancer, Liver disease, Alcohol consumption, Risk factors
Aims: Alcohol increases the risk of liver cancer, but the incidence and predictor of liver cancer have not been well defined in alcoholic liver disease (ALD). This retrospective cohort study aimed to investigate the incidence and risk factors of liver cancer development in the patients with ALD on surveillance.

Methods: A total of 5,160 patients were diagnosed as ALD and followed for more than 6 months from April 2004 to December 2017 in our single center. ALD cases were identified by the ICD10 of K70. Surveillance for liver cancer was based on liver ultrasound and/or serum tumor marker such as alpha fetoprotein (AFP) and carbohydrate antigen 19-9 (CA 19-9). Liver cancer incidence and related risk factors were analyzed by Kaplan-Meier analysis and competing risk Cox model.

Results: During a median follow-up of 5.4 years, a total of 153 patients were newly diagnosed as liver cancer including 146 cases of HCC, 6 cases of Intrahepatic cholangiocarcinoma, 1 case of combined HCC-CCC, retrospectively. Overall liver cancer incidence was 0.9% at 2 years, 2.9% at 5 years, 5.2% at 10 years and 8.7% at 15 years. In patients with liver cirrhosis, liver cancer incidence was 3.8% at 2 years, 13.3% at 5 years, 24.1% at 10 years, and 33.5% at 15 years. Cox multivariate analysis showed that the independent factors related to liver cancer development were male sex (hazard ratio [HR], 2.84; 95% confidence interval [CI], 1.60-5.04; P < .01), old age (HR, 1.05; 95% CI, 1.03-1.06; P < .01), cirrhosis (HR, 22.69; 95% CI, 12.63-40.78; P < .01), low serum platelet count (≤110,000/μL; HR, 1.83; 95% CI, 1.24-2.71; P = .002), positive serum Hepatitis B surface antigen (HBsAg) (HR, 3.10; 95% CI, 2.07-4.64; P < .01), and positive serum anti-HCV antibody (HR, 2.07; 95% CI, 1.18-3.66; P = .012).

Conclusions: Liver cancer incidence among alcoholic liver disease was 0.9%, 2.9%, 5.2%, 8.7% at 2, 5, 10, 15 years, respectively. Male sex, old age, cirrhosis, serum platelet count, positive serum HBsAg, and positive anti-HCV antibody were independent risk factor for liver cancer development in patients with ALD.

Keywords: Alcoholic liver disease, Liver cancer, Surveillance, Incidence, Risk factors
by ELF and/or FS nearly eliminated the need for liver biopsy and accurately identified patients with advanced fibrosis due to NASH with misclassification rates similar to liver biopsy.

Keywords: NASH, NAFLD, Gilead, Selonertib, ASK-1 inhibitor, STELLAR, Fibrosis, Non-invasive test

**O-009**

Development of Diagnostic Marker for NASH and Evaluation of Hepatic Steatosis and Fibrosis Using Biochemical Marker, TE, and MRI in Biopsy-Proven NAFLD Patients

Young-Sun Lee¹, Sung Won Chang¹, Ha Seok Lee¹, Ji Hoon Kim¹, Hee Sun Park², In Hee Kim³, Baek-hui Kim⁴, Chang Hee Lee⁵, Jong Eun Yeon⁶, So Young Kwon⁶, and Kwan Soo Byun¹

¹Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea; ²Department of Radiology, Konkuk University School of Medicine, Seoul, Korea; ³Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea; ⁴Department of Pathology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea; ⁵Department of Radiology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea; ⁶Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Republic of Korea

**Aims:** Nonalcoholic fatty liver disease (NAFLD) is becoming a major cause of chronic liver disease. The development of non-invasive evaluation of severity in this broad spectrum disease is urgently needed. In this prospective cross-sectional study, we aimed to evaluate hepatic steatosis and fibrosis using non-invasive tests including biochemical marker, transient elastography (TE), and magnetic resonance imaging (MRI). In addition, we tried to develop non-invasive diagnostic marker for NASH using biochemical parameters and MRI parameters.

**Methods:** This is a prospective cross-sectional study including patients with biopsy-proven NAFLD. All patients underwent biochemical, TE, and MRI within 6 months of liver biopsy. For evaluation of biochemical fibrosis marker, AST/platelet ratio index (APRI) and fibrosis-4 (FIB-4) index were calculated in all patients. MRI examination included mDIXON, MR spectroscopy (MRS), T1 mapping and MR elastography (MRE). TE measured liver stiffness and controlled attenuation parameter (CAP).

**Results:** 123 patients with biopsy-proven NAFLD were enrolled from October 2016 to March 2019. Mean age and BMI were 50.69 ± 13.57 years and 29.59 ± 4.64 kg/m², respectively. Female was dominant (n=72, 58.5%) and other co-morbidities were checked, such as diabetes (n=52, 42.3%), hypertension (n=53, 43.1%) and dyslipidemia (n=39, 31.7%). For diagnosis of severe steatosis (stage 2-3), CAP (0.706; 95% CI, 0.595-0.802) showed lower AUROC compared with mDIXON (0.832; 95% CI, 0.733-0.905; P=0.027) and MRS (0.842; 95% CI, 0.744-0.913; P=0.029), respectively (Figure 1). For diagnosis of advanced fibrosis (stage 3-4), diagnostic accuracy of MRE was superior (0.889; 95% CI, 0.748-0.915) comparing with APRI (0.686; 95% CI, 0.623-0.725, P=0.003), FIB-4 (0.808; 95% CI, 0.743-0.845, P=0.018), and TE (0.829; 95% CI, 0.683-0.870, P=0.016) (Figure 2). Age, BMI, DM, dyslipidemia, AST, platelet are associated with NASH in univariate. In multivariate analysis AST, PLT, and MRE were significant factor for diagnosis of NASH.

**Conclusions:** MRI (mDIXON, MRS and MRE) showed significant diagnostic accuracy to identify severe steatosis and advanced fibrosis compared to other non-invasive markers in patients with biopsy-proven NAFLD. AST, PLT, and MRE were significant factor for diagnosis of NASH. Non-invasive modalities using AST, platelet, and MRI could be potential tools for diagnosis of NASH.

Keywords: NAFLD, NASH, MRI, Elastography

---

**Table 1: Diagnostic Performance of NTIs to Discriminate Advanced Fibrosis (F3-F4)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predicted Value</th>
<th>Negative Predicted Value</th>
<th>AUROC <strong>b</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>FIB-4 (F3, F4)</td>
<td>92%</td>
<td>89%</td>
<td>92%</td>
<td>90%</td>
<td>0.889 (95% CI, 0.748-0.915)</td>
</tr>
<tr>
<td>ELF (F3, F4)</td>
<td>85%</td>
<td>92%</td>
<td>90%</td>
<td>92%</td>
<td>0.832 (95% CI, 0.733-0.905)</td>
</tr>
<tr>
<td>mDIXON (F3, F4)</td>
<td>78%</td>
<td>82%</td>
<td>80%</td>
<td>84%</td>
<td>0.842 (95% CI, 0.744-0.913)</td>
</tr>
</tbody>
</table>

---

**Figure 1.**

**Figure 2.**
The Liver Week 2019

O-010

The Impact of Controlled Attenuation Parameter on Liver Stiffness Measurement Using Transient Elastography in Patients with Nonalcoholic Fatty Liver Disease

Dong Hyeon Lee, Won Kim*, Sae Kyung Joo, Yong Jin Jung, Kook Lae Lee, Byeong Gwan Kim

Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea

Aims: According to a recent report, severe steatosis is likely to affect liver elasticity (E) as measured by transient elastography (TE) in subjects with non-alcoholic fatty liver disease (NAFLD). However, little is known about the impact of controlled attenuation parameter (CAP) as assessed by TE on the measurement of liver E in subjects with NAFLD.

Methods: Five hundred fifty-nine subjects with biopsy-proven NAFLD were included in this prospective analysis. All patients underwent TE with CAP measurement. Logistic regression analysis and discriminant function analysis were used for calculating two kinds of CAP-adjusted E. Area under ROC curves (AUROC) were used to determine the optimal cut-offs, sensitivity, and specificity of CAP-adjusted E values for detecting significant fibrosis (≥F2) and advanced fibrosis (≥F3).

Results: For diagnosing significant fibrosis, the AUROCs for TE (CAP-adjusted E) were 0.817 (optimal cut-off, -0.189; sensitivity [se], 72.68%; and specificity [sp], 79.78%) in model 1 (adjusted for CAP) and 0.812 (optimal cut-off, -0.042; se, 67.60%; sp, 82.70%) in model 2 (adjusted for CAP, platelet, albumin, and PT INR) by formula calculated using discriminant function analysis, while, for diagnosing advanced fibrosis, those for TE (CAP-adjusted E) were 0.908 (optimal cut-off, 0.274; se, 80.49%; sp, 93.43%) in model 1 and 0.916 (optimal cut-off, 0.205; se, 82.05%; sp, 89.38%) in model 2 by formula calculated using discriminant function analysis. The AUROCs (for ≥F2, 0.821 and for ≥F3, 0.914) for TE (E) were not significantly different from those for TE (CAP-adjusted E).

Conclusions: There was a significant positive correlation between CAP-adjusted E and fibrosis stages in subjects with NAFLD. However, CAP-adjusted E was not superior to E in diagnosing significant fibrosis and advanced fibrosis.

Keywords: NAFLD, LSM, CAP, Fibrosis

O-011

Serial Liver Stiffness and Controlled Attenuation Parameter Measurements by Transient Elastography in Patients with Type 2 Diabetes

Hye Won Lee1,2,3,4, Grace Lai-Hung Wong1,2,3, Raymond Kwok4, Henry Lik-Yuen Chan1,2,3, Juliana Chung-Ngor Chan2, Alice Pik-Shan Kong2, Vincent Wai-Sun Wong1,2,3

1Institute of Digestive Disease, Department of Medicine and Therapeutics, and 2State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong SAR, China; 3Yonsei University College of Medicine, Seoul, South Korea; 4Department of Gastroenterology, Blacktown Hospital, Sydney, Australia

Aims: Type 2 diabetes is an important risk factor for non-alcoholic fatty liver disease (NAFLD) and advanced fibrosis. Current European guidelines recommend repeating non-invasive tests of fibrosis in NAFLD patients at 3-yearly intervals, but data are largely lacking. Here we report the changes in the liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) by transient elastography (TE) in patients with type 2 diabetes at 3 years.

Methods: We recruited patients with type 2 diabetes from a complication screening facility in Hong Kong in 2013-2014 and repeated the assessment in 2016-2018. The primary endpoint was the proportion of patients who progressed to chronic liver disease with advanced fibrosis. The secondary endpoint was the proportion of patients who experienced a change in the CAP.

Results: A total of 611 diabetic patients with valid LSM (mean age, 57.7 ± 10.9 years; 342 males [56.0%]) were included in this study (568 also had valid CAP). Overall, there was moderate correlation between baseline and follow-up LSM (r=0.689, P<0.001). At baseline, 487 (79.7%) patients had an LSM <10 kPa and 21 (4.3%) had follow-up LSM ≥10 kPa. BMI, ALT and ALT were independent factors for predicting LSM increase. Among the remaining 124 (20.3%) patients with LSM ≥10 kPa at baseline, 70 (56.5%) had follow-up LSM <10 kPa. Among 198/568 (34.9%) patients with CAP <248 dB/m at baseline, 103 (52.0%) had CAP increased to ≥248 dB/m (55 [27.8%] ≥280 dB/m suggestive of severe steatosis). Among the 370/568 (65.1%) patients with a CAP ≥248 dB/m at baseline, CAP decreased to <248 dB/m in 45 (12.2%) patients.

Conclusions: The prevalence and incidence of NAFLD in patients with type 2 diabetes are high. While patients with advanced fibrosis are common in this population, the incidence of progression to advanced fibrosis is relatively low. Our results support one-off fibrosis testing in diabetic patients but not routine 3-yearly assessments in all patients.

Keywords: Diabetes, NAFLD, Controlled attenuation parameter, Liver stiffness measurement

O-012

Relationship between Incident Nonalcoholic Fatty Liver Disease and Body Composition Parameters at Baseline and during Follow-Up: A 8-Year Longitudinal Study

Hwi Young Kim1, Su Jung Baik2, Hye Ah Lee3, Byoung Kwon Lee4, Hye Sun Lee1, Tae Hun Kim1, and Kwon Yoo1

1Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Republic of Korea; 2Healthcare Research Team, Health Promotion Center, Gangnam Severance Hospital, Seoul, Republic of Korea; 3Clinical Trial Center, Ewha Womans University Medical Center, Seoul, Republic of Korea; 4Biostatistics Collaboration Unit, Medical Research Center, Yonsei University College of Medicine, Seoul,
Aims: Association between nonalcoholic fatty liver diseases (NAFLD) and relative skeletal muscle mass has been documented in several studies. We investigated the effects of baseline values and changes of body composition and development of incident NAFLD in a large-scale longitudinal cohort study.

Methods: In this 8-year longitudinal study, we included a total of 9967 subjects without NAFLD at baseline who underwent two or more comprehensive health check-up examinations between January 2008 and December 2016. We explored association between development of incident NAFLD and body composition parameters at baseline as well as their changes, including body weight-adjusted soft lean mass and percentage fat.

Results: Study subjects were categorized according to their BMI as follows: underweight (BMI<18.5), n=710 (7.1%); lean (18.5≤BMI<23), n=5457 (54.8%); overweight (23≤BMI<25), n=2182 (21.9%); obese (BMI≥25), n=1618 (16.2%). During follow-up, incident NAFLD was observed in 2395 subjects (24.0%). Subjects with incident NAFLD were older (47.1 vs. 45.6 years), male-predominant (55.2% vs. 32.9%), had higher baseline BMI (23.7 vs. 21.8), and were more frequently associated with MetS (53.1% vs. 33.6%), compared to those without (all P<0.001). Among the subgroups by BMI, incident NAFLD developed in 2.0% in the underweight group, 40.0% in the lean group, 27.6% in the overweight group, and 30.4% in the obese group, respectively (P<0.001). Baseline risk factors for incident NAFLD in each BMI subgroup were as follows: i) underweight group: higher percentage fat (HR=1.0; 95% CI, 1.00-1.05; P<0.001), and triglyceride level (HR=1.0; 95% CI, 1.00-1.02; P=0.01); ii) lean group: higher percentage fat (PF; HR=1.1; 95% confidence interval [CI], 1.02-1.08; P<0.001) and triglyceride level (HR=1.0; 95% CI, 1.00-1.02; P=0.01) and tri-glyceride level (HR=1.0; 95% CI, 1.00-1.02; P=0.01) for each tertile of weight/height (Wt/Ht); iii) overweight group: higher percentage fat (HR=1.0; 95% CI, 1.00-1.05; P<0.001), and tri-glyceride level (HR=1.0; 95% CI, 1.00-1.02; P=0.01); iv) obese group: higher percentage fat (HR=1.0; 95% CI, 1.00-1.05; P<0.001), and tri-glyceride level (HR=1.0; 95% CI, 1.00-1.02; P=0.01). Of the entire study population, 5033 subjects underwent health examination three or more times during the study period, with their second examination after a median of 1.2 years (IQR, 1.0-2.0) from their first examination. In these 5033 subjects, significantly positive correlations were observed between weight gain between the first and second examinations and harmful changes in MetS components (increased systolic and diastolic blood pressure, TG and glucose and decreased HDL cholesterol; all P<0.0001). Highest tertile of PF change was significantly associated with incident NAFLD in both overweight (HR=1.8; 95% CI, 1.2-2.6; P<0.001) and obese groups (HR=1.9; 95% CI, 1.3-2.7; P<0.001).

Conclusions: High baseline level or increase during follow-up of percentage fat mass was associated with increased risk of NAFLD development over time in lean, overweight and obese population. Lifestyle intervention to reduce fat mass as well as to increase in relative skeletal mass may be needed in lean population to prevent new NAFLD.

Keywords: Fatty liver, Longitudinal study, Body composition, Risk factor
MAGE-1-Targeting Aptamer Inhibits Hepatocellular Carcinoma Cell Growth via PFKFB4 Suppression and ROS Overproduction

Yun Bin Lee1, Eun Ju Cho1, Jeong-Hoon Lee1, Su Jong Yu1, Yoon Jun Kim1, Eun Ju Oh1, Jung In Kim1, Jong Hun Im2, Jung Hwan Lee2, Jung-Hwan Yoon3

1Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; 2Aptamer Initiative, POSTECH Biotech Center, Pohang University of Science and Technology, Pohang, Republic of Korea

Aims: Aptamers are short synthetic oligomers that bind to protein targets on cancer cells. The melanoma antigen-1 (MAGE-1), a member of MAGE gene family which encode tumor-specific antigens for autologous cytotoxic T cell recognition, is highly expressed in hepatocellular carcinoma (HCC) suggesting the possibility of a novel therapeutic target. We generated aptamers targeting MAGE-1 and assessed those therapeutic potentials in the treatment of HCC.

Methods: MAGE-1 expression on the surface of HCC cells (SNU-761, Huh7, and SNU-3058) was assessed by immunofluorescence staining. Flow cytometry was performed to determine the binding affinity of the MAGE-1 aptamers, which were synthesized through systematic evolution of ligands by exponential enrichment (SELEX) method, to HCC cells. Cell proliferation was analyzed using the MTS assay.

Results: MAGE-1 was highly expressed on the surface of SNU-761, Huh7, and SNU-3058 cells. Ten SELEX-derived MAGE-1 aptamers were evaluated by flow cytometry for selection of high-affinity aptamers to HCC cells. Among MAGE-1 aptamers analyzed, one which showed high affinity to SNU-3058 cells (HCC cell line derived from hypovascular HCC), was selected for MTS assay. MAGE-1 aptamer treatment suppressed HCC cell growth compared to control aptamer. In a microarray, PFKFB4 gene expression was reduced by MAGE-1 aptamer treatment with a –1.77-fold change in SNU-3058 cells. Knockdown of PFKFB4 in cancer cells is known to be associated with reactive oxygen species (ROS) production and cell death. Suppression of PFKFB4 expression after MAGE-1 aptamer treatment in SNU-3058 cells was confirmed by real-time polymerase chain reaction. ROS production was increased by treatment of MAGE-1 aptamer or transfection of PFKFB4 siRNA.

Conclusions: We demonstrated that newly developed MAGE-1 aptamer can bind to HCC cells with high affinity and inhibit HCC cell proliferation via PFKFB4 gene suppression and ROS overproduction. Further investigation of MAGE-1 aptamer as a novel targeted therapy for HCC is needed.

Keywords: MAGE-1, Aptamer, HCC, Liver cancer, PFKFB4, ROS

O-015

Kinase Suppressor of Ras 1 Promotes Development of TAZ-Mediated Intrahepatic Cholangiocarcinoma

Hyuk Moon1, Kyungjoo Cho1, Soonyoung Shin1,2, Simon W. Ro1,2, Beom Kyung Kim3, Seung Up Kim1,2, Jun Yong Park1,2, Sang Hoon Ahn1,2, Do Young Kim1,2, Kwang-Hyub Han1,3

1Yonsei Liver Center, Severance Hospital, 2Brain Korea 21 PLUS project for Medical Science College of medicine, 3Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea

Aims: Liver cancer is a major cause of cancer-related deaths worldwide, of which Intrahepatic cholangiocarcinoma (ICC) is the second most common malignant tumor. Kinase suppressor of ras 1 (KSR1) is a scaffold protein for the RAF-MEK-ERK cascade and promotes phosphorylation of MAPK and ERK kinase (MEK) by RAF. In this study, we have investigated the role of KSR1-dependent signaling pathways in YAP/TAZ-mediated hepatic carcinogenesis.

Methods: Transposons were constructed encoding KSR1 and an activated form of TAZ (TAZS89A). Transposons were hydrodynamically delivered to livers of 5-week-old C57BL/6 mice. Mice were monitored at least twice per week and sacrificed when moribund. Tumor-bearing livers were formalin fixed for hematoxylin–eosin staining and immunohistochemistry.

Results: Analysis of gene expression levels in human ICC samples deposited in The Cancer Genome Atlas (TCGA) revealed that KSR1 was significantly upregulated in human ICC, compared with non-tumoral surrounding livers (P<0.01). Furthermore, simultaneous expression of KSR1 and an activated form of TAZS89A promoted tumorigenesis in mice liver. Histological analysis revealed that these tumors were ICCs, as also indicated by strong immunoreactivity for the CK19 and EpCAM. Interestingly, western blotting of the ICC tissues showed that AKT1 phosphorylation was higher than in normal tissue control, and was positively correlated with KSR1 expression.

Conclusions: KSR1 has been known as a positive regulator of MAPK signaling. In this study, we found a new function of KSR1 that induces activation of AKT signaling. KSR1 promotes TAZ-mediated liver tumorigenesis, and is a key molecule in ICC as a positive regulator of AKT signaling.

Keywords: Intrahepatic cholangiocarcinoma, KSR1, YAP/TAZ, Tumorigenesis
**O-016**

**Loss of ARID1A Serves as Prognostic Biomarker for Hepatocellular Carcinoma and Has Synthetic Lethality with PI3K/mTOR Inhibition**

Sun Young Yim¹, Yun Seong Jeong², Ji-Hyun Shin², Tae Hyung Kim¹, Yeon Seok Seo¹, Ji Hoon Kim¹, Hyung Joon Yim¹, Ju-Seog Lee², Soon Ho Um³

¹Internal Medicine, Korea University Hospital, ²Systems Biology, The University of Texas MD Anderson Cancer Center

**Aims:** Based on the recent study from The Cancer Genome Atlas (TCGA) project, ARID1A was one of the most frequently mutations in hepatocellular carcinoma (HCC). Since clinical significance of ARID1A in HCC is not clarified despite its high prevalence, the role of ARID1A was evaluated.

**Methods:** By analyzing the gene expression of livers from Arid1a-knockout mice, a hepatic Arid1a-specific gene expression signature was identified (P<0.05 and log, ratio >0.5 fold difference). From this signature, a prediction model was developed to identify tissues lacking Arid1a activity and was applied to gene expression data from three independent cohorts of HCC patients to stratify patients according to ARID1A activity. The molecular features associated with loss of ARID1A were analyzed using TCGA multi-platform data, and Ingenuity Pathway Analysis (IPA) was done to uncover potential signaling pathways associated with ARID1A loss. Sensitivity of ARID1A-wild-type, -deficient, and -knockout HCC cells to PI3K/mTOR inhibitor GSK2126458 was tested.

**Results:** ARID1A inactivation was clinically associated with poor prognosis in all three cohorts and was consistently related to poor prognosis subtypes associated with previously reported gene signatures (high NCI proliferative, hepatic stem cell, significance of Hippo pathway, and SNUR high recurrence). Immune activity, indicated by significantly lower IFNG6 and cytolytic activity scores and enrichment of regulatory T-cell composition, was lower in the ARID1A-low subtype. IPA results revealed PI3K/mTOR as activated upstream regulators of the ARID1A signature. Sensitivity to GSK2126458 was significantly higher in ARID1A-deficient and -knockout cells than in ARID1A-wild-type cells (P<0.05).

**Conclusions:** ARID1A inactivation is significantly associated with poor prognosis and activation of the PI3K/mTOR pathway. ARID1A status could be used for identification of HCC tumors sensitive to PI3K/mTOR inhibition.

**Keywords:** ARID1A, Hepatocellular carcinoma, Genomics, Survival

**Figure 1.**

**O-017**

**Identification of the Novel Exosomal Protein Markers of Hepatocellular Carcinoma**

Hyun Jung Cho¹, Jung Woo Eun¹, Baek Geum Ok², Chul Won Seo²¹, Hye Ri Ahn¹, Young-hwan Ahn¹, Jinhee Jung¹, Soon Sun Kim¹, Sung Won Cho¹, and Jae Youn Cheong⁴

¹Department of Gastroenterology, Ajou University School of Medicine, Suwon, South Korea; ²Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, South Korea

**Aims:** The marker of hepatocellular carcinoma-derived exosomes (HEX) is not yet fully identified. In this study, we tried to reveal novel biomarker of hepatocellular carcinoma (HCC) by identifying the specific protein markers of HEX.

**Methods:** Exosomes were isolated from human HCC cell lines (Hep3B and Huh-7) and immortalized normal hepatocyte cell line (THLE-2). Proteomic analysis was performed for screening the overexpressed proteins in HEX compared to exosome derived normal hepatocyte. To select potential candidate of novel protein maker of HEX among the screened overexpressed proteins of HEX, various public data set including TCGA, ICGC, and GSE77314 were analyzed. To validate clinical implication of the selected proteins, serum ELISA was performed in the cohort of liver disease including 22 HCC patients and 22 chronic liver disease patients without HCC.

**Results:** A total of 757 differentially expressed spots in HEX were identified by deep sequencing. Among them, 54 spots overexpressed more than 2 folds in HEX compared to normal hepatocyte-derived-exosome were selected and purified. ID conversion by using DAVID software were performed for naming the spots. As a result, 22 overexpressed exosomal proteins in HCC cell lines were identified. To select final candidates, the expression level of the 22 candidate proteins were analyzed in various public database and 4 proteins were finally selected as the potential novel protein marker of HEX. Serum ELISA was performed to validate whether these 4 potential HEX protein markers could distinguish HCC patients in an independent co-
Identification of Resistance-Associated Pathways
Murine Hepatocellular Carcinoma

**Results:**

**Methods:**

**Keywords:** Hepatocellular carcinoma, Exosome, Protein, Biomarker

**Conclusions:**

**Aims:** Tyrosine kinase inhibitors (TKIs) play an important role in the latest treatment of advanced hepatocellular carcinoma (HCC). Despite the fact that lenvatinib and regorafenib as multiple target receptor tyrosine kinase inhibitors showed statistically significant non-inferiority over sorafenib and survival advantages in progressive HCC patients on sorafenib treatment, respectively, those also acquire resistance to both drugs in long-term treatment. We aimed to establish lenvatinib and regorafenib resistance in vivo models and to identify those molecular genetic features that affect resistance of both drugs.

**Methods:** RIL-175 HCC cells (2X10⁵) were injected subcutaneously into the C57BL/6 mice. When the average volume of tumors reached to 300 mm³, mice were randomly divided into 3 groups and received the following treatments: 1) vehicle control, 2) lenvatinib (5 mg/kg/day, PO) and 3) regorafenib (10 mg/kg/day, PO). Tumors were monitored 3 times per week by using Vernier caliper measurement of length (L) and width (W) of the tumor. Tumors volume increase more than 30% in 3 days, reached to 900 mm³ (for at least 15 days) were considered end points. Total RNA samples were extracted from xenograft tissue and subjected to gene expression analysis using Affymetrix Clariom-S Array.

**Results:** The result of microarray analyses showed that there were 31 statistically significant molecules in the lenvatinib resistance model and 81 molecules in regorafenib resistance model. There were equally significant changes in genes involved in metabolism, human disease, and environmental information processing in both groups which were distinguished from genes related focal adhesion in the lenvatinib resistance group and choline metabolism in cancer, MAPK signaling pathway, and renin secretin in the regorafenib resistance group. Moreover, three molecules of the highest signal intensities (volume) in each group were Adh7, Gstm1 and Mgst1 in the lenvatinib resistance model (Table 1) and Gsta4, Gsta2 and F2r in the regorafenib resistance model (Table 2).

<table>
<thead>
<tr>
<th>Gene symbol</th>
<th>Gene ID</th>
<th>Fold change</th>
<th>DEG*</th>
<th>Volume</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adh7</td>
<td>13529</td>
<td>-2.9134774</td>
<td>Downregulated</td>
<td>7.397120</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gstm1</td>
<td>11482</td>
<td>-2.063645</td>
<td>Downregulated</td>
<td>7.494585</td>
<td>0.010</td>
</tr>
<tr>
<td>Mgst1</td>
<td>56932</td>
<td>-2.475955</td>
<td>Downregulated</td>
<td>6.985016</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Differentially expressed genes

**Conclusions:** Our study well-established lenvatinib and regorafenib resistance in vivo models and identified potential key molecules in both resistance HCC cells. The pathways that play an important role in the resistance mechanism of lenvatinib and regorafenib might be different. Further studies are needed to overcome resistance mechanisms to both drugs.

**Keywords:** Hepatocellular carcinoma, Lenvatinib resistance, Regorafenib resistance, In vivo model

---

**O-018**

Establishment of Tyrosine Kinase Inhibitors-Resistant Murine Hepatocellular Carcinoma in Vivo Models and Identification of Resistance-Associated Pathways

Minseok Albert Kim¹, Su Jong Yu¹², Hyojin Noh³, Heejoon Jang³, Sun Woong Kim¹, Cheol-Hyung Lee¹, Yun Bin Lee¹², Eun Ju Cho³, Jeong-Hoon Lee¹, Yoon Jun Kim¹, Jung-Hwan Yoon¹

¹Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; ²Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea.

**Aims:** Tyrosine kinases inhibitors (TKIs) play an important role in the latest treatment of advanced hepatocellular carcinoma (HCC). Despite the fact that lenvatinib and regorafenib as multiple target receptor tyrosine kinase inhibitors showed statistically significant non-inferiority over sorafenib and survival advantages in progressive HCC patients on sorafenib treatment, respectively, those also acquire resistance to both drugs in long-term treatment. We aimed to establish lenvatinib and regorafenib resistance in vivo models and to identify those molecular genetic features that affect resistance of both drugs.

**Methods:** RIL-175 HCC cells (2X10⁵) were injected subcutaneously into the C57BL/6 mice. When the average volume of tumors reached to 300 mm³, mice were randomly divided into 3 groups and received the following treatments: 1) vehicle control, 2) lenvatinib (5 mg/kg/day, PO) and 3) regorafenib (10 mg/kg/day, PO). Tumors were monitored 3 times per week by using Vernier caliper measurement of length (L) and width (W) of the tumor. Tumors volume increase more than 30% in 3 days, reached to 900 mm³ (for at least 15 days) were considered end points. Total RNA samples were extracted from xenograft tissue and subjected to gene expression analysis using Affymetrix Clariom-S Array.

**Results:** The result of microarray analyses showed that there were 31 statistically significant molecules in the lenvatinib resistance model and 81 molecules in regorafenib resistance model. There were equally significant changes in genes involved in metabolism, human disease, and environmental information processing in both groups which were distinguished from genes related focal adhesion in the lenvatinib resistance group and choline metabolism in cancer, MAPK signaling pathway, and renin secretin in the regorafenib resistance group. Moreover, three molecules of the highest signal intensities (volume) in each group were Adh7, Gstm1 and Mgst1 in the lenvatinib resistance model (Table 1) and Gsta4, Gsta2 and F2r in the regorafenib resistance model (Table 2).

**Conclusions:** Our study well-established lenvatinib and regorafenib resistance in vivo models and identified potential key molecules in both resistance HCC cells. The pathways that play an important role in the resistance mechanism of lenvatinib and regorafenib might be different. Further studies are needed to overcome resistance mechanisms to both drugs.

**Keywords:** Hepatocellular carcinoma, Lenvatinib resistance, Regorafenib resistance, In vivo model

---

**O-019**

Generation of Induced Secretome from Adipose-Derived Stem Cells Specialized for Disease-Specific Treatment: An Experimental Mouse Model

Say-June Kim¹, Kee Hwan Kim²

¹Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, ²Uijeongbu St. Mary’s Hospital, The Catholic University of Korea, Republic of Korea

**Aims:** Recently, the exclusive use of mesenchymal stem cell (MSC)-secreted molecules, named as the secretome, rather than cells has been evaluated for overcoming the limitations of cell-based therapy while maintaining its advantages. The goal of this study was to improve cell-free therapy by adding disease-specificity through stimulation of MSCs using disease-causing materials.

**Methods:** We collected the secretory materials (named as inducers) released from AML12 hepatocytes that had been pretreated with thioacetamide (TAA) and generated the TAA-induced secretome (TAA-secretome) after stimulating adipose-derived stem cells (ASCs) with the inducers. The TAA-secretome was intravenously administered to mice with TAA-induced hepatic failure and those with partial hepatectomy.

**Results:** TAA-secretome infusion showed higher therapeutic
potential in terms of (a) restoring disorganized hepatic tissue to normal tissue, (b) inhibiting proinflammatory cytokines (interleukin-6 and tumor necrosis factor-a), and (c) reducing abnormally elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase) compared to the naïve secretome infusion in mice with TAA-induced hepatic failure. However, the TAA-isecretome showed inferior therapeutic potential for restoring hepatic function in partially hepatotomized mice.

**Conclusions:** Our results suggest that appropriate stimulation of MSCs with disease-causing agents leads to the production of a secretome specialized for treating a specific disease. Additionally, isecretome therapy is expected to open a new way of developing various specific therapeutics based on the high plasticity and responsiveness of MSCs.

**O-020**

**Clinical Impact of Circulating Exosomal microRNA as a Novel Biomarker of Liver Fibrosis**

Young Chang1, Jae Young Jang2*, Tom Ryu1, Han Seul Park2, Soon Won Jeong2, Jeong-Ju Yoo2, Jae Young Jang1, Jeong-Ju Yoo2, Sae Hwan Lee1, Sang Gyu Kim1, Young Seok Kim3, Hong Soo Kim3, So Young Jin3, Seonho Ryu1

1Institute for Digestive Research, Digestive Disease Center, Department of Internal Medicine, Soonchunhyang University College of Medicine, Seoul, Korea, 2Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, Korea, 3Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea, 4Department of Pathology, Soonchunhyang University College of Medicine, Seoul, Korea, 5Soonchunhyang Institute of Medi-bio Science (SIMS), Soonchunhyang University, Cheonan, Korea

**Aims:** Many approaches have been suggested to diagnose liver fibrosis non-invasively including various serum biomarkers and ultrasound-based elastography, but none of them have yet to replace liver biopsy. Circulating microRNA (miRNAs) have been suggested as possible diagnostic tools for liver diseases in various circumstances. We investigated whether circulating exosomal miRNAs associated with liver fibrosis and its clinical impact as a biomarker of liver fibrosis.

**Methods:** This study prospectively enrolled a total of 85 patients who underwent liver biopsy in three large-volume hospitals in Korea. Exosome was extracted from the serum samples followed by quantification of exosomal miRNAs using targeted RT-qPCR. A novel model to discriminate advanced fibrosis using miRNA level was derived by multivariate logistic regression. The performance of the models were evaluated and compared by area under the ROC curve (AUC) and DeLong’s test.

**Results:** The level of miR-122 and miR-194 decreased as the pathologic fibrosis stage progressed 0 to 4. Patients with biopsy-proved advanced fibrosis showed significantly lower level of miR-122 (P<0.001) and miR-194 (P=0.073) than those without advanced fibrosis. miR-122 exhibited a fair performance in discriminating advanced fibrosis with AUC of 0.77. When combined with Fibrosis-4 score (FIB-4) and transient elastography (TE), miR-122 represented improved discrimination function with AUC of 0.86, which was higher than any other non-invasive modalities including TE alone (AUC of 0.80). In subgroup patients who had non-viral etiology of liver disease, the performance of miR-122 was better than that of whole study population with AUC of 0.87. Furthermore, the combination model of miR-122, FIB-4 and TE showed the best discrimination function with AUC of 0.90, which was significantly higher than that of TE alone (AUC, 0.83; DeLong’s test P=0.046).

**Conclusions:** Circulating exosomal miR-122 can serve as a novel biomarker in discriminating advanced liver fibrosis especially combined with other non-invasive tests such as FIB-4 and TE.

**Keywords:** Exosome, MicroRNA, Fibrosis, Biomarker

**O-021**

**New Therapeutic Strategies for Hepatic Fibrosis Using Stem Cell Printing Three-Dimensional Liver Patch**

Sung Min Kim1, Wonil Han2, Wonhee Hur1, Gil Won Lee3, DongJun Park1, Byung-Yoon Kang1, Narendra K. Singh1, Hyungseok Lee4, Jinah Jang3, Dong-woo Cho1, Seung Kew Yoon1

1The Catholic University Liver Research Center & WHO Collaborating Center of Viral Hepatitis, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2Division of Integrative Biosciences and Biotechnology, Pohang University of Science and Technology (POSTECH), Pohang, South Korea; 3Department of Mechanical Engineering, Pohang University of Science and Technology (POSTECH), Pohang, South Korea; 4School of Interdisciplinary Bioscience and Biotechnology, POSTECH, Korea, Department of Creative IT Engineering, POSTECH, Pohang, Korea

**Aims:** Liver cirrhosis is a major source of liver cancer which is the leading cause of death worldwide. Mesenchymal stem cell (MSC) therapy is being used as a liver transplant alternative therapy in liver cirrhosis patients. However, MSC therapy has a low delivery efficiency. Therefore, to overcome this problem, we established a patch-shaped cell therapy agent (liver patch)
Development of a Prognostic Score to Predict Mortality in Patients with Pediatric Acute Liver Failure

Eun Joo Lee1, Ju Whi Kim1, Jin Soo Moon1, Yu Bin Kim1, Seok Hee Oh2, Kyung Mo Kim3, and Jae Sung Ko4

1Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea; 2Departments of Pediatrics, Asan Medical Center Children’s Hospital, University of Ulsan College of Medicine, Seoul, Korea

Aims: The aim of this study was to develop a new prognostic score based on change in serial laboratory data in patients with pediatric acute liver failure (PALF).

Methods: We retrospectively collected data on patients with PALF at the Seoul National University Children Hospital (SNUCH) and the Asan Medical Center (AMC). Daily morning laboratory records were obtained for up to 7 days after diagnosis of PALF; (1) total bilirubin (TB) (mg/dL), international normalized ratio for prothrombin time (INR) at enrollment (2) peak TB, peak INR, peak ammonia (mmol/L) (3) a) the difference between the peak TB and TB at enrollment (i.e., △peak TB), b) the difference between the peak INR and INR at enrollment (i.e., △peak INR), c) the maximum change in serial TB (i.e., △daily TB), d) the maximum change in serial INR level (i.e., △daily INR).

Results: 42 patients of derivation cohort (SNUCH) and 33 patients of validation cohort (AMC) were enrolled. Multivariate logistic regression was conducted to predict death in derivation cohort and a new score was developed. PALF-Delta score (PALF-Ds) = [0.232 * △peak TB (mg/dL)] + [2.267 * △daily INR] + [0.01 * peak ammonia (mmol/L)] - 4.514. PALF-Ds showed excellent accuracy in both cohort with AUC 0.922 in derivation cohort (sensitivity 81%, specificity 91%) and AUC 0.951 in validation cohort (sensitivity 93%, specificity 90%).

Conclusions: A prognostic scoring system using the change of TB/INR might be useful for predicting death in patients with PALF.

Keywords: Pediatric acute liver failure, Prognostic score

Postoperative Hepatic Decompensation in Patients with Cirrhosis Undergoing Major Surgery: Prognostic Value of Liver Stiffness

Hana Park1, Joo Ho Lee2,3, Yeonjung Ha1, Mi Na Kim1,2, Seong Kyu Hwang2,3, and Young Eun Chon2,3

1Health Screening and Promotion Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 2Department of Internal Medicine, Institute of Gastroenterology, CHA Bundang Medical Center, CHA University, Seongnam, Korea; 3CHA Bundang Liver Center; CHA Bundang Hospital, Seongnam, Korea

Aims: Patients with liver cirrhosis are at fear of postoperative hepatic decompenation, despite the need for significant surgery. This prospective study investigated the prognostic value of liver stiffness measurement (LS) for predicting the development of hepatic decompenation after major surgery requiring general anesthesia.

Methods: This prospective study enrolled 132 consecutive patients with compensated liver cirrhosis (Child-Pugh Class A) who underwent a preoperative liver stiffness (LS) measurement and major surgery between Jan 2016 to September 2018. Definition of hepatic decompenation included at least one sign of liver function impairment (jaundice, ascites, hepatic encephalopathy, or coagulopathy). Predictors of hepatic decompenation were assessed with logistic regression analysis.

Results: Seventy four (56.1%) patients had hepatitis B virus infection and 123 (93.2%) patients had Child-Pugh score 5. The mean LS value was 14.0 kPa. Thirteen (9.8%) patients had hepatic decompenation after major surgery. LS value, and Child-Pugh score were significantly associated with hepatic decompenation in the univariate analysis, but LS value was the only significant predictor in subsequent multivariate analysis (cutoff, 15.0 kPa; P=0.001; odds ratio; 36.3; 95% confidence interval, 4.4–300.4).
Clinical Application of New EASL Clinical Practice Guideline for Malnutrition in Cirrhosis Patients

Jin Hwa Park, Dae Won Jun, Dae Hyun Lim, Won Woo Seo, Ji Hyun Yeo, Na Ryung Choi, Jai Hoon Yoon, Kang Nyeong Lee, Hang Lak Lee, Oh Young Lee, Byung Chul Yoon, and Ho Soon Choi

Department of Internal Medicine, University of Hanyang College of Medicine, Korea

Aims: Recently, clinical practice guideline for nutritional evaluation of cirrhosis patients developed by European Association for the Study of the Liver (EASL). We tried to apply nutrition assessment according to the EASL Clinical Practice Guideline to clinical practice and analyzed the prevalence of malnutrition and its association with related factors.

Methods: From April, 2018 to January, 2019, 309 patients who visited liver clinic in Hanyang University Hospital were enrolled. Sarcopenia was assessed by hand strength measurement and bioelectrical impedance analysis. Subjective global assessment (SGA) and dietary intake assessment was performed. Based on these, malnutrition was defined according to the EASL Clinical Practice Guideline. Cohen's kappa analysis was used to calculate the degree of agreement between the two groups in which malnutrition was diagnosed by different methods.

Results: The prevalence of malnutrition diagnosed according to the EASL clinical guideline was 34.0% and there was no difference by etiology. The prevalence of sarcopenia was 5.5%, malnutrition assessment by SGA was 13.6%, and impaired dietary intake was 27.5%. The prevalence of malnutrition was increased according to disease severity (Child A; 31.3%, Child B; 41.4%, Child C; 71.4%) (P=0.006). Lower body mass index (BMI ≤ 18.5 kg/m²; 60.0%, BMI ≥ 18.5 kg/m² & < 25 kg/m²; 33.9%, BMI ≥ 25 kg/m²; 32.8%) showed relationship with greater prevalence of malnutrition, but no statistically significant. The prevalence of malnutrition was 72.4% in patients intake protein less than 1.0g/kg. Low protein intake and severe disease activity are confirmed to risk factor of malnutrition in multi-variant analysis.

Conclusions: Prevalence of malnutrition in cirrhosis patients diagnosed by EASL clinical practice guideline was 34.0%, and there was no difference by etiology. Low protein intake and severe disease activity are independent risk factors for malnutrition.

Keywords: Liver cirrhosis, Malnutrition, EASL guideline
O-026

Preliminary Efficacy and Safety of 8-Week Glecaprevir/Pibrentasvir in Patients with HCV Genotype 1–6 Infection and Compensated Cirrhosis: The EXPEDITION-8 Study


1Weill Cornell Medical College, Center for Liver Disease and Transplantation, New York, NY, USA; 2Department of Hepatology, Hôpital Henri Mondor, Université Paris-Est, Paris, France; 3AbbVie Inc., North Chicago, Illinois, USA; 4Vall d’Hebron University Hospital and CiBER-HED del Instituto Carlos III, Barcelona, Spain; 5Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan; 6Louisiana Research Center, Shreveport, LA, USA; 7Hepatology Center of Budapest, Budapest, Hungary; 8Director of GHGCPR Research Institute, Puerto Rico; 9GHWC and Gastroenterology Section, San Juan, Puerto Rico; 10Private Practice, Bakersfield, California, USA; 11AbbVie Ltd. Korea, Korea

Aims: The pangenotypic direct-acting antivirals glecaprevir (identified by AbbVie and Enanta) coformulated with pibrentasvir (G/P) are approved to treat chronic HCV genotype (GT) 1–6 infection. Eight-week G/P achieved high SVR12 rates in Phase 2 and 3 studies, but was not studied in patients with compensated cirrhosis. Based on the high SVR12 rates demonstrated in treatment-naïve patients with HCV GT1–6 infection and compensated cirrhosis treated with 12-week G/P, this study evaluates the efficacy and safety of an 8-week G/P treatment duration in that population.

Methods: EXPEDITION-8 is an ongoing phase 3, non-randomized, single arm, open-label, multicenter study conducted in adults with chronic HCV GT1–6 infection with compensated cirrhosis who are HCV treatment-naïve. A recently approved protocol amendment enabled the inclusion of HCV GT3-infected patients, who are not included in this analysis. G/P (300 mg/120 mg) is being dosed orally once-daily with food for 8 weeks. The primary efficacy endpoint is the SVR12 rate. Secondary endpoints are on-treatment virologic failure and relapse rates. Adverse events and clinical laboratory abnormalities are being monitored in all patients.

Results: In total, 280 treatment-naïve patients with compensated cirrhosis have enrolled and are included in the analysis. The majority of patients were white (80%), male (60%), and with a Child-Pugh score of 5 (90%); the distribution of genotypes were as follows: GT1 (82%), GT2 (9%), GT4 (5%), GT5 (<1%), and GT6 (3%). At baseline, median and range values for key characteristics were as follows: HCV RNA 6.3 (3.4–7.5) log10 IU/mL, FibroScan score 20.7 (2.5–70.6) kPa, platelet count 152 (42–788) x 10^9 cells/L, total bilirubin 0.7 (0.2–2.4) mg/dL and albumin 4.2 (2.7–5.1) g/dL. To date, 116 patients have completed the post-treatment week 12 visit; Figure 1 shows preliminary efficacy results for those with available post-treatment week 4 and/or 12 data. No virologic failures have occurred. Adverse events (AEs) have been mostly mild, with the most common (at least 5%) AEs being pruritus and fatigue (both 9%), headache (7%) and nausea (6%). No AEs have led to discontinuation of G/P; 5 serious AEs have occurred, none of which were deemed related to G/P.

Conclusions: In this ongoing study, G/P for 8 weeks in treatment-naïve patients with HCV infection and compensated cirrhosis has been well-tolerated and achieved high rates of SVR, with no virologic failures to date. Updated efficacy and safety data will be presented at the meeting.

Keywords: Hepatitis C, Liver cirrhosis, RNA virus infection

O-027

Ledipasvir/Sofosbuvir for 12 Weeks Is Effective in HCV-Infected Asian Patients with Difference Liver Fibrosis Stages: Integrated Analysis of Clinical Studies

Chun-Jen Liu1, Masashi Mizokami2, Lai Wei3, Young-Suk Lim4, Sang Hoon Ahn5, Seung Woon Paik6, Ju-Hyun Kim7, Qing Xie8, Jin Youn9, Chen-Yu Wang9, Joe Llewellyn9, Anu Osinusi10, Gerald...

Conclusions: In this ongoing study, G/P for 8 weeks in treatment-naïve patients with HCV infection and compensated cirrhosis has been well-tolerated and achieved high rates of SVR, with no virologic failures to date. Updated efficacy and safety data will be presented at the meeting.

Keywords: Hepatitis C, Liver cirrhosis, RNA virus infection
Aims: Ledipasvir (LDV)/sofosbuvir (SOF) fixed-dose combination is approved as a 12-week regimen for patients with HCV genotype 1, 2, 4-6 infection in several Asian countries. This integrated analysis describes the efficacy and safety of LDV/SOF treatment in HCV-infected genotype (GT) 1 and 2 Asian patients across the spectrum of fibrosis stages.

Methods: This is a retrospective analysis from 797 Asian patients with GT 1 or 2 HCV infection treated with LDV/SOF for 12 weeks in 4 phase 3 studies. Fibrosis stages were defined by liver biopsy, transient elastography, or Fibrotest. Efficacy was assessed by sustained virologic response 12 weeks after treatment (SVR12). Safety data was analyzed.

Results: 797 Asian subjects were treated with LDV/SOF for 12 weeks. 56% were female, 70% had IL28B CC genotype, 45% had prior treatment failure and 78% were infected with genotype 1. Overall 68% were F0-F2, 14% were F3, and 18% were F4. In complete analysis, the overall SVR rate was 99% (786/791, 99% [788/796] in Intend-to-treat analysis), and was 99% (617/619) and 98% (169/172) in subject infected with HCV genotype 1 and genotype 2, respectively. The SVR rate was 99% (535/536), 97% (109/112), and 99% (142/143) in subjects with F0-F2, F3, and F4 fibrosis respectively. Among previously treated subjects, the SVR rate was 99% (218/219), 97% (6062), 99% (7778) in F0-F2, F3, and F4 subjects respectively. The treatment was well tolerated with 2% (9/796, 6 in F0-F2, 1 in F3 and 2 in F4 subjects) severe adverse events and 0.4% (3 in F0-F2 subjects) discontinuations due to adverse event.

Conclusions: 12 weeks of LDV/SOF treatment is highly efficacious and well tolerated in Asian patients with GT1 and GT2 HCV infection regardless of fibrosis stages.

Keywords: HCV, Asian, Fibrosis, Ledipasvir, Sofosbuvir
# Use of Ribavirin for Chronic Hepatitis C Treatment on Direct-Acting Antiviral Era: Real World Practice

Hoon Gil Jo¹, Jung Hwan Yu⁷, In Hee Kim⁵, Dae-Ghon Kim⁵, Gum Mo Jung³, Yong Keun Cho⁷, Myeong Jun Song⁷, Sung-Bum Cho⁶, Eun Young Cho¹

¹Department of Internal Medicine, Wonkwang University School of Medicine, Korea; ²Department of Internal Medicine, Chonbuk National University School of Medicine, Korea; ³Departments of Internal Medicine, Presbyterian Medical Center, Korea; ⁴Department of Internal Medicine, Konkuk University School of Medicine, Korea; ⁵Department of Internal Medicine, Catholic University School of Medicine, Korea; ⁶Department of Internal Medicine, Chonnam University School of Medicine, Korea; ⁷Department of Internal Medicine, Inha University School of Medicine, Korea

**Aims:** Ribavirin is still used with DAA, and it is still necessary to monitor the anemia. The aim of this study was to identify factors predictive of anemia during the treatment and to investigate the ribavirin reduction behavior and its effects during the treatment with DAA in the real-world practice.

**Methods:** SOF and RBV treatment group from May 2016 to April 2017 and PR treatment group from 2008 to 2012 were enrolled. The medical records of the subjects were analyzed.

**Results:** There were 221 (93 males and 138 females) in SOF+RBV group and 178 (99 males and 79 females) in PR group, and SVR was 85.15% in PR group and 98.1% in SOF+RBV group. There was no significant difference in incidence of hemoglobin <10 g/dL between the two groups (P=0.414). During SOF+RBV treatment, the patients who reduced the dose of ribavirin were 18.9% (40/212): 22 with hemoglobin <10 g/dL, 10 with significant reductions from baseline hemoglobin, 6 due to side effects. Dose reduction of ribavirin was associated with low WBC, ANC, hemoglobin, hematocrit, platelet values, and high MCV values at the beginning of treatment. Ribavirin reduction was associated with low WBC, ANC, hemoglobin, hematocrit, platelet values, and high MCV values at the beginning of treatment. Also, it was associated with cirrhosis, older age, lower BMI, and longer treatment duration. Multivariate analysis showed that only MCV values were associated with ribavirin reduction (P=0.010). Accordingly, in the results of verifying the significance of MCV value, the change in MCV values affected SVR on PR group, but it was not associated with SVR in SOF+RBV group. MCV values and its change in the SOF+RBV group were associated with the incidence of anemia and reductions in the ribavirin dose during the treatment.
Conclusions: The incidence of anemia during the treatment with DAA was similar to that with the PR treatment, and the baseline MCV value could predict development of anemia during DAA plus ribavirin treatment. Therefore, patients who have high baseline values of MCV require close monitoring of anemia during the treatment.

Keywords: Chronic hepatitis C, Sofosbuvir, Ribavirin, Pegylated interferon

Design and Validation of Risk Prediction Model for Hepatocellular Carcinoma Development after Sustained Virological Response in Patients with Chronic Hepatitis C

Ho Soo Chun¹, Beom Kyung Kim¹,², Jun Yong Park¹,², Do Young Kim¹,², Sang Hoon Ahn¹,², Kwang-Hyub Han¹,², Cheol-Hyung Lee¹, Yun Bin Lee¹, Eun Ju Cho³, Su Jong Yu¹, Yoon Jun Kim¹, Jung-Hwan Yoon¹, Jeong-Hoon Lee³, and Seung Up Kim¹,²

¹Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; ²Yonsei Liver Center, Severance Hospital, Seoul, Republic of Korea; ³Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea

Aims: Hepatocellular carcinoma can develop after hepatitis C virus eradication. We developed a new hepatocellular carcinoma risk score (HCC-SVR score) based on independent predictors for chronic hepatitis C after sustained virological response.

Methods: Between 2003 and 2016, 1,193 patients with chronic hepatitis C who achieved sustained virological response through antiviral therapy were included (669 for training cohort, 524 for validation cohort). The HCC-SVR score was developed using multivariate Cox proportional hazards regression modelling.

Results: Hepatocellular carcinoma occurred more frequently in older, male patients and was associated with liver cirrhosis; hypertension; diabetes; lower platelet count; higher alpha-fetoprotein, aspartate, and alanine aminotransferase; lower total cholesterol; and higher fibrosis-4 index (FIB-4) (all \(P < 0.05\)). FIB-4 (hazard ratio = 1.080), male gender (hazard ratio = 8.189), and higher alpha-fetoprotein (hazard ratio = 1.060) independently predicted hepatocellular carcinoma (all \(P < 0.05\)). HCC-SVR score successfully predicted hepatocellular carcinoma development risk (area under receiver operating characteristic curve [AUC] = 0.771, 0.991, and 0.739 at 2, 6, and 10 years, respectively). The cumulative incidence rate of hepatocellular carcinoma differed significantly among groups stratified by HCC-SVR risk score (0–2 points, low; 3–7 points, intermediate; 8–9 points, high risk) (all \(P < 0.05\) by log-rank test). HCC-SVR score was maintained in a validation cohort (n = 524) (AUC = 0.728 at 2 years, 0.809 at 6 years, and 0.970 at 8 years).

Conclusions: The HCC-SVR score enables risk stratification for hepatocellular carcinoma development at sustained virological
Tumor Marker-Based Characterization of Patients with Intermediate-Stage Hepatocellular Carcinoma Deemed to Have a Grave Prognosis


1 Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 2 Korean Liver Cancer Study Group, Seoul, Korea; 3 Department of Internal Medicine, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea; 4 Department of Internal Medicine, Samsung Medical Center, Seoul, Korea; 5 Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Korea; 6 Department of Radiology, Seoul National University College of Medicine, Seoul, Korea.

Aims: For patients with intermediate-stage hepatocellular carcinoma (HCC), the definition of refractoriness to transarterial chemoembolization (TACE), which might be candidate for systemic therapy, is still controversial. We sought to derive and validate a tumor marker-based algorithm to guide the retreatment of intermediate-stage HCC with TACE.

Methods: The multiple study cohorts comprised a total of 482 consecutive patients who underwent TACE for treatment-naive intermediate-stage HCC. We derived a prediction model for overall survival (OS) using pre- and post-TACE MoRAL score (i.e., MoRAL score=11×[PIVKA-II] + 2×[α-fetoprotein (AFP)], which was proven to reflect both tumor burden and biologic aggressiveness of HCC in explant liver, from the training cohort (n=193). These results were externally validated in both an independent hospital cohort (from two large-volume centers, n=140) and a Korean National Cancer Registry sample cohort (n=149).

Results: Multivariable analyses indicated that the changes in MoRAL score (ΔMoRAL) after initial TACE was an independent predictor of OS (MoRAL-increase vs. MoRAL-non-increase: adjusted hazard ratio [HR]=2.18, 95% confidence interval [CI]=1.37–3.46, P=0.001; median OS=18.8 vs. 37.8 months) (Figure 1A). In a subgroup of patients with high baseline MoRAL score (≥89.5, 25th percentile and higher), the prognostic impact of ΔMoRAL was more pronounced (MoRAL-increase vs. MoRAL-non-increase: HR=3.68, 95% CI=1.54–8.76, P<0.001; median OS=9.9 vs. 37.4 months) (Figure 1B). These results were reproduced in the two external validation cohorts (Figure 2).

Conclusions: The ΔMoRAL after the first TACE, a simple and objective index, provides refined prognostication for patients with intermediate-stage HCC. Proceeding to a second TACE may not provide additional survival benefit in cases of MoRAL-increase after the first TACE in patients with high baseline MoRAL score (≥89.5) who might be candidates for systemic therapy.

Keywords: Tumor marker, Alpha-fetoprotein, Protein induced by vitamin K absence-II, TACE refractoriness

Hepatocyte-Specific MRI-Based Assessment of Indeterminate Hepatic Nodules in the Liver Transplant Evaluation of Cirrhotic Patients

Ha Il Kim, Jong Keon Jang, Jihye Lim, Seheon Chang, Jihyun An, Hye Jeong Kang, Gi-Won Song, Sung-Gyu Lee, So Yeon Kim, Ju Hyun Shim

1 Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 2 Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 3 Myongji Saint Mary’s Hospital, Seoul, Korea; 4 Gastroenterology and Hepatology, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri, Korea; 5 Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 6 Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 7 Asan Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.

Aims: We aimed to determine the identities in explants of indeterminate hepatic nodules (IDNs) that had been scanned by dynamic magnetic resonance imaging (MRI), in order to establish clinico-radiological parameters predicting which IDNs are hepatocellular carcinomas (HCCs).

Methods: This study included 88 cirrhotic patients who underwent gadoxetic acid-enhanced MRI in pre-LT workup followed...
within 90 days by primary liver transplantation (LT), in the Asan Medical Center. The MRI detected 168 hepatic nodules that were classified into 6 benign tumors, 49 HCCs, and 113 IDNs, in 5, 34, and 71 patients, respectively. We compared these pre-LT radiologic diagnoses and stagings with explant pathology on a per-lesion basis, to enable us to identify features of IDNs related to malignancy.

Results: Of the 168 nodules seen on MRI, 119 that were classified radiologically as consisting of 1 benign nodule (33.3%), 46 HCCs (93.9%), and 72 IDNs (63.7%) all turned out to be pathologic HCCs. Of 86 Milan-in patients staged by MRI, 11 progressed beyond the criteria after LT. HCC recurrence within 5 years of LT was most frequent in these recipients. High serum alpha-fetoprotein level (≥20 ng/mL) was the only per-patient factor significantly associated with malignant IDNs (Odds ratio [OR] 5.133, P=0.004). Per-tumor analysis of MRI signals revealed that arterial hyperintensity (OR, 3.45), hepatobiliary hypointensity (OR, 2.77), T2-weighted mild-to-moderate intensity (OR, 2.51), and restricted diffusion-weighted image (OR, 2.62) were significantly correlated with malignant IDN (ps<0.05). A model combining these 4 MRI factors and alpha-fetoprotein had the best performance for predicting the diagnosis of IDNs as HCCs in explanted livers.

Conclusions: Over 60% of the IDNs seen on dynamic images of cirrhotic livers proved to be HCCs when explanted livers were examined. It may be possible to identify HCCs with reasonable accuracy by means of their hepatocyte-specific MRI features in assessing patients for LT.

Keywords: Hepatocyte-specific MRI, Indeterminate hepatic nodules, Liver transplantation

O-033

Response to Sorafenib in Patients with Advanced Hepatocellular Carcinoma: Predictive Analytics Using Machine Learning with a Neighborhood-Group Detection Method

Jun Hyuk Kang1, Joong-Won Park2, Minjung Lee2, Bo Hyun Kim1
1Center for Liver Cancer, National Cancer Center, Korea; 2Department of Internal Medicine, Kangwon National University Hospital, Korea

Aims: Global guidelines indicate that sorafenib is the treatment of choice for patients with advanced hepatocellular carcinoma (HCC). However, only a few clinical markers have been suggested as predictors of the response to sorafenib. Owing to the nonlinear distribution characteristics of clinical variables, it is difficult to identify predictors by using conventional statistical analysis. To address this nonlinearity, we developed a neighborhood-group (N-group) detection method and investigated the predictors of the response to sorafenib treatment.

Methods: A previous cohort of patients that had been subjected to conventional statistical analysis (Lee M, et al. ILCA 2018 p-101; n=709) was re-analyzed. The analyses comprised: (1) calculation of the distance between all patient pairs; (2) defining N-groups based on an appropriate threshold distance and the minimum number of patients that should be included in the group; and (3) survival analysis of all N-groups. Subsequently, the clinical features of the N-groups were examined in detail to reveal the predictors related to survival differences.

Results: In total, 139 N-groups with distinct clinical features were found. In the survival analyses for all 9591 pairs of N-groups, 661 pairs of nearby N-groups were found to have significant differences in overall survival. According to the clinical characteristics of each N-group pair, various factors associated with the differences in survival were observed. The presence of portal vein thrombosis (PVT) and the absence of hand-foot syndrome (HFS) were commonly associated with poor survival. In N-group pairs without significant differences in PVT and HFS, the presence of extrahepatic metastasis and non-viral etiology was consistently associated with poor survival.

Conclusions: Through the use of an N-group detection method, we were able to identify predictors of the response to sorafenib that were consistent with the conventional analysis and additional factors. This new analytical method will provide a novel perspective for clinical analysis.

Keywords: Hepatocellular carcinoma, Sorafenib, Neighborhood-group
Deterioration of Liver Function after Transarterial Chemoembolization (TACE): Final Analysis of OPTIMIS in Korea and Rest of Asia

Keywords: Hepatocellular carcinoma, Radiofrequency ablation, Stereotactic body radiation therapy

Aims: TACE is commonly used for patients (pts) with unresectable HCC (uHCC). However, there is no global consensus on TACE use.

Methods: OPTIMIS is an international, prospective, non-interventional study of uHCC pts for whom the decision to treat with TACE was made prior to enrollment. We report practice patterns, radiologic tumor response, liver deterioration, and subsequent treatments from Korea and rest of Asia. TACE ineligibility was analyzed per study protocol-specified criteria.

Results: Globally, 1,650 enrolled pts received TACE, including 292 from Korea and 459 from rest of Asia. Of those, 85/292 pts (29%) in Korea and 193/459 (42%) in rest of Asia were TACE ineligible at inclusion (Table). Excluding pts with prior sorafenib use, 109/292 (37%) in Korea and 100/459 (22%) in rest of Asia became TACE ineligible during the study. Of those, 6/109 pts (6%) in Korea and 3/100 (3%) in rest of Asia received sorafenib immediately after TACE ineligibility. In TACE administered pts, complete and partial response rates to first TACE were 24% and 36% versus 8% and 20% in Korea and rest of Asia, respectively. In pts with available laboratory values, chronic liver function deterioration (worsening in CTCAE grade 3–90 days post TACE) after first TACE was noted in Korea and rest of Asia: bilirubin (12% and 25%), albumin (22% and 24%), ALT (4% and 27%), and AST (9% and 31%).

Table. Disease characteristics and TACE ineligibility at inclusion in Korea and rest of Asia

<table>
<thead>
<tr>
<th>Disease status</th>
<th>Korea (n=292)</th>
<th>Rest of Asia (n=459)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHS</td>
<td>25 (9)</td>
<td>33 (7)</td>
</tr>
<tr>
<td>PVT</td>
<td>30 (10)</td>
<td>22 (5)</td>
</tr>
<tr>
<td>BCLC stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>204 (70)</td>
<td>284 (62)</td>
</tr>
<tr>
<td>C</td>
<td>79 (27)</td>
<td>154 (34)</td>
</tr>
<tr>
<td>D</td>
<td>3 (1)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (2)</td>
<td>11 (2)</td>
</tr>
<tr>
<td>Ineligible for TACE per study protocol-specified criteria</td>
<td>85 (29)</td>
<td>193 (42)</td>
</tr>
</tbody>
</table>

BCLC, Barcelona Clinic Liver Cancer; EHS, extrahepatic spread; PVT, portal vein thrombosis; TACE, transarterial chemoembolization.


References:

1. Department of Internal Medicine, College of Medicine, Pusan National University and Medical Research Institute, Pusan National University Hospital, Busan, South Korea; 2. Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; 3. Department of Cancerology de l’Ouest, Nantes, France; 4. Department of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria; 5. Department of Gastroenterology/Hepatology, Endocrinology and Nephrology, Klinikum Klagenfurt am Wörthersee, Klagenfurt, Austria; 6. Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; 7. Global Medical Affairs, Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA; 8. Bayer AG, SBU Oncology, Pharmaceuticals, Wuppertal, Germany; 9. Division of Hepatology, Chang Gung University and Chang Gung Memorial Hospital, Taoyuan, Taiwan; 10. Department of Gastroenterology Asian Liver Center, Asian Medical Center, University of Ulsan College of Medicine, Seoul, South Korea.
Conclusions: TACE ineligibility criteria appear to be followed to a lesser extent in the rest of Asia compared to Korea. After the first TACE, liver function deterioration was noted in the chronic period and was higher in rest of Asia compared to Korea. In addition, radiologic tumor response rates were lower in rest of Asia compared to Korea. Our data highlight the need for evaluating TACE practice in uHCC to ensure pt eligibility for subsequent effective therapies.

Clinical Trial: NCT01933945

Keywords: Hepatocellular carcinoma, Transarterial chemoembolization, Practice patterns, Tumor response, Liver function

O-036

Distinct Mutational and Molecular Patterns Associated with Family History in Hepatocellular Carcinoma

Ji-hyun An¹, Ji-Hye Oh², Ha Il Kim³, Seheon Chang⁴, Chang Oeh Sung⁵⁶, Han Chu Lee⁷, Ju Hyun Shim⁸

¹Gastroenterology and Hepatology, Hanyang University College of Medicine, Guri, Korea; ²Medical Science, Asan Medical Institute of Convergence Science and Technology, University of UlSAN College of Medicine, Seoul, Korea; ³Gastroenterology, Asan Medical Center, University of UlSAN College of Medicine, Seoul, Korea; ⁴Pathology, Asan Medical Center, University of UlSAN College of Medicine, Seoul, Korea; ⁵Center for Cancer Genome Discovery, Asan Institute for Life Science, Asan Medical Center, Seoul, Korea; ⁶Asan Liver Center, Asan Institute for Life Science, Asan Medical Center, Seoul, Korea

Aims: Familial clustering is a common feature of hepatocellular carcinoma (HCC) as well as a risk factor for the disease. We sought to identify differences in the gene mutations and molecular alterations in patients with HCC who had a family history of the same disease versus sporadic cases.

Methods: Large genomic datasets of HCC [combined sets using whole exome sequencing and RNA-seq at Asan Medical Center (n=231) and TCGA LIHC dataset (n=316)] were analyzed to define distinct driver mutations, copy number variations, and diverse gene expressions based on the status of family history.

Results: Overall, approximately 27.3% of patients (160 out of 547) had a family history of HCC. A family history of HCC was predominantly more in female, white race, and older patients, and less in hepatitis B patients (P<0.05). Although the number of mutations was comparable between the two sets of tumors, the familial tumors contained different somatic mutation patterns with a greater frequency of alterations in TSC1, MYO18A, CNTN2, CLTC11, SYNO2, and DSCAM; and highly exclusive alterations in RPH3A, ERG, RNF146, PRKCZ, LMTK3, and FAM46D. Copy number alteration analysis disclosed distinguishable deletions in the 4q23 and 6q27 chromosome arm in the familial cases. In terms of mutational signature, signature 12 was more frequently exhibited signature 12 in HCC with family history, while signature 16 and 22 were less found. Differentially expressed transcripts in a subset of 516 tumors were significantly enriched in cellular metabolic process, especially, in pyruvate metabolism and the citric acid cycle pathway.

Conclusions: By multi-platform genomic profiling of HCC, we have refined our understanding of genetics events in familial HCC and identified clinical relevant alterations. This pathobiologic insight may serve as a fundamental backbone for precision prevention and treatment of HCC in actual practice.

Keywords: Hepatocellular carcinoma, Genomics, Family history, Mutation

O-037

Management of Pancreaticojejunostomy Stricture after Pancreatectoduodenectomy

Xu’an WANG, Wenguang WIU, Hao WENG, Xueping ZHOU, Litian CHEN, Xuefeng WANG, Yingbin LIU

Department of General Surgery, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, China

Aims: To explore the clinical management of pancreaticojejunostomy stricture (PJS) after pancreatectoduodenectomy (PD).

Methods: From July 2013 to Dec 2018, 17 patients with PJS were treated in our single center, including 10 male and 7 female, the average age was 61.3 years (49.1-73.8). All these patients had recurrent abdominal pain and acute pancreatitis. Among them, 7 were pancreatic cancer, 6 IPMN, 3 chronic pancreatitis and 1 periampullary carcinoma. The median time between PD to PJS was 38.1 months.

Results: 11 patients were successfully treated by Endoscopic dilation plus pancreatic drainage or EUS-guided rendezvous technique. Other 6 patients who failed the endoscopic technique, pancreatectoduodenectomy (PJ) reconstruction was performed for 2 cases, PJ resected followed by pancreaticogastrostomy (PG) for 3 cases, and longitudinal PJ for 1 case. None of them had severe complication.

Conclusions: PJS is a late complication of PD that was less studied, the incidence is increasing since the survival time after PD was prolonged. Endoscopic treatment is our first choice. If the endoscopic technique failed, surgical treatment remains the only option. Commonly there are 4 kinds of surgical methods could be selected. PJ reconstructed, PJ resected followed by PG, Longitudinal PJ for 1 case. And posterior direct PG.

O-038

A Inverted Mattress Technique of Pancreaticojejunostomy for Laparoscopic Pancreatectoduodenectomy

Hyung Jun KWON, Sang Geol KIM, Yun Jin HWANG

Surgery, Kyungpook National University Chilgok Hospital, Kyungpook National University School of Medicine, Republic of Korea
Aims: Laparoscopic pancreatoduodenectomy (LPD) is a challenging abdominal operation requiring complex dissection and difficult reconstruction. Especially, pancreaticojejunostomy (PJ) reconstruction is considered the “Achilles heel” of LPD because pancreatic fluid leakage from the procedure is potentially significant morbidity. In the present report, we describe our experience with our inverted mattress (IM) method for LPD.

Methods: Between May 2016 and December 2018, a total of 143 patients with periamppillary disease underwent PD at Kyungpook national university chilgok hospital. 43 patients underwent and Open PD was performed on 100 patients. The pancreatic stump was reconstructed using an our IM-PJ technique. Data on the demographic characteristics, operative outcomes and postoperative results of the cases were retrospectively collected and analyzed.

Results: Forty three patients received LPD and 7 patient was converted to open method. The mean age was 63.0 ± 12.0 years and gender ratio was 1:1. Mean ASA score and BMI were 1.8 ± 0.4 and 23.1 ± 3.4 respectively. The mean operation time was 430 ± 73.2 min. Average blood loss was 107.8±194ml. Postoperative pancreatic fistula (POPF) of Grade B occurred in 5.6% and Grade C was not occurred. Also, delayed gastric emptying (DGE) occurred in 15.8%. The mean length of hospital stay was 12.4 ± 2.7 days and no postoperative mortality occurred.

Conclusions: The results of the present study suggest the a IM-PJ method is a safe for LPD that is associated with a low risk of POPF. However, these results should be verified by performing randomized control trials.

New Onset Diabetes and Reduction of Pancreatic Volume in Laparoscopic versus and Open Pancreaticoduodenectomy

Sung Hoon Choi
Surgery, Bundang CHA Medical Center, Republic of Korea

Aims: Atrophy of the remnant pancreas might be a risk factor for new onset diabetes mellitus (DM) after pancreaticoduodenectomy (PD). There was no comparative study of laparoscopic and open PD for differences in change of remnant pancreatic volume and incidence of new onset DM after surgery.

Methods: Fifty-seven patients underwent laparoscopic PD and 43 patients underwent open PD for periamppillary pathologies between March 2014 and September 2018 were included. All patients underwent duct-to-mucosa pancreaticojejunostomy for the reconstruction of the remnant pancreas. The perioperative outcomes including the incidence of new onset DM were examined. The pancreatic volume was measured 1 week and 3 months after surgery using computer tomography volumetry.

Results: The mean age, ratio of sex, and mean body mass index of patients were comparable between the two groups. The operative time was comparable (417 ± 83 vs. 392 ± 87 min, P=0.638), but the estimated blood loss was lesser in laparoscopic group (402 ± 391 vs. 945 ± 402 ml, P=0.002). Postoperative complications greater than grade II were not different (5 vs. 5 cases, P=0.659). Incidence of new onset pancreatogenic DM was not different (7 vs. 6 cases, P=1.000). The pancreatic volume reduction rate 3 months after PD was similar in both laparoscopic and open PD (11.1 ± 17.2 vs. 10.1 ± 12.3 ml, P=0.749).

Conclusions: This study suggests that the laparoscopic PD with duct-to-mucosa pancreaticojejunostomy was safe and did not deteriorate the atrophic changes of the remnant pancreas and development of new onset DM.

Preoperative Serum Glucose to Lymphocyte Ratio as an Independent Prognostic Factor: Developing 3-Scored Survival Estimating System in Resected Pancreatic Ductal Adenocarcinoma

Incheon KANG, Chang Moo KANG
Division of HBP Surgery, Department of Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: We hypothesized that elevated glucose to lymphocyte ratio (GLR) might be a sensitive prognostic biomarker to determine the disease specific survival of pancreas ductal adenocarcinoma (PDAC). Moreover, we try to develop scoring system to predict the prognosis of PDAC by using only clinically available preoperative parameters.

Methods: Between May 1999 and August 2016, 244 patients with resectable PDAC underwent surgical resection at Severance Hospital, Korea. Medical records were retrospectively reviewed. The preoperative clinical parameters, inflammatory markers, glucose, GLR, albumin, tumor size, carbohydrate antigen (CA) 19-9, and follow up data were collected. Survival analysis and Cox regression were performed to evaluate oncologic outcomes.

Results: Among the preoperative detectable parameters, 1) GLR ≥105.5 (HR=1.6074, 95% CI: 1.119-2.308 P=0.0102), 2) CA19-9≥150 (HR=1.432, 95% CI: 0.999-2.053, P=0.0405), and 3) tumor size ≥2 cm (HR=1.586, 95% CI: 1.113-2.259, P=0.0106) were independent prognostic factor in determining long-term cancer-specific survival by multivariate analysis. We developed 3-scored survival estimating system (0 to 3) by summing these three parameters. Overall survival is significantly different according to clinically divided subgroups by 3-scored survival estimating system (P<0.001).

Conclusions: GLR is an independent prognostic factor of disease-specific survival in PDAC. Based on preoperative detectable parameters including GLR, CA 19-9, tumor size, we developed 3-scored survival estimating system which can serve as a model for assessing the possibilities of individual treatment option for PDAC patients.
O-041

Development and Validation of a Novel Topical Agent for Gallstone Dissolution
Say-June KIM¹, Kee Hwan KIM²
¹Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, ²Department of Surgery, Uijeongbu St. Mary’s Hospital, The Catholic University of Korea

Aims: Although MTBE is the only clinical topical agent for gallstone dissolution, its use is limited by its side effects mostly arising from a relatively low boiling point (55 °C).

Methods: The dissolubility of MTBE and MMP in vitro was determined by placing human gallstones in glass containers with either solvent and, then, measuring their dry weights. Their dissolubility in vivo was determined by comparing the weights of solvent-treated gallstones and control (dimethyl sulfoxide)-treated gallstones, after directly injecting each solvent into the gallbladder in hamster models with cholesterol and pigmentated gallstones.

Results: In the in vitro dissolution test, MMP demonstrated statistically higher dissolubility than did MTBE for cholesterol and pigmentated gallstones (88.2% vs. 65.7%, 50.8% vs. 29.0%, respectively; P<0.05). In the in vivo experiments, MMP exhibited 59.0% and 54.3% dissolubility for cholesterol and pigmentated gallstones, respectively, which were significantly higher than those of MTBE (50.0% and 32.0%, respectively; P<0.05). The immunohistochemical stains of gallbladder specimens obtained from the MMP-treated hamsters demonstrated that MMP did not significantly increase the expression of cleaved caspase 9 or significantly decrease the expression of proliferation cell nuclear antigen.

Conclusions: This study demonstrated that MMP has better potential than does MTBE in dissolving gallstones, especially pigmentated gallstones, while resulting in lesser toxicities.

O-042

Robotic Surgery for Gall Bladder Cancer: Operative Technique and Early Outcomes
Shraddha Patkar, Krunal Khobragade, Sagar Kurunkar, Mahesh Goel, Rajgopal Acharya
GI and HPB Surgical Oncology, Tata Memorial Hospital, India

Aims: The objective of this study was to compare the early outcomes of robotic radical cholecystectomy (RRC) with open radical cholecystectomy (ORC) for gall bladder cancer (GBC).

Methods: Patients who underwent RRC for suspected or incidental GBC between July 2015 to August 2018 were analysed. Patients who underwent ORC during the same period and fulfilled the study criteria formed the control group.

Results: During the study period, 27 patients who underwent RRC formed the study group (Group A) and 70 matched patients who underwent ORC formed the control group (Group B). Median surgical time was higher in Group A (295 versus 200 mins, P<0.001). However, median blood loss (ml) (200 versus 600 ml, P<0.001), postoperative hospital-stay (4 versus 5 days, P=0.046) and postoperative morbidity (1 versus 15 patients, P=0.035) were lower in Group A. Median lymph node yield was 10 (range=2-21) for Group A and 9 (range=2-25) for Group B, and was comparable (P=0.408). During a median follow up of 9 (1-46) months, 2 patients in Group A (no port site recurrence) and 12 patients in Group B developed recurrence.

Conclusions: RRC is safe and feasible and the short-term results are comparable to ORC.

O-043

Laparoscopic Pancreaticoduodenectomy: CUSUM Analysis in a Developing Single Surgeon
Jung Woo LEE, Dong hyun KIM, Jung il KIM, Hyun ryung KIM, Jung ho PARK
Division of Hepatobiliarypancreas, Department of Surgery, Hallym Sacred Heart Hospital, Republic of Korea

Aims: Laparoscopic pancreaticoduodenectomy (LPD) was the one of most technically challenging operations of minimally invasive surgery (MIS). This retrospective study aimed to analyze the learning curve of a single surgeon who carried out 63 LPD in a single center.

Methods: From August 2015 to August 2018, 63 patient underwent laparoscopic pancreaticoduodenectomy in hallym sacred heart hospital by a single surgeon. The patient characteristics, perioperative variables, and immediate postoperative outcomes were retrospectively collected and analysed. The cumulative sum (CUSUM) analysis was used to identify the inflexion points which corresponded to the learning curve.

Results: From the CUSUM analysis, two distinct phase of the learning curve were identified (early group:1-34 cases and late group: 35-63 cases). Among two groups, there was no significant difference in perioperative outcomes. Non-significant reduction were observed in operation time (mean, 448 min vs. 425 min, P=0.239), conversion rate (8.8% vs. 3.4%, P=0.618), postoperative complication (Clavien-Dindo grade III or higher, 26.5% vs. 20.7%, P=0.768), and intraoperative transfusion rate (35.3% vs. 20.7%, P=0.267). Except pancreas adenocarcinoma, two distinct phase of the learning curve were identified (early group: 1-31 cases and late group: 32-45 cases). there was significant difference in operation time(mean, 439 min vs. 367 min, P<0.001) and intraoperative transfusion rate (35.5% vs. 7.1%, P=0.07). Non-significant reduction were observed in conversion rate, postoperative stay, and complication.

Conclusions: Laparoscopic pancreaticoduodenectomy can be safely and feasibly performed selected cases by experienced hepatobiliary-pancreas surgeons. Conservatively, the learning curve was completed after about 30 LPD in excluding PDAC.
Upfront vs. Delayed Laparoscopic Assisted Necrosectomy for Infectected Pancreatic Necrosis

Feng CAO, Fei LI
Department of General Surgery, Xuanwu Hospital, Capital Medical University, China

Aims: To delay the surgery, percutaneous or endoscopic drainage was usually performed as the first step in step-up approach for infected pancreatic necrosis (IPN). However, drainage was unnecessary or unavailable in some patients. To explore the safety and effect of upfront laparoscopic assisted necrosectomy in treatment of IPN.

Methods: IPN patients received surgical therapy in our center between January 2015 and December 2017 were included in this study. Patients were assigned to either single or step-up group according to the received therapeutic approach. Incidence of complications, death, total number of surgical intervention and total hospital stay were compared. Logistic regression and nomogram were used to explore the risk factors and probability for patients undergoing surgical intervention ≥3 times.

Results: There were 45 and 49 patients included in single step and step-up group, respectively. No significant difference between groups in terms of new organ failure (14.29% vs. 14.33%, P=0.832), death (8.89% vs. 8.17%, P=0.949) and long-term complications (18.37% vs. 15.56%, P=0.717). However, the number of surgical intervention in single step group was significant less than in step-up group with shorter hospital stay. After multivariate analysis, CRP, IL-6 and surgical approach were independent predictors for patients undergoing surgical intervention ≥3. A nomogram was built with area under ROC curve 0.891.

Conclusions: Compared with step-up approach, single up surgery was safe and effective in selected IPN patients with less number of surgical intervention and shorter hospital stay.

Parietal Peritoneum as an Autologous Substitute for Middle Hepatic Vein Reconstruction during Living-Donor Liver Transplantation

Suk Kyun Hong, Kyung-Suk Suh, Jae-Hyung Cho, Jeong-Moo Lee, Nam-Joon Yi, Kwang-Woong Lee
Department of Surgery, Seoul National University College of Medicine

Aims: Draining the anterior section of the graft liver prevents congestion and preserves the graft function when using right lobe for living-donor liver transplantation (LDLT). Autologous, cryopreserved, or artificial vascular graft can be used as an interpositional vascular substitute. However, they are not always available, time-consuming, expensive, or associated with a risk of infection. The parietal peritoneum can be a good alternative to solve these problems. This study reports the first 16 cases of LDLT using parietal peritoneum for middle hepatic vein reconstruction.

Methods: Between May 2016 and February 2019, 16 patients underwent LDLT using right lobe with reconstruction of middle hepatic vein using the patients’ own parietal peritoneum. This study was reviewed and approved by the institutional review board of the author’s institution.

Results: V5 was reconstructed in 16 patients and V8 in 11 patients. The mean hospital stay was 17.4 days. The 7-days and 32-days patency rates were 56.3% and 37.5%. All patients survived with tolerable liver function tests. There were 3 patients with early major complication; one experienced middle hepatic vein thrombosis which required aspiration thrombectomy and stent insertion and the other one experienced bile duct leakage which required endoscopic biliary drainage. There were 3 patients experienced late major complication including one portal vein stenosis, one bile duct stricture, and the other one bile leakage. There was no infection related complication. After initial experience, all of the recent 6 cases showed good patency until discharge and are under follow up.

Conclusions: Parietal peritoneum can be safely used as an autologous substitute for middle hepatic vein reconstruction during LDLT.

Keywords: Peritoneum, Living donor liver transplantation, Graft, Middle hepatic vein
ed. All operations were performed identical procedures for dissection and hemostasis and were totally robotic approach.

**Results:** 22 cases of left hemipatectomy, 1 case of extended left hemipatectomy, 14 cases of right hemipatectomy, 2 cases of right anterior sectionectomy, 6 cases of right posterior sectionectomy, and one cases of central bisectionectomy were performed. Total operation time was 378.58 ± 124.31 (190–696) minutes and estimated intraoperative blood loss was 276.67 ± 397.41 mL (minimal – 2600mL). Overall complications were developed in 16 cases (34/8%). In terms of severe surgical complications, there were 3 cases of postoperative fluid collection treated with drainage and one case of bile leakage treated with percutaneous trans-hepatic biliary drainage. Only one case out of 46 cases was converted to the conventional open left hemipatectomy by bleeding.

**Conclusions:** In this study, robotic anatomic major liver resection might be safely performed even by robotic beginners but advanced open and laparoscopic liver surgeons.

**Selective Occlusion of the Hepatic Artery and Portal Vein Improves Liver Hypertrophy for Staged Hepatectomy**

Changku JIA

Hepatobiliary Pancreatic Surgery, Affiliated Hangzhou First People’s Hospital,Zhejiang University School of Medicine,China

**Aims:** To evaluate the safety and feasibility of a new method of selective occlusion of the hepatic artery and portal vein (SOAP) for staged hepatectomy (SOAPS) in patients with hepatocellular carcinoma (HCC).

**Methods:** Ten patients with unresectable HCC due to insufficient volume of future liver remnant (FLR) were chosen to undergo SOAPS. SOAP without liver partition was performed in the first stage of hepatectomy. The second stage of hepatectomy, including right hemipatectomy, right trisectionectomy and left trisectionectomy, was performed when the FLR was sufficient.

**Results:** None of the patients developed hepatic failure and no deaths occurred following SOAP. The FLR in all patients increased by an average of 144.3 mL after SOAP. The average ratio of FLR to standard liver volume increased from 32.6% to 44.7%. The second stage of hepatectomy was performed 8 to 18 days after SOAP. The average time interval between the two stages was 14.4 days. No in-hospital deaths occurred after SOAPS. The AFP level in 8 patients reduced to normal within two months after SOAPS. Of these 10 patients, 4 patients died of intrahepatic recurrence, lung metastasis or bone metastasis. Six months after SOAPS. Of these 10 patients, 4 patients died of cancer. All operations were performed with robotic approach.

**Conclusions:** In this study, robotic anatomic major liver resection might be safely performed even by robotic beginners but advanced open and laparoscopic liver surgeons.

**Clinical Outcomes of Laparoscopic Living Donor Right Hepatectomy without Pringle’s and Hanging Maneuver**

Young Seok HAN, Ja Ryung HAN, Heon Tak HA, Jae Min CHUN, Yoon Jin HWANG

Hepatobiliary Pancreas Surgery and Liver Transplantation, Kyungpook National University, School of Medicine, Kyungpook National University Hospital, Republic of Korea

**Aims:** Careful preparation and blood-saving surgery will significantly lower the postoperative morbidity in laparoscopic liver resection (LLR). To reduce bleeding during hepatectomy, it is
significant to decrease central venous pressure (CVP) and apply Pringle’s & hanging maneuver (P&H). However, P&H are cumbersome and has the potential for further injury by excessive mobilization and dissection of inferior vena cava and right lobe of liver, especially in living liver donors. We would like to present the experience and outcomes of laparoscopic living donor right hepatectomy (LDRH) performed without P&H.

**Methods:** Between December 2014 and October 2018, among 97 cases of living donor right hepatectomy, 50 donors underwent LDRH. During LDRH, mean pneumoperitoneal pressure was 12 mmHg and CVP was less than 5 mmHg. The right liver was mobilized to the inferior half portion of retrohepatic IVC and large right inferior hepatic veins were preserved. The caudal approach without P&H was applied for liver parenchymal transection. The V5 and V8 for reconstruction were also preserved until just before the right hepatic duct transection.

**Results:** Mean total operation time was 367 minutes and the warm ischemic time was 9.2 minutes. No donors required blood transfusion, conversion to open surgery, and re-operation. The postoperative course was uneventful. All donors’ liver function was recovered to normal range within 2 weeks and mean postoperative hospital stay was 8 days.

**Conclusions:** Conclusively, LLR under low CVP and constant pneumoperitoneal pressure without P&H can help reduce blood loss and prevent further liver graft injury by excessive mobilization of liver.

### O-050

**Right and Ventral Margins of Paracaval Portion of Caudate Lobe: Studies from Cadaveric Dissection and 3D Reconstruction Analysis Using Synapse 3D Software**

Xue-Yin Shen¹, Sung-Yeon Hong¹, Xu-Guang Hu², Mi-Na Kim¹, Bong-Wan Kim¹, Hee-Jung Wang²

¹Department of Hepatobiliary Surgery, Ajou University Hospital, Republic of Korea, ²Department of Hepatobiliary Surgery, Jiangxi Cancer Center, China

**Aims:** As the hilar cholangiocarcinoma holds the possibility of metastasis via minute bile duct branches to caudate lobe, total caudate lobectomy along with hepatic resection is necessary. This study was designed to figure out the utility of using Synapse 3D in the right and ventral margins of caudate lobe before caudate lobectomy.

**Methods:** 18 cadaveric liver specimens were dissected and by calculating the distance from the right side of inferior vena cava (IVC) and height from the hilar plate of a rightmost branch, we figured out the right margin and ventral margin of paracaval portion, respectively. 39 preoperative liver computed tomography images were obtained from donors and reconstructed by Synapse 3D software.

**Results:** In the respect of right margin, the mean length in Synapse 3D group was 1.7 cm, greater than 1.2 cm of cadaveric dissection group meaningfully (P<0.05). Synapse 3D showed 4 types of ventral margin. Type 1: the ventral margin of paracaval portion is restricted to the dome-like area between the middle hepatic vein (MHV) and right hepatic vein (RHV) insertion to the IVC (30 cases, 76.9%); Type 2: ventral margin extends beyond this dome-like area (7 cases, 17.9%); Type 3: ventral margin extends beyond the RHV (1 case, 2.6%); Type 4: ventral margin extends beyond both RHV and MHV-RHV dome-like area (1 case, 2.6%).

**Conclusions:** The image of the right margin and ventral margin of the paracaval portion can be reconstructed and measured by Synapse 3D, we think it is beneficial for more precise caudate lobectomy clinically.

### O-051

**Short Term Result of Parenchymal Sparing Anatomical Liver Resection Based on Portal Ramification of the Right Anterior Section: A Single Center Experience**

Giang NGUYEN, Anh PHAM, Ha NGHIEM, Hung NGUYEN, Duc PHAM

Hepatobiliary and Pancreatic Surgery, Vietnam National Cancer Hospital, Vietnam

**Aims:** Anatomical liver resection is the treatment of choice for hepato cellular carcinoma (HCC). However, the remnant liver volume is equally important in patient selection for operation. Recent appreciation of the liver segmentation divided the right anterior section (RAS) into segment 5-segment 8 or ventral-dorsal segment. Thus, we aim to evaluate the short term results of parenchymal sparing liver resection based on portal ramification of the right anterior section.

**Methods:** From July 1 to December 30, 2018, 12 patients with HCC underwent parenchymal sparing right hepatectomy. The portal ramification of RAS were analyzed using the Multidetector Computed Tomography scan. The procedures were performed by 4 liver surgeons.

**Results:** Among 12 patients, there were 10 men and 2 women. The mean age was 60.6 ± 6.9 years. The right hepatectomy with segment 8 parenchymal sparing was performed in 1 patient with cranio-caudal type of the RAS. In 11 patients with ventro-dorsal type, we performed 10 ventral-segment preserving right hemihepatectomy and 1 dorsal preserving mesohepatectomy. The mean operative time was 262.5 ± 40.1 minutes with a mean estimated blood loss of 404.2 ± 362.4 ml. One liver failure was reported (Clavien-Dindo classification, grade 2). The mean length of hospital stay was 10.9 ± 3.9 days. There was no reported 30 days mortality.

**Conclusions:** The pre-operative evaluation of RAS’s anatomy is very important to decide the method of parenchymal sparing
Improved Outcomes of Laparoscopic Liver Resection for Hepatocellular Carcinoma Located in Posterosuperior Segments of the Liver

Yujin Kwon1, Jai Young Cho2, Ho-Seong Han2, Yoo-Seok Yoon1, Young Rok Choi2, Boram Lee3

1Department of Surgery, Seoul National University College of Medicine, Republic of Korea; 2Department of Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea

Aims: Laparoscopic liver resection (LLR) is widely adapted for hepatocellular carcinoma (HCC), while LLR in posterosuperior (PS) segments is still challenging. However, with recent improvement of techniques and accumulation of experiences, LLR in PS segments is feasible. We compared outcomes of LLR for HCC located in PS segments before and after the adaptation of technological improvements.

Methods: We retrospectively analyzed 149 patients who underwent LLR for HCC located in PS segments from September 2003 to December 2016. The patients were divided into group 1 (n=43) and group 2 (n=106) who underwent LLR before and after 2012, when advanced techniques including use of intercostal trocars, Pringle maneuver, and semi-lateral position of patient were adapted. We also compared these patients with those who underwent open liver resection (OLR; n=124) for HCC in PS segments at the same period.

Results: Mean operative time (395 minutes vs 331 minutes; \( P=0.013 \)), intraoperative blood loss (1545 ml vs 1219 ml; \( P=0.020 \)), and hospital stay (12 days vs 9, \( P<0.001 \)) were significantly less in group 2. Postoperative complication rate (18.6% vs 18.9%; \( P=0.970 \)), open conversion rate (23% vs 17%; \( P=0.374 \)), 5-year overall survival (79% vs 89%; \( P=0.607 \)) and 5-year disease free survival (52% vs 53%; \( P=0.657 \)) rates were not significantly different between the groups. The proportion of LLR increased (36% vs 69%, \( P<0.001 \)). Compared to OLR group, complication rate (40.3% vs 18.8%; \( P=0.001 \)) and hospital stay (18 days vs 10 days; \( P<0.001 \)) were significantly lower in LLR group.

Conclusions: The complexity of LLR for HCC in PS segments has been gradually overcoming by the adaptation of advanced techniques.

Keywords: Hepatocarcinoma, Complication, Survival, Prognosis

Combinatorial Effect of Ezetimibe and Empagliflozin on NAFLD in Choline Deficient High Fat Diet-Induced Murine Model

Dong Yun Kim1, Kyu Sik Chung3, Kyung Joo Cho2, Heon Yung Gee3, Jun Yong Park3,4

1Department of Pharmacology, Yonsei University Graduate School of Medicine, Seoul, Rep. of South Korea; 2Department of Medicine, Yonsei University Graduate School of Medicine, Seoul, Rep. of South Korea; 3Division of Gastroenterology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Rep. of South Korea; 4Yonsei Liver Center, Severance Hospital, Seoul, Rep. of South Korea

Aims: Sodium-glucose cotransporter 2 inhibitor (SGLT2i) and ezetimibe, a cholesterol-lowering drug by targeting NPC1L1, have shown therapeutic potential for non-alcoholic fatty liver disease (NAFLD). As SGLT2i and ezetimibe have different pharmacological mechanisms, we hypothesized that the combination of empagliflozin (selective SGLT2i) and ezetimibe could improve NAFLD additively.

Methods: We used the choline-deficient high fat diet (CD-HFD)-induced murine model of NAFLD that has key features of human metabolic syndrome. 6 week-old C57BL/6j mice were fed with CD-HFD for 8 weeks. Then these mice were divided into four groups: vehicle, ezetimibe (10 mg/kg), empagliflozin (10 mg/kg), and ezetimibe (10 mg/kg) + empagliflozin (10 mg/kg). After 8 weeks, mice were sacrificed and subjected to blood measurements, and tissues for RNA isolation, lipid measurements and histology.

Results: CD-HFD-fed mice group exhibited liver weight gain with lipid accumulation and increased serum alanine aminotransferase (ALT). Ezetimibe, empagliflozin, and combination therapy significantly reduced liver steatosis. However, the histological NAFLD activity score (NAS) was most improved in the ezetimibe/empagliflozin group (0.667) than in the ezetimibe group (2.0, \( P=0.032 \)) or empagliflozin group (2.33, \( P=0.043 \)). Hepatic lipid contents were also significantly lower in the ezetimibe/empagliflozin group compared to other groups. In the insulin tolerance test, glucose level was most reacted in ezetimibe/empagliflozin group. Hepatic expression of lipogenesis genes such as Acc1 (Acetyl-CoA carboxylase 1) and Fas (fatty acid synthase) were significantly decreased in the ezetimibe/empagliflozin group. But hepatic expression of \( \beta \)-oxidation-related genes or esterification genes were not significantly decreased in the ezetimibe/empagliflozin group.

Conclusions: These findings suggested combined administration of empagliflozin and ezetimibe can additively improve NAFLD through decreasing lipogenesis process.

Keywords: NAFLD, CD-HFD, Ezetimibe, Sodium-glucose co-transporter 2, Combination therapy
Nicotinamide Riboside Does Not Attenuate Steatosis but Improve Inflammation in Non-Alcoholic Steatohepatitis Induced by Methionine-Choline Deficient Diet

Soon Sun Kim1, Hye Eun Byun2, Jung Mi Kim3, Eun Jung Woo1, Chul Won Suh2, Keum Ok Baek1, Jin Hee Cheong1, Young Hwan Ahn1, Hyo Jung Cho1, Jae Youn Cheong1, and Sung Won Cho1

1Department of Gastroenterology, Ajou University School of Medicine, 2Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, Republic of Korea

Aims: Mitochondria dysfunction is one of important pathophysiologic mechanisms in non-alcoholic fatty liver disease. Nicotinamide adenine dinucleotide (NAD+) supplementation by nicotinamide riboside (NR) was reported to improve hepatocyte mitochondria function. We evaluate the efficacy of NR administration in non-alcoholic steatohepatitis (NASH) induced by methionine-choline deficient (MCD) diet in mice.

Methods: Mice were fed MCD diet or normal chow diet for 8 weeks. NR, a precursor of NAD+ biosynthesis, was added either as a preventive strategy (NR-prevention group) or as a therapeutic intervention (NR-therapy group) in MCD diet group.

Results: MCD diet induced severe macrovesicular fat change and moderate periportal inflammation in mice. NAD+ content in liver lysate and mitochondria decreased in MCD diet group and increased in both NR-prevention and NR-therapy groups (mitochondria NAD+ [pmole/10⁶ cells]; 3938.5, 1208.0, 3104.5, and 2503.0 in control, MCD diet, NR-prevention and NR-therapy group, respectively, \( P < 0.001 \)). NR administration also increases the hepatic β-oxidation and mitochondrial complex content and activity (citrate synthase activity [fold change]; 1.00, 1.20, 1.70 and 2.20, in control, MCD diet, NR-prevention and NR-therapy group, respectively, \( P < 0.001 \)). Inflammatory transcripts (tumor necrosis factor-α, MCP-1, interleukin-1β, and interleukin-6) increased in MCD diet group and decreased with NR treatment (tumor necrosis factor-α relative mRNA expression; 1.01, 4.97, 1.58 and 1.28 in control, MCD diet, NR-prevention and NR-therapy group, respectively, \( P < 0.001 \)). However, histologic liver tissue sections did not show the improvement of steatosis and only showed modest improvement of periportal inflammation in NR-prevention and NR-therapy group.

Conclusions: Hepatic NAD+ repletion by NR administration does not attenuate steatosis but improve inflammation in NASH by MCD diet.

Keywords: Non-alcoholic fatty liver disease, Mitochondria, Nicotinamide adenine dinucleotide, Inflammation

PNPLA3 Genetic Polymorphisms Associated with the Development of Non Alcoholic Fatty Liver Disease in Korea Biobank Network

Sooyeon Oh1, Keong Won Hong2, Eun-Ji Kim3, Young-Eun Chon3, Seong-Gyu Hwang3, Joo-Ho Lee3, Sang Woon Choi1

To elucidate the mechanisms by which etezipime or SGLT2i therapy decreases hepatic steatosis in the CD-HFD mice, we performed expression of genes involved in fatty acid and glucose metabolism in the liver. Expression of the microsomal gene such as fatty acid synthase (FAS) and acetyl-CoA carboxylase 1 (ACC1) was significantly repressed by etezipime/SGLT2i combination treated mice, while expression of FAS and ACC1 was not affected by any treatment. In conclusion, etezipime/SGLT2i combination therapy in CD-HFD mice reduces steatosis and improves hepatic fatty acid metabolism. Expression data were normalized to the housekeeping gene GAPDH. *P<0.05 versus CD-HFD.
Aims: The patatin-like phospholipase domain-containing protein-3 (PNPLA3) rs738409 genotype (major genetic variant associated with non-alcoholic fatty liver disease [NAFLD]) confers high cross-ethnicity risk for NAFLD and non-alcoholic steatohepatitis (NASH) development. This study aimed to investigate the correlation between gene polymorphism of PNPLA3 and genetic susceptibility of NAFLD and NASH using the Korea Biobank Project (KBP) database.

Methods: Our study population comprises the city cohorts (n=3698) and rural cohorts (n=6030) of Korean Genome and Epidemiology Study provided by KBP. Genotype data of single nucleotide polymorphisms (SNPs) were retrieved by using Affy 6.0 and Illumina Exome Chip ver 1.1 of KBP network from January 2004 to December 2012. PNPLA3 SNPs were assessed for the risk of NAFLD and NASH development by chi-square tests followed by logistic regression analyses. NAFLD was diagnosed when the individuals had a radiologic evidence of fatty liver, and had neither viral hepatitis nor history of alcohol drinking. Among the NAFLD patients, NASH was diagnosed if the patient had serum ALT > 50 IU/L.

Results: The total population (n=9,728) has had an average of 56-year, and 26% were male gender. In terms of PNPLA3 rs738409 genotypes, there were 628 (17%) GG, 1803 (49%) GC, and 1262 (34%) CC genotype in city cohorts, whereas there were 981 (16%) GG, 2968 (49%) GC, and 2081 (35%) CC genotype in rural cohorts. Radiologic exam data were available in 3698 subjects in city cohorts and 2236 subjects in rural cohorts. There were 61 (1.6%) NAFLD subjects in city cohorts (n=3698), and 59 (2.6%) NAFLD subjects in rural cohorts (n=2236). Among them, 12 (19%) subjects had NASH in city cohorts and 15 (25%) had NASH in rural cohorts. Age and sex matched case-control analysis could not be done because of the relatively low prevalence of NASH (1.6 – 2.6%) in our cohorts and a potential selection bias. In the unmatched case-control analyses, 61 NAFLD subjects and 1,658 healthy control subjects were enrolled in city cohorts, and 59 NAFLD and 1,089 healthy control subjects in rural cohorts. In univariate analysis, there was no significant association between the PNPLA3 rs738409 genotypes and the development of NAFLD both in city cohorts and in rural cohorts (P>0.05), neither was between the NASH development and the PNPLA3 rs738409 genotypes. Nevertheless, in logistic regression analysis with adjustment for age and sex, PNPLA3 rs738409 GG genotype showed a tendency towards NAFLD development (Adjusted OR = 1.27, P=0.07) in the unmatched combined cohorts (n=2,867).

Conclusions: Using the city and rural cohorts of KBP database, no significant association was observed between the PNPLA3 rs738409 genotypes and risk of NAFLD or NASH. Further studies with higher quality and larger population will be needed to obtain a more precise estimate of the genetic effects on NAFLD susceptibility including PNPLA3.

Keywords: Single nucleotide polymorphism, Korean, PNPLA3, Non-alcoholic fatty liver disease
**O-057**

**Serum MFG-E8 Level as a Potential Biomarker for the Evaluation and Prediction of the Metabolic Syndrome**

Han Ah Lee, Hyung Joon Jo, Yeon Seok Seo, Hyun Gil Goh, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Sang Jun Sub, Young Kuk Jung, Ji Hoon Kim, Hyung Joon Yim, Jong Eun Yeo, Do Sun Lim, Kwan Soo Byun, Soon Ho Um

1Division of Gastroenterology & Hepatology, Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea
2Division of Cardiology, Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

**Aims:** Diagnosis and prediction of metabolic syndrome (MS) is cumbersome and so MS often goes unnoticed. Thus, better biomarkers for earlier diagnosis are needed. Serum milk fat globule-EFG factor 8 protein (MFG-E8) is an inflammatory glycoprotein that mediates the clearance of apoptotic cells.

**Methods:** Serum samples of 556 subjects in the Korea University Metabolic syndrome cohort was analyzed.

**Results:** Age was 55.1±6.5 years and 277 subjects (49.8%) were men. Diabetes, hypertension, and MS was present in 103 (18.5%), 299 (53.8%), and 236 subjects (42.4%), respectively. Serum MFG-E8 level was significantly correlated with diastolic blood pressure (Pearson’s correlation coefficient 0.146, P<0.001), mean arterial pressure (0.120, P=0.005), serum total cholesterol (0.121, P=0.005), high-density lipoprotein cholesterol (0.160, P<0.001), triglyceride (0.618, P<0.001), glucose (0.213, P<0.001) levels and pulse wave velocity (0.134, P=0.002). The area under the receiver operating characteristic curve (AUROC) of serum MFG-E8 level for the prediction of MS was 0.644 (95% confidence interval [CI], 0.597-0.691; P<0.001), and the optimal cutoff value was 4745.1 pg/mL (sensitivity 41.9%, specificity 82.5%). In 320 subjects without MS at baseline, MS was developed in 122 subjects (38.1%), and serum MFG-E8 level was significantly higher in these patients than other subjects (4029.0±1321.9 pg/mL vs. 3636.4±1315.3 pg/mL, P=0.010). AUROC of serum MFG-E8 level for the prediction of development of MS in subjects without MS at baseline was 0.595 (95% CI, 0.532-0.658; P=0.004), and the optimal cutoff value was 3732.5 pg/mL (sensitivity 57.4%, specificity 58.6%). When subjects were classified according to the cutoff of 3732.5 pg/mL of serum MFG-E8 level, the prevalence of development of MS was significantly higher in subjects with serum MFG-E8 level >3732.5 pg/mL than in those with serum MFG-E8 level >3732.5 pg/mL (46.1% vs. 31.0%, P=0.005).

**Conclusions:** Serum MFG-E8 might be used as a biomarker for the diagnosis and screening those at risk of developing metabolic syndrome.

**Keywords:** Serum milk fat globule-EFG factor 8, Metabolic syndrome, Biomarker, Diagnosis

---

**O-058**

**Long-Term Risk of a Nonalcoholic Fatty Liver after Tamoxifen Use in Breast Cancer: Propensity Score Matching Analysis**

Jeong-Ju Yoo, Sang Gyune Kim, Young Seok Kim, Young Don Kim, Gab Jin Cheon

1Department of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon, Korea
2Department of Internal Medicine, SoonChunHyang University School of Medicine, Seoul, Korea
3Department of Internal Medicine, SoonChunHyang University School of Medicine, Cheonan, Korea
4Department of Internal Medicine, Gangneung Asan Hospital, Gangneung, Korea

**Aims:** Fatty liver has been known to be the common side effect of tamoxifen, but there are few related studies considering the prevalence rate. The purpose of this study was to determine the effect of tamoxifen on the development or aggravation of fatty liver and to identify risk factors in large patient populations.

**Methods:** This was a single-center, retrospective study performed from January 2007 to July 2017. Consecutive 911 patients were classified into three groups according to the treatment method; tamoxifen group, aromatase inhibitor (AI) group, and control group. Propensity score matching method was used between the groups. The incidence or severity of fatty liver was judged by non-contrast computed tomography or abdominal ultrasound.

**Results:** Median treatment duration was 49 months and the median observational period was 85 months. Tamoxifen significantly increased fatty liver development or aggravation compared to AI or control groups [hazard ratio (HR) 1.598, 95% confidence interval (CI) 1.173-2.177, P=0.003] after adjusting other factors. When subgroup analysis was performed depending on basal fatty liver status, tamoxifen had more effect on fatty liver aggravation (HR 2.103, 95% CI 1.156-3.826, P=0.015). However, the development or aggravation of fatty liver did not significantly increase the mortality of breast cancer patients.

**Conclusions:** Tamoxifen significantly increases the development or aggravation of fatty liver compared to other treatments in breast cancer patients. Therefore, when tamoxifen is used for a long-term period, close monitoring for fatty liver is necessary, especially in high-risk patients, e.g. basal fatty liver or high body mass index.

**Keywords:** Nonalcoholic fatty liver disease, Tamoxifen, Aromatase inhibitor

---

**O-059**

**Combined Use of Rosuvastatin and Ezetimibe Improves Hepatic Steatosis in Patients with Dyslipidemia**

Won Dong Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang Hyub Han, Seung Up Kim

1Department of Internal Medicine, Yonsei University College of Med-
Aims: Rosuvastatin and ezetimibe are beneficial for dyslipidemia control. We investigated whether the combined use of rosuvastatin and ezetimibe improves hepatic steatosis (HS) in patients with dyslipidemia.

Methods: Between January and August 2018, 114 patients with dyslipidemia treated with 6-month combined use of rosuvastatin and ezetimibe were considered eligible for this retrospective cohort study. The degree of HS was assessed using the hepatic steatosis index (HSI). The HS improvement was defined as ≥ 5% reduction in the HSI score from the baseline. The presence of fatty liver was defined as HSI ≥ 36.

Results: The mean age of the study population (50 men and 64 women; 49 non-diabetic and 65 diabetic) was 57.4 years. The mean body mass index, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, and HSI was 25.1 kg/m^2, 207.4 mg/dL, 126.1 mg/dL, 52.9 mg/dL, 146.4 mg/dL, and 36.1, respectively. During 6-month treatment, HS burden was similarly maintained (mean HSI=36.3 at 3 months and 36.4 at 6 months; all P>0.05 vs. baseline). On multivariate analyses, ultrasonographic fatty liver (hazard ratio [HR]=3.212, 95% confidence interval [CI] 1.041-9.913) and HSI ≥ 36 (HR=3.501, 95% CI 1.226-10.001) were selected as independent predictors of HS improvement (all P<0.05). However, when 53 (46.5%) patients with fatty liver (HSI>36) were selected, HS burden was significantly improved (mean HSI=40.8 at baseline → 39.3 at 3 months → 39.7 at 6 months; all P<0.05 vs. baseline).

Conclusions: The combined use of rosuvastatin and ezetimibe for dyslipidemia control did not improve HS burden in all patients with dyslipidemia, but improved HS burden in the subgroup with fatty liver.

Keywords: Rosuvastatin, Ezetimibe, Dyslipidemia, Diabetes mellitus

O-060

Weight Change and Resolution of Fatty Liver in Normal Weight Individuals with Non-Alcoholic Fatty Liver Disease

Joo Hyun Oh¹, Tae Jin Kwon¹, Dong Hyun Sinn¹, Danhee Kang², Soo Jin Cho³, Seung Woon Paik⁴, Eliseo Guallar⁵, Juhee Cho⁴, Geum-Youn Gwak¹

¹Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine; ²Department of Clinical Research Design and Evaluation, SAIHST; ³Center for Health Promotion, Samsung Medical Center; ⁴Center for Clinical Epidemiology, Samsung Medical Center; Seoul, South Korea; ⁵Departments of Epidemiology and Medicine and Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, USA

Aims: Obesity is a well-known risk factor for non-alcoholic fatty liver disease (NAFLD), and weight reduction is primarily recommended for managing the disease. However, some NAFLD patients show normal weight (lean NAFLD), and whether weight reduction can be recommended for lean NAFLD individuals remains unclear. We investigated the association between weight changes and resolution of fatty liver in patients with NAFLD.

Methods: We conducted a retrospective cohort study of 16,738 adult men and women (average age, 50.5 y; lean NAFLD, 2,383 participants) with NAFLD at baseline who underwent repeated health check-up examinations including body weight measurements and abdominal ultrasonography from January 2003 through December 2013. NAFLD was defined by ultrasonography and exclusion of secondary causes.

Results: During 68,389 person-years of follow-up (median follow-up of 3.00 years), 5,819 patients had fatty liver resolution. Compared with participants who had no weight reduction or
increased weight, the fully adjusted hazard ratios for fatty liver resolution in participants with 0–4.9%, 5–9.9%, and 10% or more weight reduction were 1.67 (95% confidence interval [CI] = 1.57, 1.77), 3.36 (95% CI = 3.09, 3.65), and 5.50 (95% CI = 4.83, 6.27), respectively. The association between weight reduction and fatty liver resolution was stronger in overweight/obese NAFLD participants but was also evident in lean NAFLD participants in a dose-dependent manner. In spline regression models, the association between weight change and the fatty liver resolution was linear among participants with normal weight.

Conclusions: In a large cohort of NAFLD participants, weight reduction showed a dose-dependent effect on fatty liver resolution in lean NAFLD participants. Lean NAFLD might be considered for metabolically obese individuals who may benefit from weight reduction.

Keywords: Lean, Weight change, Non-alcoholic fatty liver disease
Th17 ratio than nontolerant group. The levels of gene expression related to the signal transducer and activator of transcription 3 (STAT3) pathway including hypoxia-inducible factor 1α (HIF-1α), CCL2, Pim1, Fos-related antigen 1 (FRA1) were more decreased in tolerant patients compared to non-tolerant patients. Moreover, Retinoic-acid-orphan-receptor-C (RORC) which is the regulator of IL-17/Th17 were more decreased in tolerant patients than non-tolerant patients.

Conclusions: This gene analysis in IS drug withdrawal study suggest that increase pattern of Treg/Th17 ratio as tolerance signature is appropriate to the decrease of gene expression associated with STAT3 pathway and IL-17/Th17 pathway.

Keywords: Liver transplantation, Tolerance, Stat3, IL-17, Regulatory T cell, Helper T 17 cell

O-063

Silent Allograft Fibrosis in 10-Year Post-Transplantation Histology of Pediatric Liver Transplantation: Is It Really Silent?

Jinsoo RHU, Suk-Koo LEE, Sanghoon LEE, Jong Man KIM, Gyu-Seong CHOI, Jae-Won JOH

Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Aims: This study sought to analyze factors related to long-term allograft fibrosis in clinically stable pediatric liver transplantation patients.

Methods: Pediatric patients who underwent liver transplantation at Samsung Medical Center from January 1997 to January 2008 were reviewed. Ten-year protocol biopsies were examined by an expert pathologist specializing in liver transplantation. The degrees of inflammation and fibrosis were classified based on Banff criteria and the METAVIR system, respectively. Analysis of risk factors for allograft fibrosis was performed using logistic regression.

Results: Sixty-six clinically silent pediatric patients who underwent 10-year post-transplantation biopsy were included. Protocol biopsy revealed nine cases (13.6%) with a rejection activity index ≥3 based on Banff classification and 31 cases (47.0%) with METAVIR fibrosis stage ≥F1. All the characteristics among the patients were similar except for experience of rejection when classified by Banff criteria (29.4% in normal, 60.9% in indeterminate, and 55.6% in mild rejection, P=0.039) and METAVIR staging (34.3% in F0, 36.8% in F1, and 83.3% in F2, P=0.009). More than three events with aminotransferase level elevated above 50U/L was the only significant factor for METAVIR ≥F1 (OR=3.351, CI 1.160–9.643, P=0.026) However, mean total bilirubin ≥1.0mg/dL during the entire period (OR=10.388, CI 1.414–76.322, P=0.021) and experience of rejection (OR=10.403, CI 1.788–60.531, P=0.009) were significant risk factors for METAVIR stage F2.

Conclusions: Even in clinically silent pediatric liver transplantation patients, long-term fibrosis occurs frequently, and repeated elevation of aminotransferases was related to METAVIR stages ≥F1, while experience of rejection and elevated mean total bilirubin ≥1.0mg/dL were related to METAVIR stage F2.

O-064

Clinical Features and Prognosis of DIHBS (Diffuse Intrahepatic Biliary Stricture) after Adult ABO-Incompatible Living Donor Liver Transplantation

Jae Hyun KWON, Gi-Won SONG, Shin HWANG, Ki-Hun KIM, Chul-Soo AHN, Deok-Bog MOON, Tae-Yong HA, Dong-Hwan JUNG, Gil-Chun PARK, Young In YOON, Hwuil-Dong CHO, Yongkyu CHUNG, Sang-Hyun KANG, I-Ji JEONG, Jin Uk CHOI, Sung-Gyu LEE

Division of Liver Transplantation and Hepatobiliary Surgery, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Republic of Korea

Aims: Despite the advancement in desensitization protocol, diffuse intrahepatic biliary stricture (DIHBS), an attenuated form of antibody mediated rejection (AMR), remains an unresolved problem. As a high-volume LT center, we retrospectively review clinical outcome and prognosis of recipients who developed DIHBS after ABOi LDLT.

Methods: From November 2008 to December 2017, total of 497 cases of ABO incompatible LDLT were performed at Asan Medical Center. Among them, twenty-four patients (4.83%) developed DIHBS. Retrospective review of medical records of these patients was carried out.

Results: Median time of diagnosis for DIHBS after ABOi LDLT was 2.8 months. In patients with DIHBS, the 3-year patient survival rate was 69.9%. Causes of patient death in nine patients were recurrent HCC in four patients, biliary sepsis in two patients, graft failure (not associated with AMR) in one patient, post-operative bleeding after re-LT in one patient, and pneumonia in one patient. Nine patients (37.5%) received re-transplantation. Graft survival rates at 3-year was 40.6%. Both patient survival and graft survival rates were significantly lower than ABOi LDLT recipients without DIHBS (both P<0.001). Between ABOi LDLT patients with or without DIHBS, there were no significant differences in pre-operative isoagglutinin (IA) titer, post-operative peak bilirubin, AST, ALT, IA titer, and pre- and post-operative frequency of total plasma exchange (TPE).

Conclusions: In this study, DIHBS developed usually before 3 months after ABOi LDLT. DIHBS significantly affects short and long-term outcome in ABOi LDLT. In patients who demonstrated DIHBS, over half of the patient progress to graft failure and need re-LT.

O-065

Impact of the Baseline Anti-A/B IgG Titer on the Clinical Outcome in ABO-Incompatible Liver Transplantation

Juhun Lee, Deok Gie Kim, Jee Youn Lee, Seok Jeong Yang, Jae

www.theliverweek.org
Geun Lee, Myoung Soo Kim, Soon Il Kim, and Dong Jin Joo

Aims: The use of ABO incompatible (ABOi) living donors is an attractive solution for expanding the liver donor pool. We investigated the impact of the baseline anti-A/B IgG titer on the transplant outcomes in ABOi liver transplantation (LT).

Methods: We analyzed 394 adult patients who underwent living donor LT (303 ABO compatible LT and 91 ABOi LT) between 2012 and 2018. ABOi LT patients were categorized by baseline IgG titer: low IgG titer (≤ 1:64, n=51) versus high IgG titer (≥ 1:128, n=40). All ABOi LT patients received desensitization therapy including rituximab and plasmapheresis.

Results: Patients with high IgG titer experienced antibody re-bound (≥ 1:64) more frequently than those with low IgG titer during the first month after LT (35.0% vs. 15.7%, P=0.033). Patient survival rates for ABO compatible, low IgG titer, and high IgG titer were 85.0%, 91.5%, and 74.4%, respectively, at 3 years post-transplantation (P=0.006). High IgG titer (HR, 2.76; 95% CI, 1.39-5.48; P=0.004) and MELD score of >20 (HR, 2.32; 95% CI, 1.22-4.41; P=0.010) were independent risk factors for mortality. Infection was the leading causes of death in all groups, but the proportion was significantly higher in high IgG titer group than in other groups (81.8% vs. 30.8% vs. 33.3%).

Conclusions: Patients with high IgG titer (≥1:128) are associated with a higher risk of death after ABOi LT than those with low IgG titer (≤1:64). Thus, ABOi LT patients with high IgG titer should be managed with great care.

Keywords: Liver transplantation, ABO incompatibility, Desensitization

O-066

Comparative Analysis of Bile Microbiology and Antibiotic Susceptibilities between Liver Transplant Recipients and Normal Population: Multicenter Cohort Study

Suk-Won Suh, Seung Eun Lee, Yoo-Shin Choi, YoungRok Choi, Jae-hong Jeong

Aims: Biliary complications are still unresolved problems after liver transplantation (LT), up to 28%-32%, especially in living donor LT. Effective antibiotics should be administered to control the cholangitis, however immunosuppression after LT may have changed the microbiology of infected bile. The aim of this study was to compare bile microbiology and antibiotic susceptibilities between liver transplant recipients and normal population.

Methods: Between 2008 and 2017, the microbiologic culture and antibiotics sensitivity tests were compared on the patients who underwent percutaneous trans-hepatic biliary drainage because of biliary complications after LT (n=59) and cholecystectomy under the diagnosis of gallbladder disease (n=271) at multiple centers.

Results: The most frequently isolated microorganisms were similar between two groups; Enterococcus (42.4% vs. 29.4%) followed by Escherichia (22.0% vs. 19.0%), Pseudomonas (16.9% vs. 8.8%), and Klebsiella (10.2% vs. 10.1%). For Enterococcus and Escherichia, two most frequently isolated organisms, gentamicin and imipenem showed similar high sensitivity for both organisms in two groups. According to the period, within or after 6 month of LT, Enterococcus (23.7% vs. 18.6%) was consistently frequently isolated, but others were different; Klebsiella (8.5% vs. 1.7%), Escherichia (3.4% vs. 18.6%) and Pseudomonas (3.4% vs. 13.6%).

Conclusions: Microbiologic culture and antibiotics sensitivity tests were similar between liver transplant recipients and normal population, however there was some difference of frequent isolated microorganisms by the period after LT.

Keywords: Bile microbiology, Antibiotic susceptibilities, Liver transplant
Aims: The transient elastography (TE)-based risk prediction models predict hepatocellular carcinoma (HCC) development. We investigated the influence of antiviral therapy (AVT) on TE-based risk prediction model in patients with chronic hepatitis B (CHB).

Methods: Patients with CHB who initiated AVT were retrospectively recruited from 13 referral Korean institutes. The mREACH-B model was selected for the analysis.

Results: A total of 253,002 patients met inclusion and exclusion criteria in 2007, with 320,245 in 2011 and 418,099 patients in 2016. Cases and non-CHB controls were matched in a 1:4 ratio using propensity score matching method.

Conclusions: The mREACH-B score was dynamically changed during AVT. Thus, repeated assessment of the mREACH-B score is required to predict the changing risk of HCC development in patients with CHB undergoing AVT.

Keywords: Transient elastography, Risk prediction, Hepatocellular carcinoma, Chronic hepatitis B

Increased Clinical and Economic Burden of Chronic Hepatitis B (CHB) Patients Compared to Non-CHB from 2007 to 2016 in Korea

Dae Won Jun1, Hyunwoo Oh1, Hyun Jung Ahn2, Bo Ok Kim1, Mindie H. Nguyen3

1Hanyang University Hospital, Seoul, South Korea; 2Kantar Health, Seoul, South Korea; 3Stanford University Medical Center, Palo Alto, California, United States of America

Aims: CHB prevalence in Korea ranges from 2-7% and is attributable for ~64-70% of hepatocellular carcinoma (HCC) cases. This study aims to characterize the distribution and trend in demographics and comorbidity among CHB patients in Korea between 2007 and 2016.

Methods: We used the Health Insurance Review & Assessment Service (HIRA) Database to identify patients ≥18 years with CHB as identified by ICD-10 codes (B18.1). Demographic and comorbidity data was reported cross-sectionally for 2007, 2011, and 2016. Cases and non-CHB controls were matched in a 1:4 ratio using propensity score matching method.

Results: A total of 253,002 patients met inclusion and exclusion criteria in 2007, with 320,245 in 2011 and 418,099 patients in 2016. The mean age of patients was 47 years (SD 13.3) in 2007 and increased to 52 years (SD 12.5) in 2016 (P<0.0001). As shown in Table 1, by 2016, CHB patients in Korea had significantly (P<0.001) higher comorbidity burden compared to matched non-CHB with (37% with hyperlipidemia, 29% with hypertension, 20% with diabetes, 4% with osteoporosis/bone fracture, and 3% with chronic kidney disease ; all of which have increased significantly from 2007 (all P<0.001). The average Devo-Carlson comorbidity index (DCCI) was also calculated and the score was higher in CHB group compare to matched control group (2.22 vs 1.15, P<0.0001). In addition, CHB patients showed a higher prevalence of concomitant medication and had significantly higher rates of health care resource utilization (HCRU), such as hospitalization and outpatient visits, compared to non-CHB patients, which significantly increased until 5 years of AVT (12.2%, P=0.05). The mREACH-B scores at baseline, 1 year, and 2 years of AVT independently predicted HCC development (hazard ratio=1.199-1.262) (all P<0.05). The cumulative incidence rate of HCC was significantly different at 5 years of AVT among risk groups (high vs. high-intermediate vs. low-intermediate vs. low) from baseline (4.5% vs. 3.2% vs. 1.5% vs. 0.8%) and 1 year (11.8% vs. 4.6% vs. 1.8% vs. 0.6%) (all P<0.05, log-rank tests).

Conclusions: The mREACH-B score was dynamically changed during AVT. Thus, repeated assessment of the mREACH-B score is required to predict the changing risk of HCC development in patients with CHB undergoing AVT.

Keywords: Transient elastography, Risk prediction, Hepatocellular carcinoma, Chronic hepatitis B
Conclusions: Between 2007-2016, the Korean CHB population has significantly aged with more comorbidities, and HCRU including renal and metabolic bone disease that may affect CHB management. As CHB treatment is lifelong, careful selection of NUCs treatment and monitoring should be considered in aging Korean CHB populations.

Keywords: Comorbidity, HBV, Burden of HBV, Increased clinical and economic burden

Comparison of Tenofovir and Entecavir on the Risk of Hepatocellular Carcinoma and Liver-Related Events in Patients with Chronic Hepatitis B: A Propensity Score Analysis

Sung Won Lee1,2, Jung Hyun Kwon1,2, Hae Lim Lee1,2, Sun Hong Yoo1,2, Hee Chul Nam1,2, Pil Soo Sung1,2, Soon Woo Nam1,2, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,2, Nam Ik Han1,2, Jeong Won Jang1,2

1Division of Hepatology Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea; 2The Catholic University Liver Research Center

Aims: The use of tenofovir (TDF) and entecavir (ETV) in chronic hepatitis B (CHB) patients has led to a decrease in the incidence of hepatocellular carcinoma (HCC) and liver-related events. However, whether there is a difference between the two highly-potent agents in the extent of improving such clinical outcomes has not been clarified thus far. Therefore, we aimed to compare the effects of TDF and ETV on the risk of HCC and liver-related events.

Methods: A total of 7,015 consecutive CHB patients who were treated with TDF or ETV between February 2007 and January 2018 at the liver units of the Catholic University of Korea were screened for study eligibility and 4,014 patients were finally analyzed. Primary endpoints were HCC and occurrence of liver-related events within 5 years after the initiation of antiviral therapy. Liver-related event was defined as either liver transplantation (LT) or liver-related death.

Results: No difference was observed between TDF and ETV in the incidence rates of HCC in the entire cohort (HR, 1.047; 95% CI, 0.780-1.406, PSM model, \( P = 0.757 \)) and subgroups of treatment-naïve, treatment-experienced, chronic hepatitis and cirrhotic patients. However, TDF significantly lowered the risk of liver-related events compared to ETV in the entire cohort (HR, 0.380; 95% CI, 0.173-0.834, PSM model, \( P = 0.015 \)).

Conclusions: This study has demonstrated the intermediate-term clinical outcomes in CHB patients who received TDF or ETV treatment. There was no difference in the risk of HCC between the two drugs but TDF significantly lowered the risk of liver-related events compared to ETV.

Keywords: Tenofovir, Entecavir, Hepatocellular carcinoma, Chronic hepatitis B

The Risk of Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Who Received Tenofovir vs. Entecavir Treatment

Terry Cheuk-Fung Yip1,2, Vincent Wai-Sun Wong1,2,3, Henry Lik-Yuen Chan1,2,3, Yee-Kit Tse1,2, Grace Lai-Hung Wong1,2,3

1Institute of Digestive Disease, 2Department of Medicine and Therapeutics, and 3State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong SAR, China

Aims: A recent study suggested patients received tenofovir disoproxil fumarate (TDF) treatment have a lower risk of hepatocellular carcinoma (HCC) than those received entecavir (ETV).
We aimed to compare TDF and ETV on the risk of HCC in a territory-wide cohort of patients with chronic hepatitis B (CHB).

**Methods:** Consecutive adult CHB patients who were initially treated with ETV or TDF for at least 6 months between January 2008 and June 2018 were identified using Clinical Data Analysis and Reporting System in Hong Kong. Patients who had cancers or liver transplantation before or within the first 6 months of treatment were excluded. Missing data were replaced by multiple imputation. Propensity score (PS) weighting was used after multiple imputation to balance the clinical characteristics between two treatment groups; PS included all covariates in the multivariable analysis, serum creatinine, and renal replacement therapy. Fine-Gray model was used to adjust for competing risk of death.

**Results:** 29,350 CHB patients were identified. Their mean age was 52.9±13.2 years, 18,685 (63.7%) were male; 1,309 (4.5%) and 28,041 (95.5%) first received TDF and ETV, respectively. TDF-treated patients were younger (43.2 vs. 53.4 years) and less likely to be cirrhotic (35 [2.7%] vs. 3,650 [13.0%]). At a median (interquartile range) follow-up of 3.6 (1.7–5.0) years, 8 (0.6%) TDF-treated and 1,386 (4.9%) ETV-treated patients developed HCC. The 5-year cumulative incidence (95% confidence interval [CI]) of HCC in TDF-treated and ETV-treated patients was 1.1% (0.5%-2.3%) and 7.0% (6.6%-7.3%), respectively (Figure). TDF use was associated with a lower risk of HCC than ETV use with (weighted subdistribution hazard ratio [SHR] 0.36, 95% CI 0.16-0.80, \(P=0.013\)) and without (adjusted SHR 0.32, 95% CI 0.16-0.65, \(P=0.002\)) PS weighting.

**Conclusions:** TDF treatment is associated with a lower risk of HCC than ETV treatment in a territory-wide cohort of CHB patients.

**Keywords:** Nucleos(t)ide analogues, Hepatocellular carcinoma, Chronic hepatitis B

---

**O-071**

**Hepatitis B Immunology**

Ashish Kumar Vyas1,4, Pooja Negi1, Sharda Patra2, Jaswinder Singh Maras, Shiv Kumar Saran1, Nirupma Trehanpati1

1Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, INDIA; 2Lady Harding Medical College & Smt. S. K. Hospital, New Delhi, INDIA; 3Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, INDIA; 4Current affiliation-All India Institute of Medical Sciences, Bhopal, MP, INDIA

**Aims:** Vertical transmission of Hepatitis B virus (HBV) from infected mother to the newborn is the main cause of chronicity of HBV infection. However, there is rather scanty information on the role of maternal immunity in maternofetal transmission. Our aim is to understand the role of immunity of HBV infected mother in vertical transmission.

**Methods:** A total of 18461 pregnant females were screened for HBsAg. Fifty HBsAg+ve pregnant mothers and their newborns were recruited in this study and tested for transmission of HBV (HBsAg, HBV DNA); 22 were positive and rest were negative. PBMCs from the transmitting (Gr. A, n=22) and non-transmitting (Gr. B, n=28) mothers were analyzed for different immune cell subsets by flow cytometry including dendritic cells (DCs), CD4, CD8, TFh and B cells. The HBV-specific responses of different cells were assessed using pooled surface and core overlapping HBV peptides. Next-generation sequencing (NGS) was performed in PBMCs; qRT-PCR and ELISA was performed to validate the flow data.

**Results:** Mothers in Gr. B then A had higher frequencies and greater HBV specific DC, CD4, CD8, TFh and B cell-mediated protective responses. RNAseq showed increased expression of CD4, CD8, B, TFh, and Immune-related genes in Gr. B compared to Gr. A. Frequency of TFh cells inversely correlated with HBV DNA and IL-21. ROC analysis gave the cut-off values with the highest specificity and sensitivity to predict the involvement of TFh and B cells in HBV vertical transmission.

**Conclusions:** Serum IL-21 levels, TFh, and plasma B cells are useful predictors of vertical transmission of HBV from infected mothers to the newborns. Our study first time showed defective maternal immunity influences the chances of HBV transmission into their newborns. These cells can be used as a therapeutic target for protection of vertical transmission.

**Keywords:** Hepatitis B, Vertical transmission, Immune responses, T follicular helper cells

---

**O-072**

**Sustained Response without Nucleos(t)ides after Pegylated Interferon Represent Favorable Outcome: Up to 13 Years Follow-Up**

Soon Kyu Lee1, Jung Hyun Kwon1, Jeong Won Jang1, Hee Chul Nam1, Yoon-Jung Kim1, Sun Hong Yoo1, Soon Woo Nam2, Si Hyun Bae1, Jong Young Choi1, Seung Kew Yoon1

**Aims:**

To evaluate the long-term safety and efficacy of pegylated interferon (PegIFN) treatment for chronic hepatitis B (CHB) patients who achieved sustained virologic response (SVR) with or without nucleos(t)ide analogues (NAs).

**Methods:**

A total of 268 CHB patients who achieved SVR with PegIFN were enrolled. Median age was 43 (range 16-68) years, and 140 (52%) were male. The primary endpoint was relapse-free survival. The primary analysis involved a comparison of relapse-free survival between patients treated with PegIFN monotherapy (group 1) and those treated with PegIFN plus lamivudine (group 2). The secondary analysis compared the relapse-free survival of patients treated with PegIFN monotherapy to those treated with PegIFN plus nucleos(t)ide analogues (group 3). The mean follow-up duration was 13.1 years (range 3.4-13.5 years) for all patients.

**Results:**

The 13-year Kaplan-Meier estimated relapse-free survival rates were 78.6% (95% CI: 72.0-85.1%) for group 1, 85.5% (95% CI: 79.5-91.2%) for group 2, and 65.3% (95% CI: 58.1-72.8%) for group 3. The difference in relapse-free survival between group 1 and group 2 was statistically significant (log-rank test, \(P=0.002\)). The difference in relapse-free survival between group 1 and group 3 was also statistically significant (log-rank test, \(P=0.003\)).

**Conclusions:**

PegIFN monotherapy represents a favorable outcome for patients with CHB who achieve SVR, especially when compared to PegIFN plus nucleos(t)ide analogues treatment. However, the long-term efficacy of PegIFN monotherapy remains to be evaluated in a larger, randomized controlled trial.

**Keywords:** Hepatitis B, Pegylated interferon, Relapse-free survival, Chronic hepatitis B
Novel Deep Neural Network-Based Liver Transplantation Criteria for Hepatocellular Carcinoma: A Multi-center Study

Aims: Pegylated interferon (PEG-IFN) treatment with a high rate of off-therapy host immune control is still an attractive treatment for chronic HBV infection. There remains uncertainty about the prognosis of sustained responder after PEG-IFN treatment who don’t need nucleos(t)ides (NAs). We investigated the long-term outcomes of PEG-IFN treatment focused on tolerant patients without NAs up to 13 years.

Methods: A consecutive 172 patients treated with PEG-IFN for chronic hepatitis B or compensated liver cirrhosis between 2005 and 2014 were enrolled and finally 122 patients who fully completed PEG-IFN treatment were analyzed. The definition of response for PEG-IFN treatment at 6months post-treatment were as follows: HBeAg positive patients, achieve both virologic response (VR, ≤2,000 IU/ml of HBV DNA) and serologic response (HBeAg loss or seroconversion); HBeAg negative patients, reach VR. During follow-up period, we analyzed the number of patients with HBsAg loss, starting NAs due to viral activation and disease progression including liver cirrhosis and hepatocellular carcinoma (HCC).

Results: The median follow-up period of 122 patients were 7.2 years (range, 1.1 -13.2 years). Of 122 patients, 43 patients (35.2%) had a response at 6 months post-treatment. During follow-up, 69 patients (56.6%) started NAs and the patients who had a response for PEG-IFN significantly lower rate of starting NAs (14/43 vs 55/79, P<0.001). HBsAg loss occurred in 9 patients (7.4%) and sustained responders without further NAs treatment had significantly high rate of HBsAg loss compared to the patients with starting NAs (13.2% vs. 2.9%, P=0.01). Eight patients (6.6%) developed disease progression including HCC (n=3). All of them were non-sustained responders who started NAs after PEG-IFN therapy compared to sustained responders (P=0.03).

Conclusions: Sustained responders without further NAs treatment after PEG-IFN treatment had a favorable clinical outcome in HBsAg loss and no disease progression up to 13 years.

Keywords: Pegylated interferon, HBV, HCC, Liver cirrhosis, Nucleos(t)ides, HBsAg loss

Results: The median follow-up was 78.1 (interquartile range, 39.0–110.5) months. The 203 patients (36.1%) had HCC exceeding MC and portal vein invasion was observed in 83 (14.7%). The optimal model consisted of seven layers including two residual-blocks. Through the performance assessment in validation cohort, DNN model showed better discrimination.
function compared to MC (c-index: 0.75 vs. 0.64), and calibration was confirmed by Hosmer-Lemeshow test (P>0.05). The high-risk group (probability cut-off=0.5) presented significantly higher tumor-recurrence rate than low-risk group (cut-off=0.5) in the validation cohort (hazard ratio, 2.67; 95% confidence interval, 1.36–5.25; P<0.001; see Figure). The expected probabilities of tumor recurrence at years 1, 3, and 5 were 7.0%, 12.0%, and 12.0% in low-risk group; and 27.4%, 29.7%, and 30.9% in high-risk group, respectively. The largest weighted parameter in DNN model was tumor size and followed by alpha-fetoprotein, age, and PIVKA-II.

Conclusions: The DNN model presented better prediction ability of tumor-recurrence after LT than MC. New model is considered as optimal LT criteria in HCC patients, in that it can evolve with further data.

Keywords: Deep learning, Milan criteria, Liver transplantation, Hepatocellular carcinoma

Bioelectrical Impedance Analysis for Predicting Postoperative Complications and Survival after Liver Resection for Hepatocellular Carcinoma

Gil Ho Lee1, Hyo Jung Cho2, Garam Lee2, Han Gyeol Kim3, Hee Jung Wang2, Bong Wan Kim2, Mi Young Lee1, Jin Hee Cheong1, Young Hwan Ahn1, So Young Yoon1, Choong Kyun Noh1, Chul Won Suh1, Jung Woo Eun1, Jaeyoung Cheong2, Sung Won Cho2, and Soon Sun Kim1

1Department of Gastroenterology; 2Department of Surgery, Ajou University School of Medicine; 3Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, Korea

Aims: Bioelectrical impedance analysis (BIA) provides information on body composition and nutritional status in patients with cancer. However, it is unclear whether the preoperative edema index or phase angle, obtained from BIA, predicts postoperative complication or mortality in patients with hepatocellular carcinoma (HCC). Thus, we investigated whether preoperative BIA could predict postoperative complications and survival in patients with HCC.

Methods: Seventy-nine patients who underwent liver resection for HCC were prospectively enrolled and BIA was performed before surgery. The development of postoperative ascites or acute kidney injury (AKI) and patients’ survival were monitored after surgery.

Results: Among 79 patients, 35 (44.3%) developed ascites or AKI after liver resection. In multivariate analysis, a high preoperative edema index (extracellular water/total body water) (>0.384) (odds ratio 3.96; 95% confidence interval 1.03–15.17; P=0.045) and higher fluid infusion during surgery (odds ratio 1.36; 95% confidence interval 1.04–1.79; P=0.026) were identified as significant risk factors for ascites or AKI after hepatectomy. Subgroup analyses showed that the edema index was a significant predictor of ascites or AKI in patients with cirrhosis but not in those without cirrhosis. Tumor size was the only significant predictive factor for short-term survival after hepatectomy.

Conclusions: The preoperative edema index using BIA can be used as a predictor of post-hepatectomy complication, especially in patients with liver cirrhosis.

Keywords: Electric impedance, Ascites, Acute kidney injury, Carcinoma, Hepatocellular, Hepatectomy

Laparoscopic Resection vs. Percutaneous Radiofrequency Ablation for Small Single HCC: Comparison of Clinical Outcome

Dong Ho Lee1, Jin Woong Kim2, Jeong Min Lee1, Jong Man Kim1, Min Woo Lee3, Hyunchul Rhim1, Young Hoe Hur2, Kyung-Suk Suh3

1Department of Radiology, Seoul National University Hospital; 2Department of Radiology, Chosun University Hospital and Chosun University College of Medicine; 3Institute of Radiation Medicine, Seoul National University College of Medicine; 4Department of Surgery, Samsung Medical Center; 5Department of Radiology, Samsung Medical Center; 6Department of Hepato-Pancreato-Biliary Surgery, Chonnam National University Hwasun Hospital and Chonnam National University Hwasun Medical School; 7Department of Surgery, Seoul National University Hospital

Aims: To compare laparoscopic liver resection (LLR) and percutaneous radiofrequency ablation (p-RFA) as first-line treatment options in patients with single nodular hepatocellular carcinomas (HCCs) ≤3 cm.

Methods: A total of 566 patients treated by either LLR (n=251) or p-RFA (n=315) were included. The recurrence-free survival (RFS) and cumulative incidence of local tumor progression (LTP) were estimated using Kaplan-Meier methods and compared using the log-rank test. Treatment outcome of two treatment modalities was compared in subgroup of patients according to tumor location.

Results: There were no significant differences in overall survival between LLR and p-RFA (P=0.160), however, 3-year RFS was demonstrated to be significantly higher after LLR (74.4%) than after p-RFA (66.0%) (P=0.013), owing to its significantly lower cumulative incidence of LTP (2.1% at 3-years after LLR vs. 10.0% after p-RFA, P<0.001). LLR also provided significantly better local tumor control than p-RFA for subcapsular tumors (3-year LTP rates: 1.9% vs. 8.8%, P=0.012), perivascular tumors (3-year LTP rates: 0.0% vs. 17.2%, P=0.007), and tumors located in antero-lateral liver portions (3-year LTP rates: 0.0% vs. 10.7%, P<0.001). However, there were no significant differences in LTP rates between LLR and p-RFA for non-subcapsular and non-perivascular tumors (P=0.482) and for tumors in postero-superior liver portions (P=0.380).

Conclusions: LLR can provide significantly better local tumor control than p-RFA for small single HCCs in subcapsular, perivascular, and anterolateral liver portions, and thus may be the preferred treatment option for these tumors.

Keywords: Hepatocellular Carcinoma, Radiofrequency ablation, Laparoscopic liver resection, Local tumor progression
Factors and Models for Predicting Liver-Related Morbidity in Patients Undergoing Hepatic Resection for Hepatocellular Carcinoma

Jonggi Choi1, So-hyun Kim2, Seungbong Han3, Danbi Lee1, Ju Hyun Shim1, Young-Suk Lim1, Han Chu Lee1, Young-Hwa Chung1, Yung-Sang Lee4, Sung-Gyu Lee4, Ki-Hun Kim1, and Kang Mo Kim1

* These authors contributed equally to this work.

1Department of Gastroenterology, Asan Liver Center, Asan Medical Center University of Ulsan College of Medicine, Seoul, Republic of Korea; 2Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 3Department of Applied Statistics, Gachon University, Seongnam, Republic of Korea; 4Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

Aims: Hepatic resection has been a main treatment option for patients with hepatocellular carcinoma (HCC). The aim of this study was to seek predictive factors and to build predictive model for liver-related morbidity after liver resection for HCC.

Methods: A total of 1,565 patients who underwent liver resection for HCC at Asan Medical Center, between January 2016 and December 2017 were retrospectively analyzed. Laboratory tests were assessed before, and 1,2,3,5,7, and 10 days after surgery. Post-hepatectomy biochemical dysfunction (PHBF) was defined as increased INR > 1.5 or hyperbilirubinemia > 2.9 mg/dL on or after postoperative day (POD) 5. If INR or bilirubin level had increased preoperatively, PHBF was defined as increasing INR or serum bilirubin on or after POD 5, compared with the values of the previous days. Definition of post-hepatectomy liver-related morbidity included PHBF, ascites requiring diuretics or invasive drainage procedures, hepatic encephalopathy, rescue liver transplantation, and deaths from any causes within 90 days after operation.

Results: The present study analyzed 1,565 patients who underwent liver resection for HCC, including 1,258 men (80.4%) with a mean age of 58.3 years (Table 1). Major etiology of underlying liver disease was chronic hepatitis B virus infection (80.8%). Patients with cirrhosis comprised of 37.9% of patients. Patients who underwent transarterial chemoembolization (TACE) and portal vein embolization (PVE) before liver resection were 258 (16.5%) and 156 (10.0%), respectively. Of 1,565 patients, 790 (50.5%) underwent right hepatectomy and 271 (17.3%) received left hepatectomy. Segmentectomy was performed in 272 (17.4%) patients and 85 (5.4%) received bisegmentectomy. To build and validate the prediction model, study population was divided into train and test set in a 3:1 ratio. Eight-three (5.3%) patients had a bilirubin > 2.9 mg/dL or INR > 1.5 on or after POD 5. Post-operative ascites requiring diuretics or invasive drainage procedure occurred in 51 (3.3%) patients. One patient developed hepatic encephalopathy resulting from deterioration of liver function. Two patients experienced liver failure subsequently underwent rescue liver transplantation. A total of 13 mortality occurred within 90 days after operation, of which 4 patients died within 30 days. Male (Adjusted odds ratio [AOR]: 2.49, 95% confidence interval [CI]: 1.25-4.97), cirrhosis (AOR: 2.00, 95% CI: 1.27-3.15), major resection (AOR: 2.22, 95% CI: 1.42-3.45), platelet ≥150,000 (AOR: 0.96, 95% CI: 0.44-1.09), serum albumin level ≥3.5 g/dL (AOR: 0.52, 95% CI: 0.32-0.82), and INR (1.1≤INR<1.2: 1.42 [0.49-4.4], 1.1≤INR<1.2: 1.90 [0.65-5.58], and INR≥1.2: 6.32 [1.97-20.29] were selected as factors for predicting post-operative liver-related morbidity in the training cohort with an area under the receiver operating characteristics of 0.737 (95% CI: 0.689-0.784). Test set was validated with an area under the receiver operating characteristic (AUROC) of 0.740 (95% CI: 0.647-0.833).

Conclusions: We proposed point-based prediction model and points were assigned for sex (male: 3 point), cirrhosis (2 point), major resection (2 point), platelet <150,000 (1 point), serum albumin <3.5 g/dL (2 point), and INR (1.0≤INR<1.1: 1 point, 1.1≤INR<1.2: 2 point, and INR≥1.2: 5 point) based on regression coefficients. The sum of these 6 points enables predictive risk for liver-related morbidity after liver resection for HCC.

Keywords: Liver resection, Hepatocellular carcinoma, Post-hepatectomy, Liver-related morbidity

Regorafenib versus Nivolumab for Hepatocellular Carcinoma Patients Who Experienced Sorafenib Treatment Failure: A Propensity Score Analysis


1Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea; 3Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea.

Aims: Several treatment options are now available for patients with hepatocellular carcinoma (HCC) who progress during sorafenib treatment. We aimed to compare the efficacy of regorafenib and nivolumab in HCC patients who have failed sorafenib treatment.

Methods: Consecutive patients who received regorafenib or nivolumab for the treatment of HCC after sorafenib treatment failure between July 2015 and October 2018 at Seoul National University Hospital were included in this retrospective study. Primary endpoint was overall survival. Inverse probability weighting (IPW) using propensity scores was conducted to reduce the treatment selection bias.

Results: Among 151 included HCC patients, 103 patients received regorafenib and 48 patients received nivolumab. During the median (interquartile range) follow-up of 4.1 (2.8–6.2)
months, 66 of 151 patients (43.7%) died: 39 of 103 patients (37.9%) receiving nivolumab and 27 of 48 patients (56.3%) receiving sorafenib. Median survival was 6.4 months (95% confidence interval [CI], 2.4–10.4) for sorafenib and 5.9 months (95% CI, 3.7–8.1) for nivolumab (P=0.82 by log-rank test) (Fig. 1A). Overall survival was not significantly different between the groups (nivolumab vs. sorafenib: adjusted hazard ratio [aHR], 0.81; 95% CI, 0.48–1.36; P=0.42). Even after balancing baseline characteristics using IPW, overall survival was still similar between the groups (P=0.21 by log-rank test) (Fig. 1B). However, patients treated with nivolumab showed significantly prolonged overall survival compared to patients treated with sorafenib (aHR, 0.48; 95% CI, 0.25–0.91; P=0.03) after adjusting for baseline characteristics including the levels of alkaline phosphatase, aspartate aminotransferase, and MoRAL score (=11 x sqrt(PIVKA) + 2 x sqrt(AFP)), Child-Pugh class, and the presence of clinically significant portal hypertension.

Conclusions: Improved overall survival was demonstrated in patients who were treated with nivolumab compared to patients who were treated with sorafenib after rigorous adjustment for baseline demographic and clinical characteristics.

Keywords: HCC, Sorafenib, Nivolumab, Survival, Liver cancer

The Effect of Urea Cream on Sorafenib-Associated Hand-Foot Skin Reaction in Patients with Hepatocellular Carcinoma: Multicenter, Prospective Randomized Double-Blind Controlled Study

Young-Sun Lee1, Ji Hoon Kim*, Do Young Kim2, Moon Young Kim3, Hyung Joon Kim4, Yeon Seok Seo5, Ki Tae Yoon6, Jeong-Hoon Lee7, Hyun Woong Lee7, Young Kil Jung7, Hyung Joon Yim8, Byoung Kuk Jang9, Eun Sun Jang10, Jae Young Jang11, Sung Bum Cho12, Sang Yoon Hwang13

1Department of Internal Medicine, Korea University College of Medicine, 2Yonsei Liver Center, Severance Hospital, Seoul, 3Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju Severance Christian Hospital, Wonju, 4Chung-Ang university hospital, Seoul, 5Department of Internal medicine, Pusan National University school of Medicine, Pusan National University Yangsan Hospital, Pusan, 6Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, 7Department of Internal Medicine, Yonsei University College of Medicine, Seoul, 8Department of Internal Medicine, Korea University College of Medicine, Ansan, 9Department of Internal Medicine, Keimyung University School of Medicine, Daegu, 10Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, Gyeonggi, 11Division of Gastroenterology and Hepatology, Department of Internal Medicine, Soonchunhyang University School of Medicine, Seoul, 12Department of internal medicine, Chonnam National University Medical School, Chonnam, 13Department of Internal Medicine, Dongguk Institute of Radiological & Medical Sciences, Pusan, Korea

Aims: Sorafenib has recommended as first line treatment in patients with advanced hepatocellular carcinoma (HCC). Although sorafenib increase overall survival in patients with HCC, it has many side effects such as fatigue, diarrhea, vomiting, nausea, pruritus, depilation,and Hand-Foot Skin Reaction (HFSR). Among them, HFRS is the most common side effect and it is main reason for dose de-escalation or discontinuation of sorafenib in patients with HCC. In this study, we aimed that investigate the role of urea cream in preventing the occurrence of HFSR or ameliorating severity of HFSR.

Methods: Total 288 patients with HCC at 13 hospitals in Korea were randomly assigned from May 2016 to May 2018. Patients were treated with placebo cream and urea cream at the same time as starting the treatment of sorafenib. Patients were followed up for up to 12 weeks. HFSR, score for Hand-Foot Skin Reaction and Quality of Life (HF-QoL) questionnaire, and adverse event were assessed at 2, 4, 8, and 12 weeks.

Results: After exclusion of 41 patients, 247 patients with 117 patients in placebo control group and 130 patients in urea cream group were analyzed. Urea cream group showed lower cumulative incidence of any grade of HFRS (Log-rank, P=0.247) and severe HFRS of 2 or more grade Log-rank, P=0.394) without statistical significance. In the incidence by time point, development of severe HFRS of 2 or more grade were significant lower in urea cream group compared to placebo control group (13.8% vs. 23.9%, P=0.042). Urea cream group showed significant improved score of HF-QoL questionnaire comparing with placebo control group (11.8 vs. 19.7, P=0.014) at 12 weeks. There was no significant difference for overall survival (Log-rank, P=0.748) between two groups. Tumor response were also not significantly different between two groups, which objective response rate was 6.2% in placebo control group and 6.0% in urea cream group (P=0.957), and disease control rate was 44.3% in placebo control group and 42.0% in urea cream group (P=0.741).

Conclusions: Treatment of urea cream showed decreased incidence of severe sorafenib-induced HFRS at 2 weeks and decreased tendency of development of HFRS in patients with HCC. Therefore, treatment of urea cream might be considered in patient that treated with sorafenib for HCC.

Keywords: HCC, Sorafenib, Hand-foot skin reaction
Validation of the Updated Version of Korean Stroop Test in the Screening of Minimal Hepatic Encephalopathy

Eileen L. Yoon¹, Daewon Jun², Eun-Chul Jang³, Jae Youn Jeong⁴, Do Seon Song⁵, Sang Bong Ahn⁵, Hee Youn Kim⁵, Sung Eun Kim⁵, Hyoun Su Kim⁵, Soung Won Jeong⁵⁶, Sang Gyune Kim⁵⁷, Tae Hee Lee⁵⁸, Yong Kyun Cho⁵⁸

¹Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine; ²Department of Internal Medicine, Hanyang University Hospital, Hanyang University College of Medicine; ³Department of Occupational & Environmental Medicine, Soonchunhyang University Cheonan Hospital; ⁴Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine; ⁵Department of Internal Medicine, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea; ⁶Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University College of Medicine; ⁷Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, College of Medicine, The Catholic University of Daegu School of Medicine, Daegu, Republic of Korea; ⁸Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine; ⁹Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine; ¹⁰Department of Internal Medicine, Soonchunhyang University; ¹¹Department of Internal Medicine, Soonchunhyang University College of Medicine, Soonchunhyang University Bucheon Hospital; ¹²Department of Internal Medicine, Kangyang University College of Medicine; ¹³Department of Internal Medicine, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Aims: Burden of minimal hepatic encephalopathy (MHE) is significant, but no universal criteria for diagnosis have been established. We aimed to validate the updated version of Korean Stroop Test for MHE screening.

Methods: Liver cirrhosis (LC) patients without history of overt HE were recruited prospectively from 13 centers. All participants completed Korean paper-pencil test (KPPT) and the Korean stroop test. Korean stroop test consisted of two stroop-off states (color and word) and two stroop-on states (inhibition and switching). Four types of “On Time + Off Time” were analyzed (color-plus-inhibition, color-plus-switching, word-plus-inhibition, and word-plus-switching). MHE was diagnosed when KPPT scores ≥ 2.

Results: A total of 119 LC patients and 792 healthy controls were enrolled. The most common etiology of LC was alcohol (62.8%). Mean KPPT score of LC patients was 11. Prevalence of MHE was 39.5% by KPPT. Four types of “On Time + Off Time” significantly differed among healthy controls, cirrhosis patients without MHE, and cirrhosis patients with MHE. All types of “On Time + Off Time” showed positive correlation with PHES scores (all P<0.01). The highest area under the curve (AUC) among “On Time + Off Time”s, was for word-plus-inhibition (AUC=0.699, 95% Confidence Interval: 0.603–0.795, P=0.001) in discrimination of MHE. In Prothrombin time (INR) (OR 197.33, P=0.008) and word-plus-inhibition (OR 1.012, P=0.011) were significant in multivariate analysis for MHE diagnosis. The cut-off point for the highest Youden’s index value was 155 sec for word-plus-inhibition time with 78.8% of sensitivity and 60.6% of specificity. In the subgroup of patients with MELD score less than 11, On Time + Off Time for word-plus-inhibition was the only prognostic factor in the diagnosis of MHE (OR 1.008, P=0.037).

Conclusions: The Korean Stroop Test is simple and valid for screening of MHE.

Keywords: Cirrhosis, Minimal hepatic encephalopathy, Screening, Stroop test
Aims: We aimed to validate the Asian Pacific Association for the Study of the Liver acute-on-chronic liver failure (ACLF) Research Consortium (AARC) ACLF score in Korean ACLF cohort.

Methods: Data from 534 patients who included in the prospective Korean ACLF study and with AARC ACLF score. The diagnostic performances for short-term mortality were compared by the area under the receiver operating characteristic curve (AUROC).

Results: The mean age was 55 years, and 76.4% were male patients. Most patients (91.8%) had cirrhosis, and 29.4% were ACLF patients based on either AARC or European Association for the Study of the Liver (EASL) - chronic liver failure (CLIF) ACLF definition. There were no significant differences between AURO value of AARC ACLF score (AARC ACLFs) and the AURO values of other scores, such as CLIF sequential organ failure assessment (CLIF-SOFA) score, CLIF consortium organ failure score (CLIF-C OFs), Model for End-stage Liver disease (MELDs), MELD-Na score (MELD-Nas), and Child-Turcotte-Pugh score (CTPs) for predicting 28-day mortality (all \( P > 0.05 \)). However, the AURO value of AARC ACLF score for predicting 90-day mortality was significantly lower than CLIF-C OFs, MELDs, MELD-Nas, and CTPs (all \( P < 0.05 \)), except CLIF-SOFA (\( P = 0.076 \)). In the patients with ACLF according to either AARC or EASL-CLIF definition, the AURO value of AARC ACLF score was the lowest. However, there was no significant difference in predicting 28-day and 90-day mortality between AARC ACLFs and other scores. Lactate-free AARC ACLF score showed significantly higher accuracy in predicting 90-day mortality in total patients (\( P = 0.014 \)). However, the lactate-free AARC ACLFs showed similar AURO values in predicting 28-day mortality in total patients and, predicting 28-day and 90-day mortality in ACLF patients.

Conclusions: AARC ACLF score showed comparable accuracy in predicting short-term mortality compared to other ACLF scores. Lactate-free ACLFs was also an excellent prognostic score in predicting short-term mortality.

Keywords: Acute-on-chronic liver failure, Validation, APASL

O-081

Empirical Carbenapem Treatment for Spontaneous Bacterial Peritonitis Reduced in-Hospital Mortality in Cirrhotic Patients with High CLIF-SOFA Score

Sun Woong Kim, Jeong-Hoon Lee, Minseok Albert Kim, Hee Joon Jang, Yun Bin Lee, Eun Ju Cho, Su Jong Yu, Yoon Jun Kim, Jung-Hwan Yoon

Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea

Aims: The third-generation cephalosporins (TGCs) has been recommended as the first-line empirical antibiotics for spontaneous bacterial peritonitis (SBP). However, recent European studies reported that antibiotics with broad spectrum may be necessary, especially for nosocomial SBP. In this study, we aimed to evaluate whether current treatment strategy for SBP is still valid in Korea, where the resistance to antibiotics prevails.

Methods: This study retrospectively involved consecutive SBP patients between September 2012 and January 2018 at a tertiary referral center in Korea. Primary endpoint was in-hospital mortality.

Results: A total of 287 patients with SBP were included: 110 patients (38.3%) were culture-positive. Among culture-positive SBP patients, 38 (34.5%) revealed third-generation cephalosporin (TGC)-resistant organisms. In entire SBP patients, the chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score was associated with TGC-resistant organisms (adjusted odds ratio [aOR], 1.32; 95% confidence interval [CI], 1.14–1.54; \( P < 0.001 \)), whereas nosocomial infection was not (aOR, 1.16; 95% CI, 0.56–2.43; \( P = 0.68 \)) . As initial empirical antibiotics, 207 patients (71.9%) received the TGCs and 58 (20.2%) received carbapenem. In entire SBP patients, an empirical TGC treatment was not associated with higher risk of in-hospital mortality than carbapenem treatment (aOR, 1.58; 95% CI, 0.74–3.39; \( P = 0.24 \)) if antibiotics regimens were adjusted according to clinical response or culture results. However, in a subgroup with high CLIF-SOFA score (\( \geq 7 \)), TGCs as empirical antibiotics was an independent risk factor for higher in-hospital mortality (vs. carbapenem: aOR, 4.00; 95% CI, 1.14–14.03; \( P = 0.03 \)) after adjustment for CLIF-SOFA score, presence of hepatocellular carcinoma beyond Milan criteria, and nosocomial infection (see Table).

<table>
<thead>
<tr>
<th>Variable</th>
<th>In-hospital mortality OR (95% CI)</th>
<th>( P ) value</th>
<th>In-hospital mortality OR (95% CI)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGC treatment group</td>
<td>4.00 (1.14–14.03)</td>
<td>0.00</td>
<td>4.57 (1.58–13.76)</td>
<td>0.03</td>
</tr>
<tr>
<td>CLIF-SOFA score</td>
<td>1.18 (1.23–5.18)</td>
<td>0.005</td>
<td>1.00 (0.35–3.57)</td>
<td>0.93</td>
</tr>
<tr>
<td>KCC beyond Milan criteria</td>
<td>3.09 (1.38–6.93)</td>
<td>0.02</td>
<td>3.18 (0.64–15.56)</td>
<td>0.23</td>
</tr>
<tr>
<td>Nosocomial infection</td>
<td>0.43 (0.20–1.49)</td>
<td>0.43</td>
<td>1.07 (0.29–3.99)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Conclusions: TGCs still seem viable empirical antibiotics for SBP
patients. However, for patients with more severe organ dysfunction, empirical treatment with carbapenem might be more beneficial. A prospective multicenter study comparing carbapenem vs TGCs in this subgroup is warranted.

**Keywords:** Spontaneous bacterial peritonitis, Carbapenem, Third-generation cephalosporins

### O-082

**Estimating Renal Function and Predicting Prognosis of Patients with Decompensated Cirrhosis Using Serum and Urine Markers: Multicenter Prospective Observational Study**

Yeon Seok Seo\(^1\), Moon Young Kim\(^2\), Tae Hyung Kim\(^1\), Han Ah Lee\(^1\), Ki Tae Suk\(^1\), Jeong-Hoon Lee\(^1\), Sang Gyune Kim\(^1\), Ji Hoong Kim\(^1\), Hyung Joon Yim\(^1\), Soung Won Jung\(^2\), Jae Young Jang\(^1\), Young Seok Kim\(^2\), Soon Koo Baik\(^1\), Soon Ho Um\(^1\), The Korean Study Group of Portal Hypertension

\(^1\)Department of Internal Medicine, Korea University College of Medicine, Seoul; \(^2\)Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju; \(^3\)Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Korea; \(^4\)Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul; \(^5\)Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan

**Aims:** This prospective observational study was performed to evaluate the best serum and urine markers for the assessment of renal function and predicting prognosis in patients with decompensated liver cirrhosis.

**Methods:** Hospitalized patients with decompensated liver cirrhosis were included. Laboratory tests including serum creatinine and cystatin C levels and urine N-acetyl-beta-D glucosaminidase (NAG) and neutrophil gelatinase-associated lipocalin (NGAL) levels were measured at the time of hospitalization.

**Results:** Three-hundred twenty-eight patients with decompensated cirrhosis were included. Age was 57.2±12.0 years and 237 patients (72.3%) were men. Alcoholic liver disease was the most frequent underlying liver disease (223 patients, 68.0%). Acute kidney injury (AKI) was combined in 41 patients (12.5%). In 287 patients without AKI, the incidences of AKI at baseline. INR, serum creatinine and cystatin C levels, and urine NAG and NGAL levels were significantly higher in patients with AKI. During hospitalization, AKI was progressed in 37 patients (11.3%). In 287 patients without AKI, the incidences of AKI at 3, 6, 9, and 12 months were 15.4%, 22.2%, 28.6%, and 32.5%, respectively. On multivariate analysis, serum cystatin C and urine NAG levels were independent predictors of AKI. The optimal cutoff values of serum cystatin C and urine NAG levels were 1.055 mg/L (sensitivity 72.1%, specificity 59.1%) and 23.1 U/g urinary Cr (sensitivity 65.1%, specificity 70.0%), respectively. When patients were classified into 3 groups with these cutoff values of serum cystatin C and urine NAG levels (group 1, both low; group 2, one of two high; and group 3, both high), progression of AKI during hospitalization (P=0.001), incidence of AKI in patients without AKI at baseline (P=0.001), and mortality rate (P<0.001) differed significantly according to the serum cystatin C and urine NAG levels.

**Conclusions:** Serum cystatin C and urine NAG levels were useful markers for the assessment of renal function and predicting prognosis in patients with decompensated liver cirrhosis.

**Keywords:** Decompensation, Cirrhosis, Kidney injury, Cystatin C, N-acetyl-beta-D glucosaminidase

### O-083

**The Correlation between Spleen Stiffness and Portal Hypertension in Patients with Liver Cirrhosis**

Hae Won Yoo\(^1\), Sang Gyune Kim\(^1\), Jeong-Ju Yoo\(^1\), Young Seok Kim\(^1\), Moon Young Kim\(^3\), Ki Tae Suk\(^1\), Boo Sung Kim\(^1\)

\(^1\)Digestive Disease Center and Research Institute, Department of Internal Medicine, Soonchunhyang University School of Medicine, Bucheon; \(^2\)Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea; \(^3\)Division of Gastroenterology, Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea

**Aims:** The most accurate way to determine degree of portal hypertension is the measurement of hepatic venous wedge pressure (HVPG). Since it is invasive and generally difficult to measure on routine clinical practice, there are many attempts to predict portal pressure by non-invasive method. We evaluate the usefulness of spleen stiffness (SS) assessed by 2-dimensional shear wave elastography (2D-SWE) for predicting HVPG.

**Methods:** From June 2017 to April 2019, 87 patients who measured SS and HVPG simultaneously were enrolled. Thirty four patients who showed invalid measurement (n=31) and combined hematologic malignancy (n=3) were excluded. Spleen stiffness was measured by 3 examiner using 2D-SWE (LOGIQ E9, GE healthcare) from two tertiary medical center.

**Results:** Fifty four patients were eligible for analysis. Most common etiology was alcoholic hepatitis (59.3%) and followed by chronic hepatitis B (18.5%). Patients consisted of Child-Pugh class A (n=6), B (n=37), C (n=11). The mean value of HVPG was
Clinical Characteristics of Portal Hypertension in Korean Patients with Myeloproliferative Neoplasms

Jaejun Lee¹, Pil Soo Sung¹,², Ki-Seong Eom¹, Keungmo Yang¹, Hyun Yang¹,², Kwon Yong Tak¹,², Jeong Won Jang³,⁴, Si Hyun Bae¹,², Jong Young Choi¹,², Suhyun Song¹,²,³
¹The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; ²Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; ³Division of Hematology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: The Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs), which include polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF), share many common clinical and molecular characteristics, including increased risk of thrombosis. Pathogenesis of portal hypertension (PHT) in MPN was previously shown to be correlated with degree of hepatic myeloid metaplasia and fibrosis, in addition to a major pre-hepatic component from increased splanchnic venous inflow. In this study, we investigated the clinical characteristics of PHT measured as gastroesophageal varices in Korean patients with MPNs.

Methods: From Jan. 2009 to Dec 2018, 1052 patients were newly diagnosed as MPNs including PV, ET, PMF, and MPN-unclassifiable (MPN-U). Among them, 228 patients underwent contrast-enhanced abdominal imaging study, which comprised our study cohort. We retrospectively reviewed medical records of the patients in the study cohort.

Results: In the study cohort, 11 patients (5%) had PHT demonstrated by gastroesophageal varix. Among patients with PHT, five patients had PV, 2 patients had ET, 3 patients had PMF, and 1 patient had MPN-U. Median age was 60 years old and 5 patients were male. Among them, three patients had portal vein thrombosis without protein C or S deficiency. Despite the gastroesophageal varices, liver function was normal with Child Pugh score 5 in every patient with PHT. Three patients had variceal bleeding, which had not been lethal and controlled by endoscopic ligation. All the patients (100%) with PHT had JAK2 V617F mutation, but only 119 / 217 patients (55%) without PHT had JAK2 V617F mutation (P<0.003). Seven patients received hydroxyurea and two patients received ruxolitinib treatment, but both of the medication resulted in no changes in variceal size by CT imaging. Living donor liver transplantation was performed in one patient with recurrent esophageal and gastric variceal bleeding, and explant pathology showed diffuse myeloid metaplasia in whole liver without fibrosis.

Conclusions: Whether SS is associated with HVPG is unclear. Standardization of measurement methods to reduce the inter-observer difference should be implemented and re-evaluation is need thereafter.

Keywords: Spleen stiffness, 2D-SWE, HVPG, Portal hypertension

A Significant Diagnostic Role for Discrimination of Malignancy of Contrast Enhanced Ultrasound for Portal Vein Thrombosis in HCC Patients

Yu Ri Shin¹,², Jung Hyun Kwon¹, Yoon-Jung Kim⁴, Sun Hong Yoo³, Soon Woo Nam⁰
¹Department of Radiology, The Catholic University of Korea, Seoul St. Mary’s Hospital; ²Department of Internal Medicine, The Catholic University of Korea, Incheon St. Mary’s Hospital

Aims: The characterization of portal vein thrombosis (PVT) as malignant versus bland is of great significance for therapeutic strategy in the patients with hepatocellular carcinoma (HCC). The aim is to investigate quantitative time-intensity curve (TIC) parameters and qualitative CEUS characteristics for differentiation between benign and malignant PVT, compared to the diffusion-weighted MRI (DWI).

Methods: A total of 50 HCC patients who showed the PVT in liver dynamic CT or MRI were consecutively enrolled and performed CEUS. TIC parameters were analyzed and DWI was performed using b values of 0, 400 and 800 sec/mm² at 3-T unit. A thrombus
was diagnosed as malignancy if it was enhanced on MRI.

Results: There were 19 bland thrombi and 31 malignant thrombi in 50 patients as the diagnostic enhancement of MRI. All qualitative parameters of CEUS such as arterial-phase enhancement, washout in the venous phase, vessel occlusion and expansion were significantly more common in malignant thrombosis than benign thrombosis (P<0.05). Regard to quantitative parameters of CEUS, shortened time to maximum enhancement, increased area under the TIC, prolonged time between the half amplitude values in each side of the maximum, prolonged the time from injection until the peak of enhancement in malignant thrombosis, were seen compared to benign thrombosis. These parameters were correlated with tumor stage and PIVKA II (P<0.0001). After an additional CEUS evaluation, 3 patients with the enhancement PVT on MRI were considered bland thrombus, in contrast, 4 patients with no enhancement PVT on MRI were considered malignant thrombus. Overall follow-up period, 5 of 7 patients consistent with the diagnosis of CEUS.

Conclusions: The present study showed that CEUS is comparable high diagnostic accuracy to DWI-MRI. Some TIC parameters by CEUS are useful for characterization of PVT in the patients with HCC.

Keywords: Contrast enhanced ultrasonography, Portal vein thrombosis, Hepatocellular carcinoma

Comparison between Stereotactic Body Radiotherapy and Radiofrequency Ablation as First Therapy for Small Hepatocellular Carcinoma

Soo Yong Choi1, Baek Gyu Jun2, Young Don Kim3, Gab Jin Cheon3, Jeong-Ju Yoo3, Sang Gyune Kim3, Young Seok Kim2, Soung Won Jeong4, Jae Young Jang2, Sang Gyune Kim3, Young Don Kim2, Gab Jin Cheon3, Hong Soo Kim4, Sae Hwan Lee6

1Department of Internal Medicine, University of Ulsan College of Medicine, Gangneung Asan Hospital, Gangneung, South Korea, 2Department of Internal Medicine, Soonchunhyang University College of Medicine Bucheon Hospital, Bucheon, South Korea, 3Department of Internal Medicine, Soonchunhyang University College of Medicine Seoul Hospital, Seoul, South Korea, 4Department of Internal Medicine, Soonchunhyang University College of Medicine Cheonan Hospital, Cheonan, South Korea.

Background/Aim: Resection or ablative therapy is not indicated for many patients with hepatocellular carcinoma (HCC) because of advanced cirrhosis or tumor location. Stereotactic body radiotherapy (SBRT) may be an alternative treatment for these patients. This study compared the therapeutic effects of radiofrequency ablation (RFA) and SBRT in patients with small (3 cm) HCC.

Methods: Data of HCC patients who underwent SBRT or RFA as an initial treatment at two tertiary referral hospitals between March 2011 and February 2017 were reviewed. The patient inclusion criteria were a single nodule measuring ≤3 cm in size and not suitable for resection.

Results: SBRT and RFA were performed in 57 (SBRT group) and 73 (RFA group) patients, respectively. In the SBRT group, 21 patients received SBRT only and 36 received SBRT combined with transarterial chemoembolization (TACE). The one-, three- and five-year overall survival rates were 97.7%, 86.4%, and 72.0%, respectively, in the SBRT group compared with 97.3%, 87.5%, and 84.8%, 70.8 and 52.6%, respectively, in the RFA group (P=0.072). Liver toxicity after treatment did not differ significantly between the SBRT (8.8%, 5/57) and RFA (2.7%, 2/71) groups (P=0.712). Liver toxicity after treatment did not differ significantly between the SBRT (8.8%, 5/57) and RFA (2.7%, 2/71) groups. liver toxicity after treatment did not differ significantly between the SBRT (8.8%, 5/57) and RFA (2.7%, 2/71) groups.
Prognostic Factors for Survival in Patients with Hepatocellular Carcinoma Treated by Trans-Arterial Radioembolization

Hee Chul Nam1,2, Pil Soo Sung1,2, Jeong Won Jang1,2, Ho Jong Chun1, Si Hyun Bae2,3, Jong Young Choi1,2, Seung Kew Yoon1,2*
1Department of Internal Medicine, College of Medicine, Seoul St. Mary’s hospital, The Catholic University of Korea, Seoul, Republic of Korea; 2Department of Radiology, Eunpyeong St. Mary’s hospital, The Catholic University of Korea, Seoul, Republic of Korea; 3Department of Radiology, College of Medicine, Eunpyeong St. Mary’s hospital, The Catholic University of Korea, Seoul, Republic of Korea

Aims: Trans-arterial radioembolization (TARE) is a form of radiation therapy performed by selective intra-arterial injection of microspheres loaded with Yttrium-90. TARE is known to be effective in the management of unresectable hepatocellular carcinoma (HCC). The aim of this study is to identify prognostic factors for overall survival (OS) and time to progression (TTP) in patients with HCC undergoing TARE.

Methods: This study included 73 consecutive HCC patients who underwent TARE from Jul 2009 to Jan 2018. The tumor responses to TARE were assessed according to modified Response Evaluation Criteria in Solid Tumors (mRECIST).

Results: The patients’ baseline characteristics were as follows; median age was 66 years, 74% of male. The median tumor size was 9cm and 41% of the patients had tumors larger than 10 cm. Multifocal HCCs identified in 58% and 26% of the patients showed infiltrative tumor. 63% of the patients did not have portal vein tumor thrombus (PVTT), 10% had VP 1-2, and 27% had VP 3-4 of PVTT. Among 73 patients, 5 (7%) obtained complete response and 25 (34%) showed partial response at 3 months after TARE. Median OS was 27.6 months and TTP was 3.2 months. Multivariate analysis revealed that the absence of PVTT (hazard ratio [HR], 0.137; 95% confidence interval [CI], 0.057-0.331, P<0.001) was independent factor for OS. The absence of PVTT (HR, 0.330; 95% CI, 0.172-0.632, P=0.001) and tumor diameter ≤10 cm (HR, 0.287; 95% CI 0.135-0.611, P=0.001) were independent prognostic factors for TTP. Subgroup analysis of 46 patients without PVTT showed that the age ≤65 (HR, 0.240; 95% CI, 0.066-0.869, P=0.030), and single number of tumor (HR, 0.015; 95% CI, 0.092-0.771, P=0.015) were identified as independent factors with improved OS.

Conclusions: TARE is an effective therapy for patients with advanced HCC. Absence of PVTT before TARE is an independent predictive factor for both OS and TTP.

Keywords: Hepatocellular carcinoma, Portal vein tumor thrombus, Transarterial radioembolization

O-088

Prediction of Overall Survival after Resection or Radiofrequency Ablation Using Surrogates for Clinically Significant Portal Hypertension in Patients with Early Hepatocellular Carcinoma

Jae Seok Bae, Dong Ho Lee, Joon Koo Han
Department of Radiology, Seoul National University Hospital

Aims: To evaluate the role of clinically significant portal hypertension (CSPH) surrogates in the prediction of prognosis and to compare the outcome of resection and radiofrequency ablation (RFA) according to the presence of surrogates for CSPH in patients with early hepatocellular carcinoma (HCC).

Methods: In this IRB-approved, single institutional study, we retrospectively enrolled 441 patients who underwent multidetector computed tomography (CT) and underwent first-line resection or RFA for single HCC ≤3 cm in diameter between January 2011 and December 2016. Upper endoscopy was performed in 211 patients. Surrogates for the presence of CSPH were considered present when at least one of the followings are present: gastroesophageal varices on upper endoscopy, thrombocytopenia (platelet count < 100 K/mm³) with splenomegaly (spleen size > 12 cm), or varices on CT. Overall survival (OS) was assessed between the treatment methods and between the patients with or without CSPH surrogates using Kaplan Meier method.

Results: The mean and median follow-up period were 52.9 ± 21.6 months and 52.0 months (0–96 months, range), respec-
Clinical Significance of the Thioredoxin System and Thioredoxin Domain Containing Protein Family in Hepatocellular Carcinoma

Sang Yeon Cho1, Sungha Kim2, Miju Son3, Woo Sun Rou4, Seok Hyun Kim5,6, Hyuk Soo Eun7,8, Byung Seok Lee1,9

1School of Medicine, Chungnam National University, Daejeon, Republic of Korea; 2Department of Clinical Research, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea; 3Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea; 4Department of Internal Medicine, School of Medicine, Chungnam National University, Daejeon, Republic of Korea

Aims: Oxidative stress occurs due to the excessive generation of cellular reactive oxygen species and antioxidant system dysfunction. The thioredoxin (TXN) system and TXN-domain-containing protein (TXNDC) family form networks maintaining the cellular reducing environment. Recently, the importance of these genes in the tumor environment has been emphasized. Therefore, we investigate the clinical significance of TXNs and TXNDC family members in HCC.

Methods: Genomic data from 367 hepatocellular carcinoma (HCC) patients who underwent hepatic resections were analyzed to determine genetic alterations in mRNA and protein levels between patients and healthy controls. In addition, functional enrichment and survival analyses were performed.

Results: HCC patients were shown to have the enhanced expression of TXN, TXNRD1, TXNDC7/9/14 mRNA and protein compared with that of controls. In accordance to the survival analyses, strong associations were found that patients with TXN, TXNRD1, and TXNDC1/7/9 alterations were proven to have poor prognosis in overall survival. Moreover, gene set enrichment analyses and network analyses revealed that positive correlations were found in mRNA expression of TXN, TXNRD1, and TXNDC7/9 genes with upregulation of the genes to tumor promoting genes, specifically mTORC1, E2F targets, and Myc targets. On the other hand, elevated expressions of TXNIP and TXNDC11 genes were correlated with suppression of the above tumor promoting genes.

Conclusions: TXN system and TXNDC family gene panel obtained from the resected tissue of the HCC patients could be used to predict survival prognosis of HCC and these genes could be considered as potential therapeutic targets for improving HCC survival.

Keywords: Thioredoxin, TXN-domain-containing protein, Hepatocellular carcinoma, Overall survival

Contrast-Enhanced Ultrasound with Perfluorobutane for Hepatocellular Carcinoma Surveillance: A Multicenter Diagnostic Trial (SCAN)

Ji Hoon Park1, Mi-Suk Park2, So Jung Lee2, Woo Kyoung Jeong3, Jae Young Lee2, Min Jung Park2,5, Sung Soo Lee1, Kyungwha Han1, Chung Mo Nam1, Seong Ho Park4, Kyoung Ho Lee1,9

1Department of Radiology, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; 2Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 3Department of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 4Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 5Department of Radiology and Institute of Radiation Medicine, Seoul National University Hospital, Seoul, Republic of Korea; 6Department of Radiology and Institute of Radiation Medicine, Seoul National University Hospital, Seoul, Republic of Korea; 7Department of Radiology and Center Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 8Yonsei Biomedical Research Institute, Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Republic of Korea; 9Department of Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; 10Program in Biomedical Radiation Sciences, Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology Seoul National University, Seoul, Korea

*Correspondence to Mi-Suk Park

Aims: Ultrasound has served as a standard surveillance tool for...
Reclassification of Microvascular Invasion in Hepatocellular Carcinoma According to Its Anatomical Location

Incheon Kang, Gi Hong Choi
Division of HBP Surgery, Department of Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: The most important factor for TNM stage in hepatocellular carcinoma (HCC) is microvascular invasion (MVI), which includes all vascular invasions detected in the microscopic examination. In this study, we classified microvascular invasion into microvessel invasion (MI) and microscopic portal vein invasion (MPVI) and evaluated their prognosis after curative resection of HCC.

Methods: This prospective, multi-institution, diagnostic trial using an intra-individual comparison design in a single arm of patients was conducted at five referral hospitals. Patients having liver cirrhosis and undergoing ultrasound for hepatocellular carcinoma surveillance were eligible for the study. All patients underwent contrast-enhanced ultrasound (Kupffer-phase ± vascular-phase ultrasound) immediately following conventional B-mode ultrasound. The primary endpoints were the detection rate of early-stage hepatocellular carcinoma and the false referral rate.

Results: From October 2014 through August 2016, 524 patients (mean age ± standard deviation, 54 ± 9 years; 184 women; 340 males) were enrolled. The detection rate of early-stage hepatocellular carcinoma was 0.6% (95% CI, 0.1%–1.7%; 3 of 524 patients) on B-mode ultrasound and 1.0% (95% CI, 0.3%–2.2%; 5 of 524 patients) on contrast-enhanced ultrasound, respectively. There was no statistically significant difference in the detection rate of early-stage hepatocellular carcinoma (P=0.16). The false referral rate was 4.6% (95% CI, 3.0%–6.7%; 24 of 524 patients) on B-mode ultrasound and 1.3% (95% CI, 0.5%–2.7%; 7 of 524 patients) on contrast-enhanced ultrasound, respectively. A statistically significant difference was observed for the false referral rate (P<0.001).

Conclusions: The use of perfluorobutane significantly reduced the false referral rate of B-mode US without significant improvement in detection rate.

Keywords: HCC, Surveillance, Ultrasound
and 58 per cent in non-curative treatment group (P=0.236). In multivariable analysis, tumor size, number of tumor and albumin level at recurrence stage were independent predictors of worse overall survival.

Conclusions: Non-curative treatment (chemoembolization) can be an alternative treatment option associated favorable overall survival for the patients of reBCLC-O when curative treatment is not feasible.

**O-093**

**Chronological Improvement in Long-Term Outcomes of Surgical Resection for Patients with Hepatocellular Carcinoma: Two Large-Volume Center Study**

Yun Bin Lee1, Jeong-Hoon Lee2, Hyo Young Lee3, Cheol-Hyung Lee1, Minseok Albert Kim1, Heejoon Jang1, Sun Woong Kim1, Suk Kyun Hong1, Eun Ju Cho1, Su Jong Yu1, Nam-joon Yi1, Kwang-Woong Lee2, Jong Man Kim1, Jae-Won Joh1, Yoon Jun Kim1, Kyung-Suk Suh2, Jung-Hwan Yoon3

1Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 2Department of Surgery, Seoul National University College of Medicine, Seoul, Korea; 3Department of Surgery, Samsung Medical Center, Sungkyunkwan University College of Medicine, Seoul, Korea

**Aims:** As the treatment for underlying liver diseases developed, clinical outcomes of patients with hepatocellular carcinoma (HCC) has been improved. We investigated whether long-term outcomes following surgical resection in HCC patients were changed over time according to the etiology of liver disease.

**Methods:** In this study, 1,631 consecutive patients who underwent surgical resection for HCC as an initial treatment between 2016 and 2013 at two large-volume centers in Korea (Seoul National University Hospital and Samsung Medical Center) were included. Study patients were divided into two groups by the year of operation: late-2000s (2006–2009: n=612) or early-2010s group (2010–2013: n=1,019). Primary and secondary endpoints were recurrence-free survival (RFS) and overall survival (OS), respectively.

**Results:** Median follow-up duration was 5.7 years in the late-2000s group and 5.0 years in the early-2010s group. Both RFS and OS were significantly longer in the early-2010s group among entire cohort (both log-rank P<0.001) (Fig. 1A–B). Multivariable Cox analyses revealed that the early-2010s group was an independent predictor of both prolonged RFS (adjusted hazard ratio [aHR]=0.69, 95% CI=0.58–0.81, P<0.001) and OS (aHR=0.30, 95% CI=0.22–0.41, P<0.001) compared to the late-2000s group. When patients were categorized into the two subgroups according to underlying liver disease (hepatitis B virus [HBV], n=1,270; and others, n=361), the aHR of RFS was similar between two subgroups (HBV subgroup: aHR=0.69, 95% CI=0.58–0.82, P<0.001; other subgroup: aHR=0.72, 95% CI=0.48–1.08, P=0.12) (Fig. 1C–D). OS of early-2010s group was also significantly improved in both subgroups (HBV subgroup: aHR=0.30, 95% CI=0.21–0.43, P<0.001; other subgroup: aHR=0.27, 95% CI=0.14–0.50, P<0.001) (Fig. 1E–F). HRs were maintained after balancing baseline characteristics using inverse probability weighting.

**Conclusions:** Long-term clinical outcomes of surgical resection for the treatment of HCC were improved over time with approximately 30% decreased risk of recurrence or death.

**Keywords:** HCC, Surgical resection, Etiology, HBV, RFS, OS, Liver cancer

**O-094**

**Is Liver Resection Justified for Multinodular Hepato-cellular Carcinoma in Patients with Cirrhosis? A Multi-center Analysis of 1,066 Patients**

Zhen-Li Li1, Xian-Hai MAO2, Ting-Hao CHEN3, Jun-Wu GUO1, Wei-Min GU4, Yu-Hao ZHOU1, Hong WANG5, Wan-Guang ZHANG6, Timothy M. PAWLICK7, Wan Yee LAU8, Lei LIANG1, Feng SHEN1, Tian YANG1

1Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, China; 2Department of Hepatobiliary Surgery, Hunan Provincial People’s Hospital, China; 3Department of General Surgery, Ziyang First People’s Hospital, China; 4The First Department of General Surgery, Fourth Hospital of Harbin, China; 5Department of Hepatobiliary Surgery, Pu’er People’s
Aims: The role of liver resection for multinodular (≥ 3 nodules) hepatocellular carcinoma (HCC) remains unclear, especially in patients with severe underlying liver disease. We aim to evaluate short-term and long-term outcomes in cirrhotic patients undergoing liver resection for multinodular HCC.

Methods: From a multicenter database, cirrhotic patients who underwent curative liver resection of HCC were enrolled and divided into two groups: the non-multinodular and multinodular HCC groups. Perioperative mortality and morbidity, and overall survival (OS) and recurrence-free survival (RFS) were compared between the two groups.

Results: Among 1,066 cirrhotic patients, 906 (85.0%) had single- or double-nodular HCC (the non-multinodular group), while 160 (15.0%) had multinodular HCC (the multinodular group). There were no any differences in postoperative 30-day mortality and morbidity between the two groups (1.8% vs. 1.9%, P=0.923, and 36.0% vs. 39.4%, P=0.411, respectively). However, the 5-year OS and RFS rates of the multinodular group were worse than those of the non-multinodular group (34.6% vs. 58.2%, and 24.7% vs. 44.5%, both P<0.001). Multivariable analyses revealed that tumor numbers ≥ 5, total tumor diameter ≥ 8 cm and microvascular invasion were independent risk factors for decreased OS and RFS after resection of multinodular HCC in cirrhotic patients.

Conclusions: Liver resection could be safely performed for multinodular HCC in patients with cirrhosis, with an overall 5-year survival rate of 34.6%. Tumor number ≥ 5, total tumor diameter ≥ 8 cm and microvascular invasion were independently associated with decreased OS and RFS after resection in cirrhotic patients with multinodular HCC.

Change in the Recurrence Pattern and Risk Factors over Time after the Complete Cure of Hepatocellular Carcinoma: Ten-Year Follow-Up Study

Han Ah Lee1, Seung Up Kim2, Hyun Gil Goh3, Tae Hyung Kim4, Sun Young Yim4, Young-Sun Lee5, Sang Jun Suh6, Young Kul Jung1, Ji Hoon Kim1, Yeon Seok Seo7, Hyung Joon Yim1, Jong Eun Yeon1, Kwang Soon Byun8, Soon Ho Um1

1Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Aims: Recurrence pattern and risk factors for recurrence after complete cure of hepatocellular carcinoma (HCC) changes over time. However, there were only few studies evaluated the recurrence of HCC in time-dependent analysis.

Methods: All patients with first diagnosed Barcelona-Clinic Liver Cancer (BCLC) stage A HCC which were completely cured with surgical resection or radiofrequency ablation (RFA) at Korea University Hospital and Yonsei University Severance Hospital were included between 2007 and 2016.

Results: In total, 1,496 patients who were cured from BCLC stage A HCC with surgical resection or RFA were included. Liver cirrhosis was combined in 919 patients (61.4%). Type of treatment was surgical resection in 991 patients (63.5%) and RFA in 570 patients (36.5%). The change of recurrence pattern over time is presented in Figure 1. Patient population and risk factors for HCC recurrence also changed with the time progression. In patients without HCC recurrence within 1 year, combined liver cirrhosis, treated with RFA, number and size of tumors, and MELD score were the independent risk factors for HCC recurrence at 1 year after treatment for HCC. While, in patients without HCC recurrence within 3 years, age, combined liver cirrhosis, and treated with RFA were the independent risk factors for HCC recurrence at 3 years after treatment for HCC. Combined cirrhosis and treatment type were two independent risk factors for HCC recurrence in almost time points. When patients were classified into four groups according to the presence of liver cirrhosis and the type of treatment, the cumulative incidences of HCC recurrence decreased with time progression in all groups, but the recurrence rate at the same time point was significantly different between groups.

Figure 1. The cumulative incidence of HCC recurrence at the time of resection or RFA, and at 1, 2, 3, 4, and 5 years after resection or RFA.

Conclusions: Recurrence pattern and risk factors for recurrence after complete cure of HCC changes with time progression. Appropriate surveillance strategy at each time point is needed.

Keywords: Recurrence, Hepatocellular carcinoma, Cirrhosis, Surveillance strategy
O-096

Surgical Resection Should Be Considered in Resectable Solitary Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis of Patients with Child A

Jong Man Kim, Sangjin Kim, Seo Hee Lee, Gyu-Seong Choi, Jae-Won Joh

Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine

Aims: Surgical resection and locoregional therapies such as combination transarterial chemoembolization (TACE) and/or radiation therapy (RT) are commonly used in those patients. The aim of present study is to compare the outcomes between surgical resection and combination therapy included TACE and RT in resectable solitary HCC with PVTT.

Methods: We prospectively enrolled in resectable solitary HCC with PVTT between 2010 and 2015. Resectability was defined by three experienced surgeons. Patients were selected using propensity score matching.

Results: All patients were Child-Pugh class A and ECOG performance grade ≤1. Forty-four patients underwent surgical liver resection (SR group) and 72 patients received combination therapies (Combination group). Age, AFP, PIVKA-II, and tumor size were significantly different between the two groups. Therefore, propensity score matching used four variables. Thirty-five patients in the SR group and 45 patients in the combination group were selected after propensity score matching. The 1-year, 2-year, and 3-year patient survival rates were 85.7%, 71.3%, and 68.2% in the SR group and 68.9%, 53.2%, and 38.1% in the combination group (P=0.008). Multivariate analysis showed that surgical resection, low platelet counts, and male are closely associated patient survival in solitary HCC with PVTT.

Conclusions: Surgical resection may improve patient survival in solitary resectable HCC with PVTT patients. Surgical liver resection is always considered as curative treatment in solitary resectable HCC with PVTT in patients with Child A.

O-097

Serine Protease HtrA2/Omi Deficiency Impairs Mitochondrial Homeostasis and Promotes Liver Fibrosis

Wonhee Hur1, Byung-Yoon Kang1, Sung Min Kim1, Gil Won Lee1, Min-Ryung Nam2, Hyangshuk Rhim1, and Seung Kew Yoon1

1The Catholic University Liver Research Center & WHO Collaborating Center of Viral Hepatitis, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2Department of Biomedicine and Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: The loss of mitochondrial function impairs intracellular energy production and potentially results in chronic liver disease. Increasing evidence suggests that mitochondrial dysfunction in hepatocytes contributes to the activation of hepatic stellate cells, thereby resulting in hepatic fibrogenesis. High-temperature requirement protein A2 (HtrA2/Omi), a mitochondrial serine protease, is responsible for quality control in mitochondrial homeostasis. However, little information is available regarding its role in mitochondrial damage during the development of liver fibrosis. This study investigated whether HtrA2/Omi regulates mitochondrial function during the development of liver fibrosis.

Methods: HtrA2/Omi expression was analyzed in liver tissues from mice model of the carbon tetrachloride (CCl4)-induced liver fibrosis and from patients with liver cirrhosis. We silenced HtrA2/Omi expression in FL83B hepatocytes with RNA interference. Hepatocytes were isolated from motor neuron degeneration 2 (mnd2)-mutant mice harboring the missense mutation Ser276Cys in the protease domain of HtrA2/Omi. For study of mitochondrial morphology and function, hepatocyte and liver tissue were analyzed by transmission electron microscopy, quantitative polymerase chain reaction, and immunoblotting.

Results: HtrA2/Omi expression considerably decreased in human and mouse fibrotic liver tissues. HtrA2/Omi knockdown in hepatocytes induced the accumulation of damaged mitochondria and provoked oxidative stress. Moreover, we found that mnd2-mutant mice altered mitochondrial morphology and function, which increased oxidative stress and promoted liver fibrosis. Conversely, the overexpression of HtrA2/Omi via hydrodynamics-based gene transfer led to the antifibrotic effects in CCl4-induced liver fibrosis mice model through decreasing collagen accumulation and enhancing anti-oxidative activity by modulating mitochondrial homeostasis in the liver.

Conclusions: These results suggest that suppressing HtrA2/Omi expression promotes hepatic fibrogenesis via modulating mitochondrial ROS generation, and these novel mechanistic insights involving the regulation of mitochondrial homeostasis by HtrA2/Omi may be of importance for developing new therapeutic strategies for hepatic fibrosis.

Supported by grants of the Basic Science Research Program through NRF-2016R1D1A1B03931395.

Keywords: Mitochondrial function, Hepatic fibrogenesis, HtrA2/Omi, Reactive oxygen species stress, Mitochondrial homeostasis

O-098

Glutamate/mGluR5 Signaling in Stellate Cells Drives Endocannabinoid-Mediated Alcoholic Steatosis

Won-Mook Choi1,2, Myung-Ho Kim1, Resat Cinar3, Bin Gao4, Hyuk Soo Eun1,2, Young-Sun Lee1,2, Won Kim1, George Kunos4, and Won-II Jeong1

1Laboratory of Liver Research, Graduate School of Medical Science and Engineering, KAIST, Daejeon, Republic of Korea; 2Department of Biomedicine and Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 3Department of Biomedicine and Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 4Department of Biomedicine and Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: The aim of present study is to compare the outcomes between surgical resection and combination therapy included TACE and RT in resectable solitary HCC with PVTT.

Methods: We prospectively enrolled in resectable solitary HCC with PVTT between 2010 and 2015. Resectability was defined by three experienced surgeons. Patients were selected using propensity score matching.

Results: All patients were Child-Pugh class A and ECOG performance grade ≤1. Forty-four patients underwent surgical liver resection (SR group) and 72 patients received combination therapies (Combination group). Age, AFP, PIVKA-II, and tumor size were significantly different between the two groups. Therefore, propensity score matching used four variables. Thirty-five patients in the SR group and 45 patients in the combination group were selected after propensity score matching. The 1-year, 2-year, and 3-year patient survival rates were 85.7%, 71.3%, and 68.2% in the SR group and 68.9%, 53.2%, and 38.1% in the combination group (P=0.008). Multivariate analysis showed that surgical resection, low platelet counts, and male are closely associated patient survival in solitary HCC with PVTT.

Conclusions: Surgical resection may improve patient survival in solitary resectable HCC with PVTT patients. Surgical liver resection is always considered as curative treatment in solitary resectable HCC with PVTT in patients with Child A.
of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; Laboratory of Physiologic Studies and the Laboratory of Liver Diseases, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA; Department of Internal Medicine, Chungnam National University, School of Medicine, Daejeon, Republic of Korea; Department of Internal Medicine, Korea University College of Medicine, Seoul, Republic of Korea; Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea

Aims: Paracrine activation of hepatic cannabinoid receptor 1 (CB1R) by hepatic stellate cell (HSC)-derived 2-arachidonylglycerol (2-AG) is one of the critical mechanisms mediating alcoholic steatosis by stimulating de novo lipogenesis in hepatocytes. However, the precise mechanism of 2-AG production in HSCs is unknown.

Methods: Levels of plasma glutamate were measured in the samples from 33 patients with biopsy-proven alcoholic liver disease and 4 healthy individuals (controls). To examine alcohol-induced glutamate excretion, endocannabinoid production and consequent steatosis, C57BL/6 wild type, global metabotropic glutamate receptor 5 (mGluR5) knockout and hepatocyte-specific xCT knockout mice were fed liquid ethanol diet for 8 weeks. In addition, mGluR5 specific antagonist or xCT inhibitor was treated to ethanol-fed mice to test their therapeutic potentials. For in vitro experiments, freshly isolated primary HSCs and hepatocytes were used. RNA sequencing, histology, immunoblots, quantitative polymerase chain reaction, and metabolite measurements were performed.

Results: We found that chronic alcohol consumption induced hepatic cysteine deficiency and subsequent glutathione depletion by impaired transsulfuration pathway. A compensatory increase in hepatic cystine-glutamate antipporter xCT resulted in significant increase of extracellular glutamate levels coupled to cystine uptake both in mice and in patients. Alcohol also induced the selective expression of mGluRs in HSCs, and mGluR5 activation stimulated 2-AG production in HSCs. Consistently, genetic or pharmacologic inhibition of mGluR5 or xCT attenuated alcoholic steatosis in mice via suppression of 2-AG production and subsequent CB1R-mediated de novo lipogenesis.

Conclusions: Our findings propose that a similar bidirectional signaling operates at a metabolic synapse between hepatocytes and HSCs through xCT-mediated glutamate/mGluR5 signaling to produce 2-AG, which induces CB1R-mediated alcoholic steatosis. This novel pathway could be a potential theragnostic target for alcoholic liver disease.

Keywords: Alcoholic fatty liver disease, Hepatic stellate cells, Endocannabinoid, Transsulfuration pathway

O-099

Src Inhibition Attenuates Liver Fibrosis by Downregulating CTGF and Phospho-Smad3

Hye-Young Seo1,2, So-Hee Lee1,2, Ji-Ha Lee1,2, Jae Seok Hwang1, Mi-Kyung Kim1,2, Byoung Kuk Jang1,2

1Department of Internal Medicine, Keimyung University School of Medicine, Daegu, South Korea; 2Institute for Medical Science, Keimyung University School of Medicine, Daegu, South Korea

Aims: The SRC kinase family comprises non-receptor tyrosine kinases that are ubiquitously expressed in all cell types. Active Src phosphorylates and thereby activates various signaling proteins such as signal transducer and activator of transcription 3, AKT, and epidermal growth factor receptor, which regulate various biological activities. Although Src is reportedly activated in pulmonary and renal fibrosis, little is known about its role in liver fibrosis. This study investigated whether inhibition of Src protects against liver fibrosis.

Methods: Liver fibrosis was induced by thioacetamide (TAA)-injection for 8 weeks in C57BL/6 mice and saracatinib was administered orally premixed with the pellet. We cultured AML12, LX2 and mouse primary hepatocytes. The effect of saracatinib on liver fibrosis was determined by Sirius red, immunohistochemistry, real-time RT PCR and western blot analysis.

Results: Expression of SRC was upregulated at the mRNA and protein levels in liver of TAA-injected mice. In addition, we confirmed that phosphorylation of SRC was increased in TAA-injection mice. The Src inhibitor saracatinib reduced TAA-induced collagen, αSMA and CTGF expression. In vitro studies also showed that TGF-β induces SRC phosphorylation and saracatinib inhibited TGF-β-stimulated CTGF and PAI-1 expression. In addition, saracatinib inhibited TGF-β-stimulated phospho-Smad3.
Conclusions: This study shows that Src is involved in TAA-induced liver fibrosis. Src inhibitors attenuated TAA-induced liver fibrosis and TGF-ß-induced CTGF expression. Furthermore, the inhibitory effect of Src inhibitors on liver fibrosis was associated with attenuation of TGF-ß-induced phospho-Smad3 expression.

Keywords: Src kinase, Saracatinib, Liver fibrosis, CTGF

Figure 1.

Figure 2.

Figure 3.

Correlation of Infiltration by T Cells and Macrophages with the Severity of Liver Damage in Drug-Induced Liver Injury: Implications in Responsiveness to Steroid Therapy

Hyun Yang1,2, Pil Soo Sung1,2, Kwon Yong Tak1,2, Jae Jun Lee1,2, Hee Chul Nam1,2, Jeong Won Jang1,3, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,3, Eun Sun Jung1,3, Jae Jun Lee1,2, Dong Wook Shin5,6, Yoon Jun Kim1, Jung-Hwan Yoon1

1 The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2 Division of gastroenterology and hepatology, Department of Internal medicine, College of Medicine, Eunpyeong St. Mary’s Hospital, The Catholic University of Korea, Seoul, Republic of Korea; 3 Department of Internal medicine, The Catholic University of Korea, Seoul, Republic of Korea; 4 Department of Family Medicine, Samsung Medical Center Supportive Care Center, Samsung Comprehensive Cancer Center; 5 Department of Digital Health, SABIST, Sungkyunkwan University, Seoul, Korea; 6 Cardiovascular Center, Seoul National University Hospital, Seoul, Korea

Aims: Drug-induced liver injury (DILI) is liver injury caused by the interplay between drugs, their metabolites and host immune response. The aim of this study is to characterize liver infiltrating immune cells in DILI and to evaluate the correlation between infiltrating immune cells and clinical outcome.

Methods: From January 2017 to February 2019, 23 patients with DILI were prospectively enrolled in this study. Diagnosis of DILI was based on patient medication history after exclusion of other etiology (virus, alcohol, autoimmune, ischemic hepatitis or extrahepatic obstruction of the bile duct). Liver biopsy was performed, and immunohistochemical stain for CD3, CD68, CD20, and CD38 was done. Experienced pathologist confirmed the pathologic and immunohistochemical findings.

Results: The causes included “health foods or dietary supplements” (8, 34.8%), “folk remedies” (6, 26.1%), “medications” (4, 17.4%), “herb” (3, 13.0%), “combined” (2, 8.7%). 18 patients (78.3%) treated with steroid. Two patients progressed to hepatic failure and recovered after steroid treatment. All patients were completely recovered from DILI at one month after diagnosis, whether they were treated with steroid or not. The frequency of infiltrated T cells, macrophages, and B cells was quantified by immunohistochemistry. The amounts of T cells, showed linearly ascending correlation with total bilirubin (r=0.370, P=0.030) and MELD (model for end-stage liver disease) score (r=0.340, P=0.047). The amounts of macrophages, showed linearly ascending correlation with total bilirubin (r=0.401, P=0.020), AST (r=0.445, P=0.010), and MELD (model for end-stage liver disease) score (r=0.402, P=0.020). The amounts of activated T cells showed linearly ascending correlation with AST (r=0.475, P=0.048).

Conclusions: In this study, we found the positive correlation between the amounts of T cells and macrophages infiltrations and deterioration of liver function in DILI. Favorable responses to steroid therapy suggest that vigorous innate and adaptive immune responses play critical roles in DILI.

Keywords: Drug-induced liver injury, Steroids, Adaptive immunity, Innate immunity
Aims: Liver enzymes, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamyltransferase (GGT), have been suggested as surrogate markers of various cardiovascular diseases. However, previous studies assessed liver enzymes only once at baseline, and the impact of variability of liver enzymes has not been examined. In this study, we investigated the association between liver enzyme variability and the risk of mortality and cardiovascular outcomes in the general population using nationally representative data.

Methods: A total of 6,496,271 subjects who participated ≥3 health examinations within 5 years from the index year (2009-2010) were included. Variability in ALT, AST, and GGT was measured using the variability independent of the mean. Multivariate Cox proportional hazards models were used.

Results: There were 106,413 deaths (1.6%), 53,385 MIs (0.8%), 65,143 AFs (1.0%), and 50,139 CHFs (0.7%) during a median follow-up of 6.0 years. In the multivariable analysis, there was increasing trends of the association between liver enzyme variability and all study outcomes. The degrees of association were largest for GGT variability. For the highest quartile of GGT variability relative to lowest one, the risk of all-cause mortality increased by 27% (hazard ratio [HR], 1.27; 95% confidence interval [CI], 1.25–1.29), myocardial infarction by 8% (HR, 1.08; 95% CI, 1.06–1.11), atrial fibrillation by 24% (HR, 1.24; 95% CI, 1.18–1.31), and congestive heart failure by 22% (HR, 1.22; 95% CI, 1.19–1.25). These findings were consistent regardless of alcohol consumption, body mass index, and degree of fatty liver measured by fatty liver index. Sensitivity analysis excluding subjects with outcomes within the first 2 years of follow-up also revealed similar results.

Conclusions: Higher visit-to-visit variability of liver enzyme was an independent predictor of all-cause mortality and cardiovascular events.

Keywords: Variability, Liver enzyme, Mortality, Cardiovascular outcome

Increased Annual Incidence of Pyogenic Liver Abscess and Its Risk Factors: An Analysis from HIRA-NPS of South Korea, 2012–2016

Jeong-Ju Yoo1, Sang Gyune Kim1, Young Seok Kim1, Soung Won Jeong2, Jae Young Jang2, Sae Hwan Lee3, Hong Soo Kim3, Baek Gyu Jun4, Young Don Kim4, Gab Jin Cheon4

1Department of Internal Medicine, Soonchunhyang University School of Medicine, Bucheon, Korea 2Department of Internal Medicine, Soonchunhyang University School of Medicine, Seoul, Korea 3Department of Internal Medicine, Soonchunhyang University School of Medicine, Cheonan, Korea 4Department of Internal Medicine, Gangneung Asan Hospital, Gangneung, Korea

Aims: The epidemiology of pyogenic liver abscess (PLA) continues to change but few population-based studies have been conducted in Korea. This study investigated the epidemiology and clinical outcomes of PLA patients in the current 5 years.

Methods: We used the Health Insurance Review and Assessment Service-National Patient Samples (HIRA-NPS) between 2012 and 2016. The HIRA-NPS, including approximately 1.4 million individuals, is a stratified random sample of 3% of the entire Korean population. The annual incidence rates, demographic data, underlying diseases, complications, and mortality rates were analyzed using the data.

Results: The annual incidence of PLA for all age groups increased gradually in Korea from 0.0273% (388 cases) in 2000 to 0.0298% (438 cases) in 2016. It occurred more commonly in the male sex, and older age (>65 years). Among the 2042 adult patients with PLA, 998 (48.9%) patients had diabetes mellitus, 108 (8%) patients colon cancer, and 346 (16.9%) patients biliary disease. Surgery due to PLA was in 44 (2.2%) patients, and 1 (0.05%) patient received enucleation due to endogenous endophthalmitis. The mortality rate was 8.2%. In particular, the mortality rate was 13.4% in patients aged over 65 and 19.3% over 85.

Conclusions: The incidence of PLA is increasing and the number of patients with comorbidity is also increasing. Especially, the mortality of PLA tends to increase in the old age. Further surveillance of epidemiology using National Health Insurance data is needed.

Keywords: Liver abscess, Epidemiology, Incidence, Mortality
### Oral Poster Presentation

<table>
<thead>
<tr>
<th>OP-001~OP-006</th>
<th>ALD &amp; NAFLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP-007~OP-012</td>
<td>Basic</td>
</tr>
<tr>
<td>OP-013~OP-018</td>
<td>HBV</td>
</tr>
<tr>
<td>OP-019~OP-024</td>
<td>Cirrhosis &amp; Liver Failure</td>
</tr>
<tr>
<td>OP-025~OP-030</td>
<td>HCV</td>
</tr>
<tr>
<td>OP-031~OP-036</td>
<td>Others</td>
</tr>
<tr>
<td>OP-037~OP-042</td>
<td>HBV &amp; Others</td>
</tr>
<tr>
<td>OP-043~OP-048</td>
<td>Liver Transplantation</td>
</tr>
<tr>
<td>OP-049~OP-054</td>
<td>Biliary and Pancreatic Disease</td>
</tr>
<tr>
<td>OP-055~OP-060</td>
<td>HBV</td>
</tr>
<tr>
<td>OP-061~OP-066</td>
<td>Cirrhosis &amp; Liver Failure</td>
</tr>
<tr>
<td>OP-067~OP-071</td>
<td>NAFLD</td>
</tr>
<tr>
<td>OP-072~OP-077</td>
<td>Liver Cancer, Basic</td>
</tr>
<tr>
<td>OP-078~OP-083</td>
<td>Liver Cancer, Clinical</td>
</tr>
<tr>
<td>OP-084~OP-089</td>
<td>Liver Cancer, Clinical</td>
</tr>
<tr>
<td>OP-090~OP-095</td>
<td>Liver Cancer, Clinical</td>
</tr>
<tr>
<td>OP-096~OP-101</td>
<td>Liver Transplantation</td>
</tr>
<tr>
<td>OP-102~OP-107</td>
<td>Surgery, Technical Issues</td>
</tr>
</tbody>
</table>
**OP-001**

**Exosomal Double-Stranded RNA Promotes Interleukin-1β Production in Kupffer Cells via Toll-Like Receptor 3 in Alcoholic Liver Injury**

Jun-Hee Lee1, Young-Ri Shim1, Wonhyo Seo2, Won-II Jeong1, Myung-Ho Kim1, Ye-eun Kim2, Tom Ryu1, Keungmo Yang1

1Lab of Liver Research, Graduate School of Medical Science and Engineering, KAIST, Daejeon, Republic of Korea; 2Laboratory of Liver Disease, National Institute on Alcohol Abuse and Alcoholism, National Institute of Health, Bethesda, MD, USA

**Aims:** Damaged hepatocytes release extracellular vesicles (EVs) into nearby milieu by various stimuli including alcohol. During alcohol metabolism, mitochondrial damage occurs by CYP2E1-mediated ROS. A recent study reported the accumulation of mitochondrial double-stranded RNA (mtdsRNA) by inhibition of mitochondrial degradosome such as PNPase. However, it has not been reported the presence of mtdsRNA in hepatocytes and its effects on alcoholic liver disease. Here, we report alcohol increases hepatic mtdsRNA and delivered mtdsRNA via hepatic exosomes could be detected by TLR3 and promotes interleukin-1β in Kupffer cells.

**Methods:** ALD is induced by binge ethanol drinking in WT and TLR3 KO mice with or without Kupffer cell deletion by clodronate. To investigate the presence of mtdsRNA, immunofluorescent staining were performed. IL-17 producing cells were identified by flow cytometry. Using differential centrifugation of hepatic EVs, microvesicles and exosomes were investigated for comparative analysis of groups. ALD is defined as liver disease with alcohol consumption history of more than 40 g/day (women) and 60 g/day (men) during the 7 days. Microbiome profiling was conducted with 16S-based Microbial Taxonomic Profiling (MTP) platform of EzBioCloud Apps (ChunLab Inc., Korea). After taxonomic profiling, comparative MTP analysis of EzBioCloud Apps was used for comparative analysis of groups.

**Results:** After binge drinking, increased IL-17 was observed in γδ T cells of WT, but not in TLR3 KO mice. In addition, IL-17 production of γδ T cells was not changed by depletion of Kupffer cells, followed by decreased IL-1β expression after binge drinking. In qPCR and western blotting, level of PNPase was significantly decreased in the liver of ethanol-fed mice. In Bioanalyzer analyses, exosomes isolated ethanol-treated hepatocytes contained much of small nucleotide RNA compared with control. After treatment with EtOH-exosomes, IL-1β expression was significantly increased in Kupffer cells of WT compared with TLR3 mice.

**Conclusions:** Accumulated hepatic mtdsRNA by alcohol-mediated suppression of PNPase, contributes TLR3 activation of Kupffer cells via exosomal delivery. Consequently, increased IL-1β expression of Kupffer cells triggers IL-17 production of γδ T cells. Therefore, mtdsRNA might be novel therapeutic targets to ALD.
Prospective Association of Soybean Products on the Risk of Non Alcoholic Fatty Liver Disease: A Nationwide Population-Based Study

Youn I Choi, Yun Soo Kim, Oh Sang Kwon, Ju Hyun Kim, Seung Kak Shin, and Dong Kyun Park
Division of Hepatology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Korea

Aims: Even though the ingredient of soy product have been ameliorated the prognosis of metabolic inflammation in experiments, there is limited real world data on the prospective effect of soy food consumption on the development of non-alcoholic fatty liver disease (NAFLD).

Methods: We used the data from the Korean Genome and Epidemiology Study health examinee study (KoGES-HEXA study) obtained during the periods from 2004-2013 (baseline) and 2012-2017 (follow up study). Soy food intake (soy bean, tofu, soy soup, and soy milk) was assessed through in-person interviews with a validated food-frequency and amount questionnaire. NAFLD was defined by fatty liver index (FLI) (>30), or hepatic steatosis index (HSI) (>30). Degree of liver fibrosis (significant fibrosis) was assessed by NAFLD fibrosis score (NFS), FIB-4, and Forns index. To reveal the association of soy food intake at baseline and the risk of newly development of NAFLD and NAFLD associated fibrosis during follow up period, univariate and multivariate analysis were done.

Results: Of 177,231 participants (40–70 years), after exclusion of participants with excess alcohol intake, baseline FLI or HSI <30, or without follow up data, we finally enrolled 40,224 participants. During median 7.1 year of period, total of 5,160 incidental cases with NAFLD were developed. Soy food consumption was inversely associated with the risk of NAFLD (HR=0.89 [0.88-0.98], P=0.04) and NAFLD associated significant fibrosis (HR=0.66 [0.48-0.89], P<0.001) in univariate analysis. The Multivariate adjusted HR of the risk of NAFLD and the NAFLD associated significant fibrosis for the upper intake quintile of soy food consumption compared with the lowest quintile were 0.79 (95% CI: 0.70-0.81).

Table 1. Univariate and multivariate analyses producing odds ratio of risk factors for the risk of NAFLD associated significant fibrosis

<table>
<thead>
<tr>
<th>Soy food consumption</th>
<th>NAFLD</th>
<th>Non NAFLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude HR [95%CI]</td>
<td>0.66 [0.48-0.89]</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Age,sex HR</td>
<td>0.72 [0.51-0.89]</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Model 1</td>
<td>0.75 [0.52-0.98]</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Model 2</td>
<td>0.76 [0.52-0.92]</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Model 3</td>
<td>0.78 [0.55-0.98]</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Model 4</td>
<td>0.79 [0.58-0.99]</td>
<td>1 (reference)</td>
</tr>
</tbody>
</table>

Model1: adjusted for age, sex, and body mass index, Model2: adjusted for age, sex, body mass index, total Calorie intake, Model3: adjusted for age, sex, body mass index, total Calorie intake, total protein intake, total lipid intake, smoking, drinking, Model4: adjusted for age, sex, body mass index, total Calorie intake, total protein intake, total lipid intake, smoking, drinking, exercise, stress index, education, income, and spouse

Abbreviation: NAFLD, non alcoholic fatty liver disease; HR, hazard ratio; 95%CI, 95% confidence interval

Conclusions: In this nationwide population based long-term follow up study, we revealed the soy food consumption had protective effect for the risk of the NAFLD and NAFLD associated with fibrosis.

Keywords: Non alcoholic fatty liver disease, Liver fibrosis, Soy bean, Hazard ratio

Evolution of Hepatic Fibrosis and Steatosis during the Long-Term Use of Metformin in Patients with Type 2 Diabetes

Ji Hye Kim, Hye Won Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, and Seung Up Kim
1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, 2Yonsei Liver Center, Severance Hospital, Seoul, Republic of Korea

Aims: The main therapeutic aim in patients with type 2 diabetes (T2D) is to control serum glucose level. Metformin has been widely used as the first-line anti-diabetic drugs. The prevalence of chronic liver diseases such as non-alcoholic fatty liver disease in patients with T2D is high. However, few studies have investigated the evolution of liver fibrosis and steatosis during the long-term use of metformin in patients with T2D.

Methods: Between 2006 and August 2010, patients with newly diagnosed T2D who received metformin were recruited. Patients with chronic liver diseases except non-alcoholic fatty liver diseases, insufficient follow-up period (< 2 years), or insufficient data were excluded. A total of 743 patients were included in the study. After baseline, each patient was followed up every year for at least 5 years.

Baseline and follow-up liver tests were performed. Liver fibrosis and steatosis were evaluated using transient elastography (FibroScan) and ultrasound. The primary outcome was the change in liver fibrosis score (FibroScan) during follow-up. Statistical analysis was performed using the Wilcoxon signed-rank test.

Results: Of the 743 patients, 686 (92.6%) completed the 5-year follow-up. The mean age of the patients was 59.2±11.2 years, and 580 (84.4%) were men. The mean body mass index was 28.4±4.4 kg/m², and 497 (71.0%) were current smokers. The mean duration of T2D was 5.0±4.9 years, and 582 (77.9%) were taking statins.

The mean change in liver fibrosis score during follow-up was 0.4±3.4 kPa (P<0.001). The mean change in liver steatosis score was -0.1±1.2 (P<0.001). The change in liver fibrosis score was not significantly different between patients taking metformin alone and those taking metformin plus other anti-diabetic drugs (P=0.074). However, the change in liver steatosis score was significantly different between the two groups (P=0.006).

Conclusions: The long-term use of metformin is associated with a significant decrease in liver fibrosis and steatosis in patients with type 2 diabetes. This finding suggests that metformin may have a beneficial effect on liver fibrosis and steatosis in patients with T2D.

Keywords: Type 2 diabetes, Metformin, Liver fibrosis, Steatosis
Fatty Liver Disease

Keywords: Non-Alcoholic Fatty Liver Disease, Diabetes, Fibrin, Fibrosis, Steatosis

Results: A total of 1,177 patients were finally enrolled. The mean age of the study population (656 men and 521 women) was 60.7 years. The mean body mass index, serum glucose, hemoglobin A1c, and aspartate and alanine aminotransferase was 25.2 kg/m², 141.9 mg/dL, 7.2%, 26.2 IU/L, and 29.5 IU/L, respectively. The mean FIB-4 and HSI was 0.17 and 27.4, respectively. At enrollment, no patient had significant liver fibrosis, but 393 (33.4%) patients had fatty liver. At 2 years of metformin treatment, the mean FIB-4 was significantly increased (0.17 → 1.44), whereas the mean HSI was decreased or maintained (27.4 → 26.6). In addition, significant liver fibrosis was developed in 69 (5.9%) patients, whereas the proportion of patients with fatty liver was decreased or maintained (33.4% → 28.5%). HbA1c level was statistically similar between patients with and without significant liver fibrosis at baseline and 2-years. Only female gender (odds ratio [OR]=3.301, 95% CI, 1.936→5.628, P<0.001) was independently associated with the risk of developing significant liver fibrosis at 2-years of metformin treatment. In the subgroup of 702 (59.6%) patients who were follow-up up to 5 years, the FIB-4 tended to increase (mean 1.80 at 5 years), whereas the HSI was maintained (mean 26.6 at 5-years). During the study period (median 97.1 months), 3 (0.3%) and 158 (13.4%) patients developed hepatocellular carcinoma and cardiovascular events, respectively.

Conclusions: During the long-term metformin treatment, female patients with T2D were significantly subject to 3-fold higher risk of liver fibrosis progression. Early recognition of liver fibrosis progression and corresponding medical interventions might be required for female patients with T2D.

Keywords: Diabetes, Metformin, Fibrosis, Steatosis

OP-005

Low Psoas Muscle Mass Is Associated with Advanced Fibrosis in Patients with Biopsy-Proven Non-Alcoholic Fatty Liver Disease

Min Kyu Kang¹, Jung Hoon Baek¹, Jung Gil Park¹, Soo Young Park², Won Young Tak³, Young Oh Kweon⁴, Se Young Jang¹, Yu Rim Lee⁵, Keun Hur³
¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Youngnam University, Daegu, Republic of Korea; ²Division of Gastroenterology and Hepatology, Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea; ³Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; ⁴Division of Cardiology and Cardiovascular Institute, Seoul, Korea; ⁵Division of Endocrinology, Department of Internal Medicine, Yonsei University, Seoul, Korea

Aims: Association of low skeletal muscle mass (LSMM) and liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) is widely evaluated using indirect and noninvasive modality. Our study is aim to investigate the association between LSMM and advanced liver fibrosis in patient with NAFLD using direct measurement of psoas muscle mass and liver histology.

Methods: We analyzed 146 NAFLD patients who underwent percutaneous liver biopsy and computed tomography, retrospectively. A receiver operating characteristic curve analysis was performed to evaluate optimal cut-off value of psoas muscle index (PMI) for LSMM to predict advanced fibrosis (F3).

Results: The optimal cut-off value of PMI to predict advanced fibrosis was 5.132 cm²/m². On the multivariate analysis, age (odd ratio [OR] 2.57, 95% confidence interval [CI] 1.25–6.30, P=0.020), LSM (OR 6.63, 95% CI 1.56–37.62, P=0.017), and platelet counts (OR 0.97, 95% CI 0.95–0.99, P=0.000) was associated with advanced fibrosis. The progression of liver fibrosis was negatively correlated with PMI (r = -0.364, P=0.002).

Conclusions: Low psoas muscle mass is independently associated with advanced fibrosis in patients with biopsy-proven NAFLD.

Keywords: NAFLD, Psoas Muscle, Liver fibrosis

OP-006

Non-Alcoholic Fatty Liver Disease Is an Early Predictor of Metabolic Disease in Metabolically Healthy Population: A Nationwide Claim Data Study

Hyeonsang Kang¹, Jeong-Hoon Lee¹, Seokhun Yang², Soongu Kwak³, Shinae Kang⁴, Seung-Pyo Lee⁵, Minseok Albert Kim⁶, Sun Woong Kim⁷, Cheol-Hyun Lee⁷, Yun Bin Lee⁷, Eun Ju Cho⁷, Su Jung Yu⁷, Yoon Jun Kim⁷, Jung-Hwan Yoon⁷
¹Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; ²Division of Gastroenterology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; ³Department of Endocrinology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Aims: Recent investigations have suggested a bi-directional relationship between non-alcoholic fatty liver disease (NAFLD) and metabolic disease. However, previous studies are limited in providing evidence as to which condition comes first because patients with NAFLD also have several concomitant metabolic syndrome components. The aim of the study is to investigate the impact of NAFLD on the development of metabolic syndrome,
prediabetes/type 2 diabetes, hypertension, and dyslipidemia in a truly metabolically healthy population.

**Methods:** This analysis included subjects who underwent health evaluation at least twice between 2009 and 2015 from the National Health Insurance Service-National Sample Cohort in Korea (n=28,880). The incidence of metabolic syndrome, prediabetes/type 2 diabetes, hypertension, and dyslipidemia was compared between the NAFLD and the non-NAFLD subjects both in the entire population and in the age, sex, smoking, and body mass index (BMI)-based propensity score-matched population (n=1,092). Univariate and multivariate standard Cox regression model was used to test whether the presence of NAFLD would be an early predictor of the incident metabolic syndrome, prediabetes/type 2 diabetes, hypertension, and dyslipidemia during follow-up.

**Results:** Presence of NAFLD was associated with significantly higher incidence of future metabolic syndrome, prediabetes/type 2 diabetes, hypertension, and dyslipidemia (age, sex, smoking and BMI-adjusted hazard ratio [aHR]=2.10, 95% confidence interval [CI]=1.18–3.71 for metabolic syndrome [Fig. 1A]; aHR=1.42, 95% CI=1.06–1.90 for prediabetes/type 2 diabetes [Fig. 1B]; aHR=2.36, 95% CI=1.35–4.12 for hypertension [Fig. 1C]; aHR=1.49, 95% CI=1.07–2.06 for dyslipidemia [Fig. 1D]) in the entire cohort.

**Conclusions:** The current study showed significant associations of NAFLD with the incidence of metabolic diseases in a non-obese population with none of the metabolic syndrome components. This enabled us to focus on the predictive impact of NAFLD on future incident metabolic syndrome, in isolation from other known metabolic confounders.

**Keywords:** Non-alcoholic fatty liver disease, NAFLD, Predictor, Metabolic disease
Molecular Diagnosis of Glycogen Storage Disease Type IX Using GSD Gene Panel

Tae Hyeong Kim1, Kwang Yeon Kim1, Moon-Woo Seong2, Sung Sup Park1, Jin Soo Moon1, Jae Sung Ko1

1Department of Pediatrics and Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea

Aim: Glycogen storage disease type IX (GSD IX) is caused by a deficiency of hepatic phosphorylase kinase (PhK). GSD type IX has been reported to be uncommon in Korea. The aim of this study is to clarify the clinical features and mutation analysis of GSD IX in Korea.

Methods: GSD gene panel was performed in GSD patients whose types were unknown at Seoul National University Hospital. GSD gene panel using hybridization capture-based next-generation sequencing contained AGL, G6PC, GBE1, GYS2, PHKA2, PHKB, PHKG2, PYGL, SLC2A2, and SLC37A4. The median duration of follow up period was 8.3 years.

Results: Nine children presented with hepatomegaly and serum ALT elevation. Among them, hypoglycemia was found in 2 (22%), hyperuricemia in 5 (56%), hypertriglyceridemia in 9 (100%), hyperlactacidemia in 5 (56%), short stature in 4 (44%), and hepatic fibrosis on liver biopsy in 7 (78%). Seven PHKA2 mutations were identified in 8 patients with GSD IXa; 1 nonsense (p.Asp757Ter), 2 splicing (c.918+1G>A, c.718-2A>G), 1 frameshift (p.Asp136ProfsTer11) and 3 missense mutations (p.Gly1210Arg, p.Glu415Asp, and p.Arg916Trp). Two mutations of PHKG2 were identified in children with GSD IXc; 1 frameshift (p.Ser262AlafsTer6) and 1 missense (p.Val221Met). Eight novel mutations are identified in Korean children with GSD IX.

Conclusions: GSD gene panel is a very useful diagnostic tool to confirm GSD type IX. GSD type IX is not rare in Korea. Liver enzymes and hypertriglyceridemia in children with GSD IX tended to improve with age.

Keywords: Glycogen storage disease, Molecular diagnosis, Gene panel

A Coagulation Factor IX-Deficient Rat as a Translational Pre-Clinical Model of Severe Hemophilia B

Jae Young Lee1, Hee Sook Bae1, Yun-Kyeong Jin1, Hee Young Kim1, Kyeong-Min Kim1, Dong Woo Song1, Ungi Kim1, Goo Jang1, Jung Min Lee1

1ToolGen Therapeutics, ToolGen Inc., Seoul, Republic of Korea; 2Laboratory of Theriogenology, Department of Veterinary Clinical Science, College of Veterinary Medicine, Seoul National University, Seoul, Republic of Korea

Aim: Glycogen storage disease type IX (GSD IX) is caused by a deficiency of hepatic phosphorylase kinase (PhK). GSD type IX has been reported to be uncommon in Korea. The aim of this study is to clarify the clinical features and mutation analysis of GSD IX in Korea.

Methods: GSD gene panel was performed in GSD patients whose types were unknown at Seoul National University Hospital. GSD gene panel using hybridization capture-based next-generation sequencing contained AGL, G6PC, GBE1, GYS2, PHKA2, PHKB, PHKG2, PYGL, SLC2A2, and SLC37A4. The median duration of follow up period was 8.3 years.

Results: Nine children presented with hepatomegaly and serum ALT elevation. Among them, hypoglycemia was found in 2 (22%), hyperuricemia in 5 (56%), hypertriglyceridemia in 9 (100%), hyperlactacidemia in 5 (56%), short stature in 4 (44%), and hepatic fibrosis on liver biopsy in 7 (78%). Seven PHKA2 mutations were identified in 8 patients with GSD IXa; 1 nonsense (p.Asp757Ter), 2 splicing (c.918+1G>A, c.718-2A>G), 1 frameshift (p.Asp136ProfsTer11) and 3 missense mutations (p.Gly1210Arg, p.Glu415Asp, and p.Arg916Trp). Two mutations of PHKG2 were identified in children with GSD IXc; 1 frameshift (p.Ser262AlafsTer6) and 1 missense (p.Val221Met). Eight novel mutations are identified in Korean children with GSD IX.

Conclusions: GSD gene panel is a very useful diagnostic tool to confirm GSD type IX. GSD type IX is not rare in Korea. Liver enzymes and hypertriglyceridemia in children with GSD IX tended to improve with age.

Keywords: Glycogen storage disease, Molecular diagnosis, Gene panel
investigate miR-101-3p’s roles in the hepatic differentiation of human BM-MSC (hBM-MSCs) and in hepatic stellate cell (HSC) activation.

Methods: To detect the miRNAs of hBM-MSC into functional hepatocytes and liver fibrotic tissue, the next-generation sequencing (NGS) was performed in hBM-MSCs before and after differentiation, hepatocyte, normal liver tissue, portal fibrotic tissue, and septal fibrotic tissue. To determine the effects miR-101-3p, hBM-MSC was treated with mimic or inhibitor during the hepatic differentiation. HSC LX2 was treated with TGF-β1 (2.5 ng/mL), and with or without miR-101-3p mimics. The role of miR-101-3p was identified through the change of liver-specific genes, EMT markers, and fibrosis genes using the quantitative real-time PCR (qRT-PCR) and western blotting.

Results: As a result of NGS analysis, miR-101-3p showed a higher expression level in differentiated hepatocyte-like cells and hepatocyte than hBM-MSC but lower expression level in liver fibrosis than normal liver. miR-101-3p caused the increase in the liver-specific gene (ALB and HNF4α) in hBM-MSC, while mesenchymal markers (SNAI1 and CDH2) and fibrosis markers (α-SMA and COL1α1) decreased in hBM-MSC and LX2. As a result, miR-101-3p mimic promoted the hepatic differentiation of hBM-MSC and inhibited the TGF-β1 mediated LX2 activation.

Conclusions: In this study, we identified miR-101-3p that can regulate the hepatic differentiation of hBM-MSC and the hepatic fibrosis. Our results demonstrate that miR-101-3p may be a biomarker, monitoring the response to therapeutic effect by BM-MSC in liver fibrosis.

Keywords: Human bone marrow-derived mesenchymal stem cells (hBM-MSCs), Hepatic differentiation, Next-generation sequencing (NGS), microRNAs (miRNAs), Fibrosis

Effect of Sericin Peptide in Animal Models of Non-Alcoholic Steatohepatitis (NASH)

Hyeon Tae Kang, Na Ryung Choi, Dae Won Jun, Jin Hwa Park, Dae Hyun Lim, Won Wu Seo, Ji Hyun Yeo, Jai Hoon Yoon, Kang Nyeong Lee, Hang Lak Lee, Oh Young Lee, Byung Chul Yoon, and Ho Soon Choi

Department of Inernal Medicine, Hanyang University College of Medicine, Korea

Aims: Sericin, a silk protein, is a component of cocoon. Previous studies have shown that sericin improves mitochondrial function in an animal model of metabolic disease. However, it is not yet known whether sericin is effective in non-alcoholic fatty liver disease.

Methods: 6 weeks old C57BL/6 mouse used. Forty mice were divided into four groups. Sericin and saline administered for 17 weeks in chow and 60% high fat diet groups, respectively. Liver biopsy, blood test, oral glucose tolerance test were performed in all animal groups. Electro-microscopy was performed to check mitochondrial function in liver tissue.

Results: There was no difference in body weight and diet intake during the study period between the control and sericin groups. However, liver weight and liver/body weight ratio were significantly lower in sericin group than in control group. In the sericin group, the AUROC of the oral glucose tolerance test was lower than that of the control group. Hepatic pJNK/JNK ratio, and pAkt/Akt ratio was decreased in active treatment group. Degree of hepatic steatosis and inflammation were lower compared to the control group in the sericin treated group. NAS scores were also lower in treatment group. Serum ALT, AST and triglyceride levels were significantly lower in sericin treated group than in control group. TNF-α and IL-6 expression was lower in liver tissues in the sericin group compared to control group. Electron microscopic findings showed abnormal mitochondria restored in sericin treated group.

Conclusions: Sericin reduced intrahepatic fat amount and intrahepatic inflammation in non-alcoholic fatty liver disease animal models.

Keywords: Sericin, Animal model, NASH
were shrunken, and some seminiferous tubules were atrophied. There were severe degenerative changes in glomerulus and tubules of kidney in the form of hyper cellularity with reduced urinary space.

Conclusions: Amoxicillin has shown toxicity to the liver, brain, kidneys, heart and testes in albino rats. Therefore, it needs special precautions when prescribing to humans.

Keywords: Amoxicillin, Drug induced liver damage, Hepatotoxicity, Toxicity


**OP-013**

Comparative Ex Vivo Analyses of Hepatitis B Virus-Specific CD8+ T Response between Patients Considered Immune Tolerant and Patients on Antiviral Treatment

Pil Soo Sung1,2,*, Dong Jun Park1,2,*, Jung-Hee Kim3, Ji Won Han1, Eun Byul Lee4, Gil Won Lee4, Hee Chul Nam2,4, Jeong Won Jang2,4, Si Hyun Bae1,2, Jong Young Choi2,4, Eui-Cheol Shin1, Su-Hyung Park1, Seung Kew Yoon1

1Department of Internal Medicine, Eunpyeong St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2Graduate School of Medical Science and Engineering, KAIST, Daejeon, Republic of Korea; 3Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic, of Korea.

Aims: Although it is generally accepted that perinatal transmission of hepatitis B virus (HBV) leads to chronic persistent infection, the underlying mechanism has not been clearly elucidated. Until recently, HBV-infected children in the IT phase were considered to have defects in mounting effective humoral and T cell responses against the infecting virus. In this study, we aimed to detect and characterize the virus-specific CD8+ T cells in patients considered immune-tolerant and under antiviral treatment.

Methods: We investigated a Korean chronic hepatitis B cohort comprising 15 patients in the immune-tolerant phase, 17 in the immune-active phase, and 13 under antiviral treatment. We performed enzyme-linked immunospot (ELISpot) assays ex vivo and intracellular cytokine staining after in vitro culture using a mixture of human leukocyte antigen A2-restricted epitopes and overlapping peptides of HBV proteins. We also performed ex vivo multimer staining assays and examined the expression of exhaustion markers and transcription factors in pentamer-positive cells.

Results: Ex vivo ELISpot revealed that HBV-specific T cell function was weaker in immune-tolerant patients than in those under antiviral treatment. Short-term culture of peripheral blood mononuclear cells revealed that some immune-tolerant patients had HBV-specific CD8+ T cells able to produce interferon-γ. We detected HBV-specific CD8+ T cells ex vivo (using the HBV core18-27 and HBV polymerase455-463 pentamer) in patients from all three groups. Pentamer-stained HBV-specific CD8+ T cells were defective in IFN-γ secretion in patients in the IT group, although those of some patients in AT group showed ex vivo IFN-γ secretion after peptide stimulation. The PD-1+ subset of pentamer+ CD8+ T cells was smaller ex vivo in the immune-tolerant phase than in the immune-active phase or under antiviral treatment. Moreover, we found that the proportion of CD127+PD-1+ HBV-specific CD8+ T cells was significantly lower in patients in the IT phase than in those in the AT phase. Interestingly, the proportion of PD-1+ CD8+ T cells and CD127+PD-1+ HBV-specific CD8+ T cells in HBV-specific CD8+ T cells correlated with patient age.

Conclusions: Overall, HBV-specific CD8+ T cells are present in patients considered immune-tolerant, although their ex vivo functionality is weaker than in patients under AT. Despite the high viral load, the proportion of PD-1 expression in HBV-specific CD8+ T cells is lower in the immune-tolerant phase than in AT phases.

Keywords: Hepatitis B virus, CD8 T cell, Immune tolerant

**OP-014**

Extremely Low Risk of Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients with Immune Tolerant Phase: A Multicenter Retrospective Cohort Study

Soo Young Park1, Hyun Woong Lee2, Dong Hyun Sinn1, In Hee Kim1, Hyung Joon Lim1, Jung Hwan Yu1, Won Young Tak1, Young Oh Kweon1, Jung Il Lee2, Kwan Sik Lee2, Wonseok Kang2, Yong Han Bahn3, Chang Hun Lee3, Sang Jun Suh3, Young Sul Jung3, Jin Woo Lee3, Han Ah Lee3, Sun Young Yim3, Soon Ho Um3, Beom Kyung Kim4, Jun Yong Park4, Do Young Kim4, Sang Hoon Ahn5, Kwang-Hyub Han6, Yoon Seok Seo7, Seung Up Kim8

1Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea; 2Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine,

Keywords: Hepatitis B virus, CD8 T cell, Immune tolerant
Aims: Patients in immune tolerant phase (IT-phase) of chronic hepatitis B (CHB) is not indicative of antiviral therapy (AVT). We investigated the cumulative incidence of HCC in patients in IT-phase, independent predictors of phase change and HCC development, and proposed the optimal cutoff HBV DNA level to define IT-phase.

Methods: A total of 946 consecutive patients in IT-phase between 1989 and 2017 were enrolled from 8 Korean tertiary hospitals. IT-phase was defined as hepatitis B e antigen positive, HBV-DNA >20,000 IU/mL, and alanine aminotransferase (ALT, ≤40 IU/L). ALT cutoff by KASL guideline was defined as 34 for men and 30 for women.

Results: The mean age of the study population (429 men and 517 women) was 36.7 years. The mean ALT and HBV DNA level was 24.6 IU/L and 316,310,000 IU/mL, respectively. No patient had liver cirrhosis. Of the study population, 476 (50.3%) stayed persistently in IT-phase, whereas 23 (2.4%), 116 (12.4%), and 331 (35.0%) patients experienced phase change into inactive carrier, minimally active, and immune active phase requiring AVT during the study period (median 63.6 [interquartile range (IQR) 29.3-103.2] months). The cumulative incidence of HCC at 10-years was 0.1%. When patients were censored at the time of phase change, the cumulative incidence was 0.2% (median follow-up 35.7 [IQR 18.0-70.4] months). On multivariate analysis, older age was the only predictor of phase change and HCC development (hazard ratio [HR]=1.067, 95% confidence interval [CI], 1.003-1.134; P<0.038). On multivariate analysis, higher HBV DNA level >10^7 IU/mL was independently associated with the reduced risk (HR=0.675, 95% CI, 0.540-0.844, P=0.001), whereas high ALT level above the cutoff by KASL guideline (HR=2.121, 95% CI, 1.717-2.620, P<0.001) was independently associated with higher risk of phase change from IT-phase to others.

Conclusions: Patients in IT-phase of CHB had an extremely low risk of HCC development. Thus, AVT should be cautiously considered for this population. In addition, we found that older age was the predictor of HCC development and that HBV DNA level >10^7 IU/mL which independently predicted phase change from IT-phase might be used to define IT-phase.

Keywords: Immune tolerant, Hepatitis B, Hepatocellular carcinoma, HBV DNA

Aims: In 2 identically-designed double-blind, randomized (2:1), Phase 3 studies, the safety and efficacy of TAF vs TDF was evaluated in subjects treated for 3 years.

Methods: 1298 HBeAg-negative and HBeAg-positive CHB patients were randomized and treated with TAF 25 mg or TDF 300 mg QD. Included in this analysis, were 1118 patients (759 HBeAg-positive and 359 HBeAg-negative); 866 of whom received TAF and 252 who received TDF for 3 years. Efficacy analyses included virologic, biochemical, and serologic responses, and pooled safety assessments included changes in bone mineral density (BMD), serum creatinine, and estimated GFR by Cockcroft-Gault method (eGFRCG).

Results: Baseline characteristics were similar between groups; mean age 39 years, 63% males, 78% Asian mostly genotypes C (48%) and D (26%); mean HBV DNA was 7.0 log10 IU/mL (34% had HBV DNA ≥8 log10 IU/mL), and 25% previously treated with nucleo(t)ides. At Week 144, high rates of virologic control were maintained in TAF vs. TDF subjects; a greater proportion of TAF vs TDF patients achieved ALT normalization (Table). Overall, adverse events (AEs) and serious AEs were similar between groups. At Week 144, greater median declines in eGFR were observed with TDF treatment; similarly, hip and
Conclusions: After three years of treatment, high and similar rates of virologic suppression were achieved and maintained and continued improvements in renal and bone safety were observed in patients receiving TAF compared to TDF.

Keywords: TAF, TDF, 144 weeks, CHB

OP-016

Predictive Score for Hepatocellular Carcinoma after Hepatitis B e Antigen Loss in Patients Treated with Entecavir or Tenofovir Disoproxil Fumarate

Tae Seop Lim, Hyun Woong Lee, Kwan Sik Lee, Jung II Lee, In Hee Kim, Chang Hun Lee, Byoung Kuk Kang, Woo Jin Chung, Jae Seok Hwang, Hyung Joon Yim, Young Kuk Jung, Sang Jun Suh, Yeon Seok Seo, Soon Ho Um, Sun Young Kim, Han Ah Lee, Jung Hwan Yu, Jin-Woo Lee, Young-Joo Jin, Young Seok Kim, Sang Gyune Kim, Jeong-Ju Yoo, Soo Young Park, Young Oh Kweon, Won Young Tak, Se Young Jung, Soon Sun Kim, Sung Won Cho, Jae Youn Cheong, Hyo Jung Cho, Seung Won Jeong, Jae Youn Chang, Seok Hyun Kim, Hyuk Soo Eun, Woo Sun Rou, Byoung Seok Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, and Seung Up Kim

1Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 2Division of Gastroenterology, Department of Internal Medicine, Mediplex Sejong Hospital, Incheon, Republic of Korea; 3Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 4Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, Jeonbuk, Republic of Korea; 5Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Republic of Korea; 6Department of Internal Medicine, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, Republic of Korea; 7Departments of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Republic of Korea; 8Department of Internal Medicine, Inha University School of Medicine, Incheon, Republic of Korea; 9Department of Internal Medicine, Soochunhyang University College of Medicine Bucheon Hospital, Bucheon, Republic of Korea; 10Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea; 11Department of Gastroenterology Ajou University School of Medicine, Suwon, Republic of Korea; 12Department of Internal Medicine, Soochunhyang University College of Medicine Seoul Hospital, Seoul, Republic of Korea; 13Department of Internal Medicine, Chungnam National University School of Medicine, Daejeon, Republic of Korea

Aims: The risk of developing hepatocellular carcinoma (HCC) after hepatitis B e antigen seroclearance (ESC) remains unclear. We established and validated a new risk prediction model for HCC development after ESC in patients with chronic hepatitis B (CHB) receiving antiviral therapy (AVT).

Methods: Between 2006 and 2016, 769 patients (training cohort) and 1,061 patients (validation cohort) with CHB who experienced ESC during AVT using entecavir (ETV) or tenofovir disoproxil fumarate (TDF) were recruited.

Results: In the multivariate analysis, male sex (odds ratio [HR]=2.092; 95% confidence interval [CI]=1.152–3.800), cirrhosis (HR=5.141; 95% CI=2.367–11.167), and fibrosis-4 index (FIB-4) of >3.25 (HR=3.25; 95% CI=1.184–3.620) were the independent risk factors for HCC development (all P<0.05). Accordingly, a novel HCC-ESC<sub>AVT</sub> model was developed (1x[sex: male=1, female=0]+3x[cirrhosis=1, non-cirrhosis=0]+1xFIB-4: >3.25=1, ≤3.25=0). The cumulative risk for HCC development was significantly different among the risk groups based on the HCC-ESC<sub>AVT</sub> category (0–1, 2–4, and 5 for the low-, intermediate-, and high-risk groups, respectively) (overall P<0.001, logrank test). The area under the receiver operating characteristic curve (AUC) for predicting HCC development 3, 5, and 10 years after ESC was 0.791, 0.791, and 0.790, respectively (all P<0.05). The predictive value of the HCC-ESC<sub>AVT</sub> model was similar in the validation cohort (AUC=0.802, 0.774, and 0.776 at 3, 5, and 10 years, respectively; all P<0.05).

Conclusions: A new HCC-ESC<sub>AVT</sub> model, which includes male sex, cirrhosis, and FIB-4 of 3.25 as constituent variables, for HCC development after ESC during AVT was established and well validated in this study.

Keywords: Hepatocellular carcinoma, Hepatitis B, Hepatitis B e antigen, Risk prediction

OP-017

Establishment of HBV-Replicating Mice Model from a Korean HBV Genome with Defective HBV-Specific T Cell Responses

Dong Jun Park, Pil Soo Sung, Jung-Hee Kim, Gil Won Lee, and Seung Kew Yoon

1The Catholic University Liver Research Center & WHO Collaborating Center of Viral Hepatitis, The Catholic University of Korea; 2Departments of Internal Medicine, College of Medicine, The Catholic University of Korea
Aims: Lack of a small animal model mimicking the human chronic hepatitis B virus (HBV) infection hampers developing the new immune-stimulating methods. We aimed to establish a mouse model that harbors replicating genotype C HBV derived from a Korean patient and to investigate HBV-specific T cell responses in the established mouse model.

Methods: pAAV_HBV 1.3 plasmid containing a greater-than-genome-length HBV genotype C fragment derived from a Korean patient (nt 1073–3215–2067. GeneBank: DQ683578.1) was constructed. To induce HBV replication in mouse liver, pAAV_HBV1.3 or pAAV-MCS was injected into the tail veins of mice. Serum levels of HBsAg were determined using the Enzyme-Linked immunosorbent assay kit. For the Enzyme-linked immunospot (ELISPOT) assay with mouse T cells, splenocytes were stimulated with overlapping peptides (OLPs).

Results: After HDI of the constructed plasmid, we monitored serum HBsAg levels in young (6-week-old) CBA/c mice. By 20 days post-HDI, serum HBsAg was detected and the level declined but remained detectable until 60 days. All mice sera were HBsAg positive at 50 days after injection, but the ALT level was not increased in mice. At 8 weeks post HDI, immunohistochemical staining for HBsAg in liver cells from infected mice revealed numerous hepatocytes expressing the HBV protein. The ELISPOT assay with splenocytes demonstrated that HBV-transfected CBA/c mice had a very low level of IFN-γ-producing HBV-specific T-cells ex vivo after being stimulated with HBsAg and HBcAg OLPs. Following intracellular cytokine staining also demonstrated poor production of IFN-γ by HBV-specific CD8+ T cells ex vivo after being stimulated with HBcAg and HBsAg OLPs.

Conclusions: We established a nontransgenic hydrodynamic transfection mouse model with HBV genotype C replication derived a Korean patient. With very low levels of interferon-γ-producing HBV-specific T-cells. This model mimics the immune tolerant phase of chronic HBV infection, and can be applied to the development of immunostimulatory therapeutics against HBV.

This research was supported by BrainKorea21.

Keywords: Hepatitis B virus, Mouse model, T cell

OP-018

Entecavir versus Lamivudine as Antiviral Prophylaxis for Patients with Hepatitis B Infection Undergoing Anticancer Cytotoxic Chemotherapy: A Randomized, Multicenter Clinical Trial

Won Kim1, Jeong Hoon Lee2, Bo Hyun Kim2, Young Seok Kim1, Hwi Young Kim3, Sohee Oh4, Sook-Hyang Jeong6

1 Department of Internal Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul National University College of Medicine, Seoul, Republic of Korea; 2 Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea; 3 Center for Liver Cancer, Research Institute and Hospital, National Cancer Center, Goyang, Republic of Korea; 4 Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, Republic of Korea; 5 Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Republic of Korea; 6 Department of Biostatistics, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea

Aims: Entecavir (ETV) is preferred to lamivudine (LAM) for the treatment of chronic hepatitis B (CH-B); however, it is unclear whether ETV would be more effective than LAM in the prophylactic setting for patients with anticancer chemotherapy. The aim of this study was to compare the efficacy and safety of ETV vs. LAM in preventing hepatitis B virus (HBV) reactivation in CH-B patients with solid and hematologic malignancies undergoing cytotoxic chemotherapy.

Methods: Randomized, open-label, controlled phase 3 study was conducted from April 2012 to June 2017 at 5 tertiary hospitals in South Korea. The study subjects were antiviral-naive 180 CH-B patients who were indicated to antiviral therapy, but not reimbursed by the National Health Insurance in 2012, and had a plan of curative or (neo)adjuvant chemotherapy for their solid (91%) or hematologic (9%) malignancies. They were allocated into either the LAM (n=92) or ETV (n=88) treatment group, stratified by malignancy types (solid or hematologic) and study sites, and received study medication until 24 week after completion of the last chemotherapy. The primary outcome was HBV reactivation, defined as either virologic breakthrough during antiviral therapy or withdrawal flare of HBV DNA level during 24 weeks after discontinuation of antivirals. Secondary outcomes included HBV-related hepatitis, emergence of genotypic resistance, hepatic decompensation, and chemotherapy disruption (TRIAL REGISTRATIONS clinicaltrials.gov Identifier: NCT01580202).

Results: On ITT analysis, HBV reactivation developed in 54.4% and 47.1% in the LAM and ETV groups, respectively (Odds ratio, 1.3; 95% confidence interval, 0.7–2.4; P=0.330). In the ETV group, the virologic breakthrough rate was significantly lower than in the LAM group, and HBV resistance was only observed in the LAM group. While development of hepatitis flare was not different between the 2 groups, chemotherapy disruption was more frequently encountered in the ETV group.

<table>
<thead>
<tr>
<th></th>
<th>Lamivudine (n=90)</th>
<th>Entecavir (n=87)</th>
<th>Difference (95% CI), %</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV reactivation</td>
<td>49 (54.4%)</td>
<td>41 (47.1%)</td>
<td>7.3 (7.4, 22.0)</td>
<td>1.3 (0.7, 2.4)</td>
<td>0.330</td>
</tr>
<tr>
<td>Virologic breakthrough</td>
<td>12 (13.3%)</td>
<td>1 (1.1%)</td>
<td>11.2 (4.8, 19.6)</td>
<td>13.5 (1.7, 108.1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Withdrawal flare</td>
<td>37 (41.1%)</td>
<td>40 (46.0%)</td>
<td>-4.9 (-19.5, 9.7)</td>
<td>1.0 (0.6, 1.9)</td>
<td></td>
</tr>
<tr>
<td>HBV-related hepatitis flare</td>
<td>4 (4.4%)</td>
<td>1 (1.1%)</td>
<td>3.3 (-1.5, 8.1)</td>
<td>4.0 (0.4, 36.5)</td>
<td>0.368</td>
</tr>
<tr>
<td>HBV resistance</td>
<td>3 (3.3%)</td>
<td>0 (0.0%)</td>
<td>3.3 (-6.4, 13.9)</td>
<td>3.0 (0.5, 19.8)</td>
<td>0.246</td>
</tr>
<tr>
<td>Chemotherapy disruption</td>
<td>1 (1.1%)</td>
<td>8 (9.2%)</td>
<td>-8.1 (-14.5, -1.6)</td>
<td>0.1 (0.0, 0.9)</td>
<td>0.017</td>
</tr>
</tbody>
</table>
Conclusions: Among CH-B patients with predominantly solid cancers on cytotoxic chemotherapy, ETV did not result in significant reduction of HBV reactivation compared with LAM. However, ETV significantly reduced the incidence of virologic breakthrough during antiviral prophylaxis compared with LAM. When prolonged chemotherapy would be expected, ETV may be preferred to LAM as an optimized prophylactic antiviral agent.

Keywords: Hepatitis B virus, Chemotherapy, Lamivudine, Entecavir

Low Apoprotein A1 as an Indicator of Poor Prognosis in Patients with Liver Cirrhosis

Chang Hun Lee, Hee Chan Yang, Sung Kyun Yim, Seung Young Seo, Sung Hun Kim, Sang Wook Kim, Seung Ok Lee, Soo Telk Lee, and In Hee Kim

Department of Internal Medicine, Chonbuk National University Medical School and Research Institute of Clinical Medicine of Chonbuk National University Hospital-Chonbuk National University Medical School, Korea

Aims: Liver cirrhosis has an appalling prognosis and numerous methods for predicting the prognosis have been extensively developed. The aim of this study was to investigate the value of apoprotein A1 in cirrhotic patients.

Methods: We retrospectively reviewed data from liver cirrhosis patients who were admitted from 2008 to 2017 in Chonbuk University Hospital. The development cohort included the first six-year populations, and the validation cohort included the following four-year populations. Apoprotein A1 level of individuals during admission was also required. Demographics and clinical parameters were evaluated and analyzed.

Results: 387 patients (296 men and 91 women) with liver cirrhosis were included for the development data set. There were 38 non-survivors (9.8%) during the 90-day follow-up, and apoprotein A1 level was significantly lower in this group (0.5 ± 0.4 vs 0.8 ± 0.4, P<0.001). The receiver operating characteristic (ROC) curve was used to evaluate the prognostic performance of apoprotein A1, and the area under ROC curve was 0.745 and the calculated optimal cut-off value was 0.36 g/L (sensitivity 60.0, specificity 84.0). We divided the patients into two groups regarding the apoprotein A1 level. Lower age, higher WBC counts, higher PT levels, lower sodium levels, higher AST and ALT levels, higher CRP levels, lower cholesterol and HDL cholesterol levels, higher CTP scores and higher MELD scores were revealed in the low apoprotein A1 group (≤ 0.36g/L) with statistical significance. The 90-day survival rate was analyzed using Kaplan-Meier curve with log-rank test and survival rate was significantly lower in the low apoprotein A1 group (P<0.001).

Conclusions: Low apoprotein A1 level considerably indicated severe disease status and was strongly associated with poor survival rate in patients with liver cirrhosis. Apoprotein A1 can be a useful marker to predict the prognosis of liver cirrhosis.

Keywords: Liver cirrhosis, Apolipoprotein A-I, Prognosis, Survival rate

Adipose Tissue Distribution in Relation to Insulin Resistance in Patients with Cirrhosis

Seong Hee Kang1,2, Hyunil Kim1, Jin Sook Lee2, Soon Koo Baik, Moon Young Kim1,2

1Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea; 2Regeneration Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea

Background: Although muscle mass and adipose tissue are associated with the risk of diabetes in the general population, it remains controversial in cirrhosis. We evaluated the association and impact on the survival adipose distribution (subcutaneous adipose tissue index [SATI] and visceral adipose tissue index [VATI]), sarcopenia, and abnormal glucose tolerance in cirrhosis.

Methods: This prospective observational study included 550 cirrhotic patients who underwent a 75-g oral glucose tolerance test and computed tomography. The patients were divided into normal glucose tolerance (NGT) and abnormal glucose tolerance (AGT) groups of patients with either impaired glucose
Efficacy of Thromboelastography for Predicting Prognosis of Korean Patients with Cirrhosis

Tae Hyung Kim, Soon Ho Um, Hyun Gil Goh, Han Ah Lee, Sun Young Yim, Young Sun Lee, Sang Jun Suh, Young Kuk Jung, Yeon Seok Seo, Ji Hoon Kim, Hwang Joon Yim, Jong Eun Yeon, Kwan Soo Byun

Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Aims: Thrombocytopenia and prothrombin prolongation are common clinical features in patients with liver cirrhosis. However, deficiency of fibrinolysis factors was also accompanied. Therefore, identification of cirrhotic patient’s hemostatic status by conventional parameters alone can mislead to wrong treatment. This study tried to evaluate the association between results of thromboelastography (TEG), which directly reflect hemostasis, and the prognosis of patients with cirrhosis.

Methods: We prospectively enrolled patients with cirrhosis and performed TEG. Patients with malignancy under treatment, and those with chronic kidney disease were excluded. Primary outcome was defined as development of major bleeding events within one month from enrollment, which are severe bleeding requiring hospitalization or transfusion. Secondary outcomes were death or urgent liver transplantation, occurrences of variceal bleeding, overt encephalopathy and portal vein thrombosis within one month.

Results: A total of 85 patients were enrolled, with an average age of 60.2 ± 10.7 years and male predominance (65.9%). Alcohol accounted for 62.4% of etiologies of cirrhosis and 54.1% of patients had Child-Pugh class A. The maximum amplitudes and angles from TEG were correlated with the platelet count (r = 0.764 and 0.652; all P<0.001). During one month after enrollment, major bleeding events were developed in 16 patients, and were significantly associated with K time, maximum amplitude, angle and lysis30 from TEG, platelet count, INR in logistic regression analyses. Among these, lysis30 of TEG served as the only independent predictive marker (hazard ratio, 0.09; P=0.037) even after adjustment for INR and platelet count. In addition, maximum amplitude was significant factor for developing overt encephalopathy, but was not independent predictor. However, results of TEG did not show any significant association with other secondary outcomes.

Conclusions: In this study, we confirmed that TEG plays a major predictor for the occurrence of short-term major bleeding in patients with cirrhosis.

Keywords: Thromboelastography, Cirrhosis, Prognosis, Bleeding

OP-022

Validation of the Animal Naming Test in the Screening of Minimal Hepatic Encephalopathy

Eileen L. Yoon1, Dae Won Jun2, Jung Eun-Chul1, Jae Yoon Jeong4, Do Seon Song5, Sang Bong Ahn6, Hee Yoon Kim7, Jung Eun Kim8, Hyo Young Su Kim9, Soung Won Jeong10, Sang Gyu-ne Kim11, Tae Hye Lee12, Yong Kyun Cho13

1Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine; 2Department of Internal Medicine, Hanyang University Hospital, Hanyang University College of Medicine; 3Department of Occupational & Environmental Medicine, Soonchunhyang University Cheonan Hospital; 4Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine; 5Department of Internal Medicine, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea; 6Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University College of Medicine; 7Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, College of Medicine, The Catholic University of Korea; 8Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine; 9Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine; 10Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine; 11Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine; 12Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine; 13Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine.
of Medicine; 13Department of Internal Medicine, College of Medicine, Soochunhyang University; 14Department of Internal Medicine, Soonchunhyang University College of Medicine, Soonchunhyang University Bucheon Hospital; 15Department of Internal Medicine, Konkuk University College of Medicine; 16Department of Internal Medicine, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Aims: Burden of minimal hepatic encephalopathy (MHE) is significant, but easy and valid screening tools for screening is an unmet need. We aimed to validate the animal naming test for MHE screening in Korea.

Methods: Liver cirrhosis (LC) patients without history of overt HE were recruited prospectively from 13 centers. All participants completed Korean paper-pencil test (KPPT) and the animal naming test (ANT). ANT consists of listing as many names of animals as possible in a minute. The number of animals listed in one minute (ANT1) was collected. MHE was diagnosed when KPPT scores ≥2.

Results: A total of 629 healthy controls and 124 LC patients were enrolled. The most common etiology of LC was alcohol (64.0%). Mean MELD score of LC patients was 11. Prevalence of MHE was 39.2% by KPPT. ANT1 was negatively correlated with education-years (p=0.298, P<0.001) in the healthy controls. ANT1 was significantly correlated with KPPT scores (p=0.387, P<0.001) in LC patients. ANT1s were significantly different between healthy controls and LC patients (P<0.001). ANT1s for healthy controls, LC patients without MHE, and LC patients with MHE were 17.4±4.6, 16.9±5.1, and 13.1±3.7, respectively. They were different when compared between LC patients without MHE and LC patients with MHE (P<0.001). ANT1 (OR 0.713, P<0.001) was the only significant factor independent of model for end-stage liver disease (MELD) score in multivariate analysis for MHE diagnosis. The cut-off point for the highest Youden's index value was 15.5 for ANT1 with 77.6% of sensitivity and 57.3% of specificity.

Conclusions: The animal naming test is an easy, simple and valid method for screening of MHE.

Keywords: Minimal hepatic encephalopathy, Cirrhosis, Screening, Animal naming test

Direct Bilirubin is More Valuable for Predicting Prognosis in Patients with Liver Cirrhosis

Joon Young Jung, Hyun Gil Goh, Han Ah Lee, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Sang Jun Suh, Young Kul Jung, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yeon, Kwan Soo Byun, Soon Ho Um

Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Aims: Most prediction models evaluating prognosis of patients with liver cirrhosis are based on serum total bilirubin level. However, because some patients with predominant indirect bilirubinemia have different predisposing factors from patients with direct bilirubinemia, direct bilirubin may have more beneficial role in predicting prognosis of cirrhotic patients.

Methods: Admitted patients clinically diagnosed with liver cirrhosis were enrolled. Patients with hepatocellular carcinoma or other malignancy were excluded. Six-month mortality was the primary outcome of this study.

Results: In total, 461 cirrhotic patients were enrolled. Age was 56.6±12.0 years and 343 patients (74.4%) were men. Alcoholic liver disease was the most frequent underlying liver disease (251 patients, 54.4%). Model of End-stage Liver Disease (MELD) score was 10.6±3.2. Among 461 patients, 86 patients (18.7%) died within 6 months. International normalized ratio (INR), serum total bilirubin (TB), direct bilirubin (DB), creatinine levels, and MELD score were significantly higher, while serum sodium level was significantly lower in patients with 6-month mortality than in those without 6-month mortality. On multivariate analysis, INR, TB, DB, albumin, and creatinine were independent predictors for 6-months mortality. Area under the receiver operating characteristic curve (AUROC) of the DB for predicting 6-month mortality was 0.871 (95% CI, 0.830-0.908), and it was significantly higher than that of TB 0.852 (95% CI, 0.809-0.894) (P=0.005). AUROC of MELD score using TB for predicting 6-month mortality was 0.892 (95% CI, 0.860-0.919). While, AUROC of MELD score using DB for 6-month mortality was 0.899 (95% CI, 0.868-0.925), which was significantly higher than that of preexist MELD score (P=0.044).

Conclusions: Direct bilirubin is might be more worthy for predicting prognosis in patients with liver cirrhosis.

Keywords: Direct bilirubin, MELD score, Liver cirrhosis, Prognosis

Impact of Relative Adrenal Insufficiency in Alcoholic Hepatitis (RAIAH)

Hyunil Kim1, Seong Hee Kang1, Soon Koo Baik2, Moon Young Kim1,2

1Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea; 2Regeneration Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea

OP-024

Impact of Relative Adrenal Insufficiency in Alcoholic Hepatitis (RAIAH)

Hyunil Kim1, Seong Hee Kang1, Soon Koo Baik2, Moon Young Kim1,2

1Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea; 2Regeneration Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea
**Background and Aims:** Relative adrenal insufficiency (RAI) is frequently observed and associated with increased mortality in patients with liver cirrhosis. However, no clinically significant data about differences in the causes of cirrhosis have been reported. In particular, clinical data regarding RAI in patients with alcoholic hepatitis, where steroids are an important treatment, have rarely been reported. We investigated the prevalence and clinical significance of RAI in patients with alcoholic liver disease.

**Method:** This prospective observational study included 111 admitted patients with alcoholic hepatitis. The peak cortisol was defined as the highest cortisol concentration whether at 30 or 60 minutes after 250 mg synacthen injection. Delta cortisol was defined as the difference between the peak and basal cortisol levels. RAI was defined as a peak cortisol level < 18 mg/dL, basal cortisol level < 15 mg/dL or delta cortisol < 9 mg/dL.

**Results:** Among the 111 patients, most patients were male (79.3%) with a mean age of 54.5 ± 11 years and median modified discriminant function (mDF) score of 27.0 (interquartile range, 15.0–45.5). RAI was identified in 78 patients (70.3%). The basal level of cortisol in patients with RAI (13.7 ± 9.9 mg/dL) was significantly lower than in those without RAI (26.8 ± 13.7 mg/dL). A significant negative correlation was observed between the mDF score and delta cortisol level (γ = −0.281, P=0.003). Eight (10.2%) of 78 patients with RAI and two of 33 (6.0%) patients without RAI received corticosteroids. However, no significant differences were observed in overall survival or the steroid treatment response between patients with and without RAI (P>0.05).

**Conclusion:** Although no independent predictor of survival or the treatment response was observed for RAI, it was frequent in patients with alcoholic liver disease and was associated with the severity of alcoholic hepatitis.

**Keywords:** Alcoholic hepatitis, Relative adrenal insufficiency, Survival

**OP-025**

Regression of Liver Fibrosis Assessed by Transient Elastography after Daclatasvir and Asunaprevir Combined Treatment in Patients with Chronic Hepatitis C with Genotype 1b Infection: Prospective Cohort Study (RELIF-C)

Hae Won Yoo1, Jun Yong Park2, Sang Gynme Kim3, Se Hwan Lee3, Young Kui Jung3, Moon Young Kim3, Dae Won Jeon4, Jaeg Young Jang3, Jin Woo Lee5, Oh Sang Kwon6

1Soochunhyang University College of Medicine Bucheon Hospital, Bucheon, Korea; 2Yonsei University Severance Hospital, Seoul, Korea; 3Soochunhyang University College of Medicine Bucheon Hospital, Cheonan, Korea; 4Korea University Ansan Hospital, Ansan, Korea; 5Yonsei University Severance Hospital, Wonju, Korea; 6Hanyang University hospital, Seoul, Korea; 7Soomchunhyang University College of Medicine Seoul Hospital, Seoul, Korea; 8Inha University hospital, Incheon, Korea; 9Gachon University Hospital, Korea

**Aims:** The development of direct acting antivirals (DAA) has made it easier to reach sustained virologic response (SVR) in patients with hepatitis C infection. However, it is not yet elucidated how much liver fibrosis get better by achievement of SVR after DAA treatment. Primary endpoint of this study is to evaluate the improvement of liver fibrosis by transient elastography (TE) after Daclatasvir/Asunaprevir (DCV+ASV) treatment.

**Methods:** Liver stiffness measurement using transient elastography as well as serum liver fibrosis scores (fibrosis-4 (FIB-4) score and the aspartate aminotransferase to platelet ratio index (APRI)) were evaluated at baseline and 48 weeks after starting DAA treatment. One hundred three patients with chronic hepatitis C Genotype 1b without resistance-associated substitution (RAS) mutation were enrolled in 9 tertiary medical centers. Patients with elevated liver enzyme (n=1) and who failed to follow-up (n=18) were excluded.

**Results:** Eighty four patients were eligible for this analysis. Mean age of patients was 68.1±9.7 years. Two patients failed to achieve SVR. Liver stiffness value after treatment with DAA was significantly decreased compared with baseline (15.0±11.0 vs. 19.8±12.4 kPa; P<0.001). Fibrosis stage assessed by TE was staged down significantly after DAA treatment (3.13±1.05 vs. 3.69±0.56, P<0.001) and 34 (40.5%) patients showed improvement in their fibrosis stage. Additionally, aspartate transaminase (31.0±23.5 vs. 65.2±37.2 IU/ml, P<0.001) and alanine transaminase (30.4±38.6 vs. 43.9±38.6 IU/ml, P<0.001) was markedly decreased after DAA treatment. Reduction in FIB-4 score (5.59±2.30 vs. 11.0±2.43, P<0.001) and APRI score (0.74±1.14 vs. 1.37±1.05, P<0.001) were also observed. In univariate analysis, improvement in fibrosis stage was associated with age, baseline liver stiffness, body mass index (BMI), platelet level, albumin level, prothrombin time. Multivariate analysis, only lower BMI showed significance with improvement in liver stage (Odd ratio, Confidence interval; 0.483, 0.249-0.937, P=0.032).

**Conclusions:** Eradication of hepatitis C virus with DAA showed improvement in liver stiffness and serum fibrosis score. Long-term follow up will be needed for prove its clinical benefit.

**Keywords:** HCV, DAA, Transient elastography, Liver fibrosis

**OP-026**

SVR Following Treatment with Direct Acting Antiviral Regimens Is Durable in More than 6,600 Patients: The Gilead SVR Registry Study

Jordan J. Feld1, Christian Schwabe2, Eric J. Lawitz3, Stanislas Pol4, Stephen David Shafran5, Robert Hyland6, Frances Chen7, Hadas Dvory-Sobol8, Anu O. Osinusi9, Diana Brainard6, Jin Youn6, Christophe Moreno10, Alessio Aghemo11, Simone L Strasser12, Stefan Zeuzem13

11,2,3,4,5,6,7,8,9,10,11,12,13
Aims: DAA therapy for HCV has provided the potential for large numbers of patients to achieve SVR raising the potential for elimination. While SVR rates are high in clinical studies and real world settings, it is important to demonstrate the durability of response. In addition, there are limited data regarding the long term outcomes of patients after achieving SVR with DAA therapy. Here we report the results of the Gilead SVR registry.

Methods: Patients were eligible for enrollment within 3 months of achieving SVR in a Gilead treatment study. Patients were followed with visits every 24 weeks for up to 144 weeks. At each visit, clinical assessment, HCV RNA measurements, and liver function tests were performed. For patients with virologic failure, sequencing and comparison with the pre-treatment baseline including phylogenetic analysis was performed differentiating relapse and reinfection.

Results: 6607 patients were enrolled. 1724 had received SOF±RBV±PEG, 2204 had received LDV/SOF±RBV, 1422 had received SOF/VEL±RBV, 597 had received SOF/VEL/VOX, and 660 had received other regimens. The majority of patients were male (62%), White (84%), non-cirrhotic (82%). Overall 99.3% of patients maintained SVR. Thirty patients experienced virologic failure of whom 8 (0.1%) had experienced relapse after completing their treatment study and 22 (0.3%) had reinfection. 232 patients experienced liver disease events, including HCC, which were most commonly observed in patients with advanced fibrosis. No patients with F0-F1 disease developed HCC; the exposure adjusted incident rates for HCC in patients with F2, F3, or F4 disease were 0.06%, 0.25%, and 0.58% respectively.

Conclusions: In this heterogeneous population SVR12 is confirmed as the optimal time to determine SVR as late relapses beyond this point are rare. In patients who achieve SVR, liver related complications are infrequent. These findings emphasize the value of SVR, regardless of fibrosis score at the time of treatment.

Keywords: SVR12, DAA, Durability, HCV
Substitution Mutations at Cys 316 of NS5B Affect Treatment with Sofosbuvir by Enhancing Replication of Genotype 1b Hepatitis C Virus

Yechan Jeong1,2, Bora Jin1,2, Hye Jung Park1,2, Hye Won Lee1,3, Kwang-Hyub Han1,2, Sang Hoon Ahn1,2, and Seungtaek Kim1,2,3
1Yonsei Liver Center, Severance Hospital, Seoul, Korea; 2Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 3Institut Pasteur Korea, Seongnam, Korea

Aims: Treatment of patients with chronic hepatitis C has been revolutionized by development of multiple direct-acting antivirals (DAAs). Most of DAAs target viral proteins such as NS3 protease, NS5A, and NS5B RNA-dependent RNA polymerase (RdRp) of hepatitis C virus (HCV). Sofosbuvir is an antiviral drug targeting NS5B RdRp as a nucleotide analog and it is very potent and safe regarding antiviral resistance. However, potential resistance-associated substitutions (RASs) in NS5B are being reported after treatment failures.

Methods: We collected blood samples from the patients who failed in ledipasvir plus sofosbuvir (Harvoni) treatment. After isolation of viral RNAs and RT-PCR, the sequences of both NS5A and NS5B were determined by population sequencing method. Potential RASs of NS5B were introduced in the genotype 1a and 1b HCV replicon by site-directed mutagenesis and the effect of those mutations on viral RNA replication was assessed in the presence of varying concentrations of sofosbuvir.

Results: Sequencing analysis identified potential RASs of both NS5A and NS5B including L159F, C316N and A207T of NS5B. Subsequent in vitro analyses using the mutant HCV replicons showed that substitutions of potential RASs in NS5B did not change the half maximal effective concentration (EC50) of sofosbuvir of mutant replicons compared to that of wild-type replicon but that some mutations including C316N enhanced viral RNA replication in a genotype-dependent manner.

Conclusions: These results suggest that the genotype-dependent enhancement of viral RNA replication by the mutations in NS5B may increase the chance of failure of the sofosbuvir-containing DAA therapies.

Keywords: hepatitis C virus, NS5B, Sofosbuvir, Resistance-associated substitution

Efficacy and Safety of 8-Weeks of Glecaprevir/Pibrentasvir in Treatment-Naive Adults with HCV Genotype 1-6 and Aspartate Aminotransferase to Platelet Ratio Index (APRI) ≤ 1

Robert J. Fontana1, Sabela Lens2, Stuart McPherson2, Magdy Elkhashbash3, Krum Katzarov4, Ana Gabriela Pires dos Santos5, Zhenyi Xue6, Roger Trinh6, Lino Rodrigues Junior6, Ariel Polcari6, Stefan Zeuzem1, Hyung Joon Yim1, Yong Kyun Won7
1Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, Michigan, USA; 2Liver Unit, Hospital Clinic, IDIBAPS and CIBERehd, Barcelona, Spain; 3Liver Unit, The Newcastle upon Tyne Hospitals NHS Foundation and Trust and Newcastle University, UK; 4Toronto Liver Centre, Toronto, Canada; 5Department of Gastroenterology, Hepato-Pancreato-Biliary (HPB) Surgery and Transplantology, Military Medical Academy, Sofia, Bulgaria; 6AbbVie, Inc., North Chicago, Illinois, USA; 7J.W. Goethe University, Frankfurt, Germany

Aims: Aspartate aminotransferase to platelet ratio index (APRI) is a low-cost, widely available, non-invasive method to assess liver disease severity. Current EASL and WHO treatment guidelines recommend APRI as an option in low- to middle-income countries and non-specialty clinics to simplify HCV management. APRI ≤ 1 has a high negative predictive value (98%) for cirrhosis compared to liver biopsy, establishing an attractive threshold to exclude liver cirrhosis. Here, we report preliminary data from the first prospective Phase 3 trial to use APRI to select patients for an 8-week treatment with the fixed-dose, pangenotypic, direct-acting antiviral combination of glecaprevir (NS3/4A protease inhibitor; developed by AbbVie and Enanta) and pibrentasvir (NS5A inhibitor) coformulated as G/P.

Methods: This prospective, single arm Phase 3 trial with 43 sites worldwide (NCT03212521) aims to evaluate the efficacy and safety of G/P (300/120mg) QD administered for 8 weeks in treatment-naive adults with chronic HCV genotypes (GT) 1-6 infection and APRI ≤ 1. Efficacy is assessed using intent-to-treat (ITT) and modified ITT analyses as the percentage of patients who received ≥1 dose of G/P and achieved sustained virologic response at post-treatment week 12 (SVR12). Safety is assessed in all patients treated with ≥1 dose of G/P.

Results: Of the 230 patients enrolled, the median APRI score was 0.41 (range from 0.13 to 1.00). Patients (n, %) were primarily white (207, 90%), <65 years of age (207, 90%), and had an APRI score ≤ 0.5 (140, 61%). Notably, 35 (15%) patients had GT3 infection, while most others had GT1 infection (151, 66%). For all patients who completed treatment (on G/P for ≥52 days), those with available post-treatment week 4 and 12 HCV RNA data (Figure) all achieved SVR4 (221/221) and SVR12 (61/61). Two patients who discontinued G/P early did not achieve SVR. Headache (13%) was the only adverse event (AE) reported in ≥10% of patients. AEs leading to G/P discon-
Efficacy and Safety of Grazoprevir/Elbasvir for Korean Patients with Chronic Hepatitis C Virus Infection: A Retrospective, Nationwide, Real-World Study

Eun Sun Jang\(^1\), Kyung-Ah Kim\(^1\), Young Seok Kim\(^1\), In Hee Kim\(^1\), Byung Seok Lee\(^1\), Youn Jae Lee\(^1\), Woo Jin Chung\(^1\), Sook-Hyang Jeong\(^*\)

\(^*\)Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Gyeonggi; \(^1\)Department of Internal Medicine, Inje University Ilsan Paik Hospital, Goyang, Gyeonggi; \(^2\)Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Gyeonggi; \(^3\)Department of Internal Medicine, Chungnam National University College of Medicine, Daejeon, Republic of Korea; \(^4\)Department of Internal Medicine, Inje University Ilsan Paik Hospital, Bucheon, Gyeonggi; \(^5\)Department of Internal Medicine, Chonbuk National University Hospital, Chonbuk National University College of Medicine, Jeonju, Republic of Korea; \(^6\)Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea

**Aims:** Grazoprevir/elbasvir had been accepted as a reimbursable treatment regimen by Korean National Health Insurance for genotype 1 or 4 chronic hepatitis C patients since May 2017 in Korea. This study aimed to clarify a real-world efficacy and safety of grazoprevir/elbasvir therapy in South Korea.

**Methods:** A total of 424 patients with chronic HCV infection who started grazoprevir/elbasvir were consecutively enrolled from 7 tertiary hospitals during May 2017 – Jun 2018. Retrospective analysis on the sustained virological response (SVR), and adverse events was performed.

**Results:** Mean age of enrolled patients was 59.0 ± 12.6 year old and 47.5% were males. Hypertension was most common (72, 29.8%) comorbid disease, following by diabetes (55, 22.7%) and chronic kidney disease (16, 6.6%). Since 29 subjects were lost to follow up before SVR evaluation, SVR rates were 85.5% (182/213) in treatment-naïve and 93.1% (27/29) in treatment-experienced patients as intention-to-treat analyses, and those were 97.8% (179/183) in treatment-naïve and 100% (28/28) treatment-experienced patients as per-protocol analyses. Any grade of adverse events had been reported in 51 (21.1%) of treated patients. Itching (29, 12%), liver function test abnormality (11, 4.6%) and fatigue (2.9%) were common adverse events. Of 4 patients who discontinued the antiviral therapy, 3 had experienced mild adverse events (1 fatigue, 1 headache, and 1 liver enzyme abnormality) but all treatment withdrawals were based on patient’s willingness, not by physician’s decision for the adverse events.

**Conclusions:** Grazoprevir/elbasvir showed high real-life efficacy and safety in Korean patients with chronic HCV infection regardless of previous antiviral treatment experience.

**Keywords:** Hepatitis C virus, Grazoprevir, Elbasvir, Real-world study, Korea
Clinical Indication and Safety of Liver Biopsy in the Era of Noninvasive Assessment of Liver Fibrosis

Jun Il Kim1, Chun Beom Lee1, Jeong-Ju Yoo1, Sang Gyune Kim1, Young Seok Kim1, Soung Won Jeong2, Jae Young Jang2, Sae Hwan Lee2, Hong Soo Kim2, Baek Gyu Jun2, Young Don Kim2, Gab Jin Cheon1

1Department of Internal Medicine, Soonchunhyang University School of Medicine, Bucheon, Korea; 2Department of Internal Medicine, Soonchunhyang University School of Medicine, Seoul, Korea; 3Department of Internal Medicine, Soonchunhyang University School of Medicine, Cheonan, Korea; 4Department of Internal Medicine, Gangneung Asan Hospital, Gangneung, Korea

Aims: Liver biopsy (LB) remains the gold standard for evaluation of liver disease. However, during the past two decades, many noninvasive tests have been developed and utilized in clinical practice to replace LB. The aim of this study is to evaluate clinical use and its safety of LB in the era of noninvasive assessment of liver fibrosis.

Methods: This retrospective study included consecutive 1945 LB cases between 2001 to 2018 in a tertiary hospital. All the LB was undertaken in ultrasound-guided with 18 gauge cutting needles. Indications of LB and adverse events (AEs) of each patient were collected.

Results: LB was performed approximately 108 times a year on average during this period. However, the number of LBs tended to decrease after 2008, when transient elastography was introduced in the institution. Chronic hepatitis B was the most common indications for LB (25.4%), followed by liver mass (19.9%), abnormal liver tests of unclear Etiology (18.5%), and nonalcoholic fatty liver disease (NAFLD) (13.1%), respectively. When classified by period, NAFLD has increased from 10.9 to 17.5% in the last 5 years compared to the last 10 years, and viral hepatitis decreased from 30.7% to 19.3%. The overall rate of major AEs was 0.05% (1 case), presented with biopsy site bleeding. Liver cirrhosis was observed in 563 cases (28.9%), and none of them experienced major AEs.

Conclusions: LB is widely used in clinical practice as an irreplaceable diagnostic tool even in the era of noninvasiveness. Also, ultrasound-guided method can be performed safely in patients with liver cirrhosis.

Keywords: Liver biopsy, Indication, Complication, Safety

Plasma Levels of Soluble Programmed Death-1 and Programmed Death-Ligand 1 in the Patients with Autoimmune Hepatitis and Primary Biliary Cholangitis

Boo-Ok Jang*, Gwang Hyeon Choi*, Yun Suk Choi, Da Woon Jeong, Jae Kyun Choi, Si Ho Kim, Kyunghan Lee, Eun Sun Jang, Jin-Wook Kim, Sook-Hyang Jeong

Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Korea

* These authors equally contributed to this study

Aims: While tissue expression of programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) was reported in autoimmune hepatitis (AIH), the profiles of plasma levels of soluble PD-1 (sPD-1) and soluble PD-L1 (sPD-L1) in AIH and primary biliary cholangitis (PBC) were not reported. This study aimed to investigate the implication of sPD-1 and sPD-L1 in AIH and PBC.

Methods: Using plasma samples obtained from the prospectively enrolled patients with AIH (n=43), PBC (n=80), and AIH-PBC variant (n=8), and age-and sex-matched healthy controls (n=57), the plasma levels of sPD-1 and sPD-L1 were measured by commercial ELISA.

Results: The mean age and female proportion (%) in AIH, PBC, AIH-PBC variant, and healthy controls was 61 years (81.4%), 56 years (86.3%), 54 years (100%) and 59 years (87.7%), respectively. The plasma sPD-1 was detected in 34.9%, 36.3%, 62.5%, and 31.6% of the patients with AIH, PBC, AIH-PBC variant, and healthy controls, respectively (P=0.40). The median plasma level of sPD-1 in either AIH PBC patients were not significantly different from healthy controls. The plasma sPD-L1 was detected in almost all the subjects. Compared to the median plasma sPD-L1 level in healthy controls (438 pg/mL), it was significantly higher in AIH patients (574 pg/mL) (P=0.001), but lower in PBC patients (191 pg/mL) (P=0.001). Moreover, plasma sPD-L1 level was significantly correlated with immunoglobulin G level (IgG) in AIH patients and with total bilirubin level in PBC patients.

Conclusions: Compared to healthy controls, the plasma level of sPD-L1 was higher in AIH with a significant correlation with IgG, while it was lower in PBC with a significant correlation with total bilirubin level.

Keywords: Soluble programmed death-1, Soluble programmed death ligand-1, Primary biliary cholangitis, Autoimmune hepatitis, Biomarker
Clinical Characteristics of Liver Cirrhosis and Hepatocellular Carcinoma Occurring after Fontan Operation

Jun Sik Yoon, Dong Ho Lee, Eun Ju Cho, Mi Kyong Song, Young Hun Choi, Gi Beom Kim, Yun Bin Lee, Jeong-Hoon Lee, Su Jong Yu, Yoon Jun Kim, Jung-Hwan Yoon, Eun Jung Bae

1Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea; 3Department of Radiology, Seoul National University College of Medicine, Seoul, Korea; 4Department of Pediatrics, Seoul National University Children’s Hospital, Seoul National University College of Medicine, Seoul, Korea

Aims: The most serious late post-Fontan complications are liver cirrhosis and hepatocellular carcinoma (HCC). The aims of this study were to investigate the cumulative incidence of cirrhosis and HCC and to identify specific features distinguishing HCC from benign arterial phase hyper-enhancing (APHE) nodules that developed after the Fontan operation.

Methods: We retrospectively enrolled 265 post-Fontan patients who had been followed for more than 5 years and had undergone ultrasound or computed tomography (CT) of the liver between 2000 and 2018. Cirrhosis was diagnosed by imaging features.

Results: During the 5103.2 person-years follow-up, the estimated cumulative incidence rates of cirrhosis at 5-, 10-, 20-, and 30-years after the Fontan operation were 2.6%, 10.8%, 35.3%, and 98.3%, respectively (Figure 1). On multiphasic CT, 17 patients had APHE nodules ≥ 1 cm showing washout in the portal venous phase (PVP)/delayed phase which met current non-invasive HCC diagnosis criteria. Among them, only six patients (35.3%, 6/17) were diagnosed with HCC. Thus, the annual incidence of HCC was 0.1% during 5097.7 person-years of follow-up after the Fontan operation. After cirrhosis developed, the annual incidence of HCC was greater: 1.1% (6 HCCs/564.7 person-years). The appearance of washout in the PVP (P=0.01) and the serum AFP level (P<0.001) were significantly associated with HCC among the APHE nodules.

Conclusions: In post-Fontan patients, cirrhosis is a frequent late complication, especially after 10 years. Diagnosis of HCC should not be based solely on the current imaging criteria, and presence of washout on PVP and high serum AFP might be helpful to differentiate HCC nodules from benign APHE nodules.

Keywords: Fontan-associated liver disease, Arterial phase hyper-enhancing nodules, Congestive hepatopathy, Congenital heart disease

The Validity of Two-Dimensional Shear Wave Ultrasound for Assessing Fibrosis Stage in Patients with Chronic Liver Disease: Comparison with Transient Elastography

Hae Won Yoo, Sang Gyune Kim, Jeong-Ju Yoo, Young Seok Kim, Soung Won Jeong, Jae Young Kang, Jae Hwan Lee, Hong Soo Kim, Young Don Kim, Gab Jin Cheon, Boo Sung Kim

1Digestive Disease Center and Research Institute, Department of Internal Medicine, Soonchunhyang University School of Medicine, Bucheon, 2Department of Internal Medicine, Soonchunhyang University School of Medicine, Seoul, 3Department of Internal Medicine, Soonchunhyang University School of Medicine, Cheonan, 4Gangneung Asan Hospital, Department of Internal Medicine

Aims: Compared to transient elastography (fibroscan), two-dimensional shear wave elastography (2D-SWE) has the advantage of performing simultaneous ultrasonographic examination and measuring liver stiffness at the same time. However, the diagnostic performance and clinical usefulness of 2D-SWE are not fully validated. In this study, we evaluated whether newly developed 2D-SWE (RS85, Samsung-shearwave imaging) is valid and reliable for predicting liver fibrosis stage when compared with fibroscan.

Methods: We prospectively enrolled 117 patients with chronic liver disease. 2D-SWE, fibroscan, laboratory test and liver biopsy were performed on a same day from two tertiary care hospital. One patient who had unreliable measurement was excluded. The measurement of 2D-SWE was considered acceptable when homogenous color pattern in a region of interest of at least 10 mm was shown at 10 different sites. Diagnostic performance was calculated using area under the receiver operating characteristics curve (AUROC).

<table>
<thead>
<tr>
<th>Fibrosis stage</th>
<th>THR†</th>
<th>SEN</th>
<th>SPE</th>
<th>AUC (95% CI)</th>
<th>Comparison of AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>F2 vs. others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D-SWE (kPa)</td>
<td>≥5.8</td>
<td>88.9%</td>
<td>74.4%</td>
<td>0.851 (0.773-0.911)</td>
<td>P=0.79</td>
</tr>
<tr>
<td>Fibroscan (kPa)</td>
<td>≥5.7</td>
<td>93.1%</td>
<td>69.8%</td>
<td>0.859 (0.781-0.916)</td>
<td>P=0.79</td>
</tr>
<tr>
<td>F3 vs. others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D-SWE (kPa)</td>
<td>≥7.5</td>
<td>95.4</td>
<td>81.7</td>
<td>0.917 (0.851-0.960)</td>
<td>P=0.14</td>
</tr>
<tr>
<td>Fibroscan (kPa)</td>
<td>≥7.2</td>
<td>95.4</td>
<td>67.6</td>
<td>0.881 (0.807-0.934)</td>
<td>P=0.79</td>
</tr>
<tr>
<td>F4 vs. others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D-SWE (kPa)</td>
<td>≥9.4</td>
<td>95.0</td>
<td>82.1</td>
<td>0.889 (0.817-0.940)</td>
<td>P=0.08</td>
</tr>
<tr>
<td>Fibroscan (kPa)</td>
<td>≥10.4</td>
<td>95.0</td>
<td>81.1</td>
<td>0.938 (0.877-0.974)</td>
<td>P=0.08</td>
</tr>
</tbody>
</table>

Results: Sixty three (54%) patients were male. Most common etiology of chronic liver disease was chronic hepatitis B (22%)
Proposal of a Cutoff for the Computed Tomography-Assessed Lumbar Skeletal Muscle Index for Diagnosing Sarcopenia in Asian Populations

Seo Yeon Gwak, Min Je Sung, Tae Seop Lim, Mi Young Jeon, Hye Won Lee, Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Seung Up Kim

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Republic of Korea; Yonsei Liver Center, Severance Hospital, Seoul, Republic of Korea

Aims: Criteria for defining sarcopenia have not been fully established. We proposed a new cutoff for the computed tomography-based skeletal muscle index (LSMI) for diagnosing sarcopenia.

Methods: Subjects who underwent comprehensive medical check-ups and those who underwent screening for live liver donation were recruited. Skeletal muscle mass was assessed using computed tomography at the L3 level and the skeletal muscle area normalized to height squared (cm²/m²) for calculating the adjusted LSMI. The cutoffs for diagnosing sarcopenia were calculated as the means minus two standard deviations.

Results: A total of 267 subjects (38 who underwent health check-ups and 229 liver donors) were selected. The mean ages and LSMIs of the study population (145 males and 122 females) were 28.9 years and 48.0 cm²/m², respectively. The LSMI was significantly higher in males than females (mean, 54.4 vs. 40.4 cm²/m², P<0.001) and significantly decreased with age (50.95 cm²/m² in those aged <26 years; 47.40 cm²/m² in those aged 26–30 years; 46.62 cm²/m² in those aged 31–35 years; 44.99 cm²/m² in those aged 36–40 years, P<0.001). The lumbar skeletal muscle area was positively correlated with body mass index, aspartate and alanine transaminase, serum albumin, gamma-glutamyl transpeptidase, serum creatinine, and triglycerides, whereas it was negatively correlated with age, female gender, platelet count, and high-density lipoprotein cholesterol level (all P<0.05). The cutoff for LSMIs for diagnosing sarcopenia were 40.0 and 30.0 cm²/m² for males and females, respectively.

Conclusions: Two-dimensional SWE has similar capabilities to fibroscan in diagnosing significant fibrosis and liver cirrhosis.

Keywords: 2D-SWE, Fibrosis, Shear wave elastography, RS85

OP-036

OP-037

Treatment Response of Noninvasive Fibrosis Markers Predicts Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients

Hee Chul Nam1,2, Si Hyun Bae1,2, Jong Young Park1,2, Seung Kew Yoon1,2, Jeong Won Jang1,2

1Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea; 2The Catholic Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Aims: Potent antiviral therapy can regress hepatic fibrosis in chronic hepatitis B patients. Non-invasive fibrosis markers such as FIB-4, APRI, and fibroscan can assess the degree of fibrosis. This study evaluated the association between treatment responses of these markers and development of HCC.

Methods: This is a single center retrospective study enrolling 2,037 patients given antiviral agents (Entecavir or Tenofovir) from April 2005 to December 2017. FIB-4 and APRI were serially assessed from the start of the treatment and their values at 6 months and at 1 year intervals for up to 8 years. Fibroscan were analyzed as well.

Results: Patients’ median age was 48 years, 61% were male, and 33% had cirrhosis. During the follow-up period, HCC de-
developed in 131 patients and median time to its occurrence was 56.9 months. Median values of FIB-4, APRI at baseline were 1.9, and 1.0, respectively. Patients were divided into four groups by the fibrosis regression at 12 months after treatment initiation (Table 1). The risk of HCC development in group 1 was significantly lower than that in group 2 or 4, but not in group 3 ($p<0.001$, Figure 1). In hepatitis patients, univariate analysis revealed that age ($\geq 60$ years), BMI ($\geq 23$), and FIB-4 response (Group 2,4) were significantly associated with HCC development. Multivariate analysis identified a lack of improvement of FIB4 (OR 4.93; 95% CI 1.74-14.00; $p=0.003$), and BMI (OR 2.69; 95% CI 1.12-6.43; $p=0.026$) to be independent prognostic factor for HCC development. In cirrhosis patients, age ($\geq 60$ years), sex (male), Child-Pugh score ($>5$), alpha-fetoprotein level ($\geq 10$ ng/mL), and fibrosis response (Group 2,4) were significantly associated with HCC development. Multivariate analysis demonstrated age (OR 2.79; 95% CI 1.73-4.49; $p<0.001$), sex (OR 2.20; 95% CI 1.39-3.49; $p=0.001$), and lack of improvement of APRI (OR 2.26; 95% CI 1.10-4.63; $p=0.027$) to be significantly associated with the development of HCC.

### Results

After 10-year follow-up period, 59 patients experienced HBsAg seroclearance (16%). Higher proportions of 181 patients with the indirect ratio of light absorbance of anti-HBc $\leq 10$ RLU, relative light unit) had HBsAg seroclearance ($n=39$, 21.5%) than 185 patients with higher levels of anti-HBc $> 10$ RLU ($n=20$, 10.8%) ($p=0.005$). For patients with levels of anti-HBc $\leq 10$ RLU, the relative risk of HBsAg seroclearance was 1.70 (95% CI, 0.985–2.925), compared to patients with higher levels of anti-HBc ($p=0.057$).

### Conclusions

The clinical utility of serial assessment of non-invasive fibrosis markers during anti-HBV therapy. On-therapy liver fibrosis regression is an independent favorable indicator of HCC risk in patients with chronic HBV infection. Our data suggests the clinical utility of serial assessment of non-invasive fibrosis markers during anti-HBV therapy. On-therapy liver fibrosis regression is an independent favorable indicator of HCC risk in patients with chronic HBV infection.

### Keywords

Chronic hepatitis B, FIB-4, APRI, Hepatocellular carcinoma

### OP-038

**Anti-HBc IgG Level in Prediction of HBsAg Seroclearance in Chronic Hepatitis B Patients with Nucleos(t)ide Analogue induced HBeAg Seroclearance**

Hyun Woong Lee¹, Saein Kim², Seung Up Kim³, Jung Il Lee⁴, Sora Kim⁵, Hye Young Chang⁶, Dokyun Kim⁷, Seok Hoon Jeong⁸, Beom Kyung Kim⁹, Jun Yong Park¹⁰, Do Young Kim¹¹, Sang Hoon Ahn¹², Kwang-Hyub Han¹³, and Seok Hoon Jeong¹³

¹Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, ²Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, ³Department of Laboratory Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine Seou, Korea

**Aims:** Although hepatitis B core antibody is outdated marker using enzyme immunoassay, the indirect ratio of light absorbance of anti-HBc IgG can be easily measured. We investigated whether the indirect ratio of anti-HBc IgG can predict HBsAg seroclearance among patients with nucleos(t)ide analogue induced HBeAg Seroclearance.

**Methods:** We performed a retrospective study from two tertiary hospital. A total of 355 chronic hepatitis B patients were included for analysis from Jan. 2008 to Dec. 2016. They were HBsAg seropositive, and experienced nucleos(t)ide analogue (entecavir, or tenofovir) induced HBeAg seroclearance. The indirect ratio of light absorbance of anti-HBc IgG levels was measured with chemiluminescent microparticle immunoassay using Architect Anti-HBc assay (Abbott Laboratories, IL, USA) before HBeAg seroclearance. We calculated cumulative incidences of HBsAg seroclearance. Association between level of anti-HBc IgG and HBsAg seroclearance were estimated by Cox proportional hazard regression.

**Table 1:** Patient groups by the response of noninvasive fibrosis markers during antiviral treatment; baseline and at 12 months after treatment initiation.

<table>
<thead>
<tr>
<th>FIB-4</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>&lt;3.25</td>
<td>&lt;1.45</td>
</tr>
<tr>
<td>Group 2</td>
<td>&lt;3.25</td>
<td>≥1.45</td>
</tr>
<tr>
<td>Group 3</td>
<td>≥3.25</td>
<td>&lt;1.45</td>
</tr>
<tr>
<td>Group 4</td>
<td>≥3.25</td>
<td>≥1.45</td>
</tr>
<tr>
<td>APRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>&lt;1.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Group 2</td>
<td>&lt;1.5</td>
<td>≥0.5</td>
</tr>
<tr>
<td>Group 3</td>
<td>≥1.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Group 4</td>
<td>≥1.5</td>
<td>≥0.5</td>
</tr>
</tbody>
</table>

**Results:** Our data suggests the clinical utility of serial assessment of non-invasive fibrosis markers during anti-HBV therapy. On-therapy liver fibrosis regression is an independent favorable indicator of HCC risk in patients with chronic HBV infection.

**Keywords:** Chronic hepatitis B, FIB-4, APRI, Hepatocellular carcinoma
Maximal Diameter of Hepatic Abscess Independently Predicts Prolonged Hospitalization and Poor Prognosis in Patients with Pyogenic Liver Abscesses

OP-039

Chang Hun Lee, Gyun Seop Lim, Myoung Soo Ha, Seung Yeon Ryu, Hee Chan Yang, Sung Kyun Yim, Seung Young Seo, Sung Hun Kim, Sang Wook Kim, Seung Ok Lee, Soo Teik Lee, and In Hee Kim

Department of Internal Medicine, Chonbuk National University Medical School and Research Institute of Clinical Medicine of Chonbuk National University Hospital-Chonbuk National University Medical School, Korea

Aims: The aim of this study was to investigate the factors associated with prolonged hospital stay and in-hospital mortality in pyogenic liver abscess patients.

Methods: We retrospectively reviewed data from pyogenic liver abscess patients who were admitted from 2005 to 2018 at Chonbuk University Hospital. Patients were categorized into 3 groups by maximal diameter of the abscess (< 5 cm, 5-10 cm, ≥ 10 cm) and compared clinical characteristics. Prolonged hospital stay was defined as hospitalization more than 14 days.

Results: A total of 482 patients (301 men and 181 women) diagnosed with pyogenic liver abscess were enrolled for the study. The patients had a mean age of 64.4 ± 14.6 years and approximately one fourth of patients had underlying diabetes mellitus, hypertension, and biliary disease, respectively. Mean maximal diameter of hepatic abscess was 5.7 ± 2.6 cm and 76.4% was single lesion. Culture positive rate of microorganism isolated from blood or pus was 40.5% and Klebsiella pneumoniae species accounted for 71.9% of total isolated microorganisms. Although there was no difference in the underlying disease or vital sign at admission, laboratory parameters indicating inflammation deteriorated with increasing size. Admission duration and in-hospital mortality were higher in the large hepatic abscess group. Next, we analyzed factors related to long-term hospitalization. Multivariate analysis revealed high baseline hsCRP and procalcitonin levels and large maximal abscess diameter were independent factors associated with prolonged hospital stay. Regarding 30-day mortality, there were 11 expired cases (3.1%) during the period. In multivariate analysis, decreased mentality at admission, baseline hemoglobin level less than 9 mg/dL, and maximal diameter of abscess were independent factors associated with 30-day mortality.

Conclusions: Large maximal diameter of liver abscess at admission indicated prolonged hospitalization and poor prognosis. More aggressive treatment strategies with careful monitoring may be required in patients with large liver abscesses.

Keywords: Liver abscess, Pyogenic, Hospitalization, Hospital Mortality

Table 1. Factors associated with prolonged hospital stay (≥ 15 days)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 65 years, yrs &lt; 65</td>
<td>0.1522</td>
<td>0.36</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.9927</td>
<td>0.93</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.6076</td>
<td>0.87</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.3741</td>
<td>0.54</td>
</tr>
<tr>
<td>DM</td>
<td>0.0917</td>
<td>1.31</td>
</tr>
<tr>
<td>Myopathy</td>
<td>0.3843</td>
<td>1.58</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0.1174</td>
<td>0.17</td>
</tr>
<tr>
<td>Previous liver abscess history</td>
<td>0.1415</td>
<td>0.37</td>
</tr>
<tr>
<td>Significant alcohol consumption</td>
<td>0.0771</td>
<td>0.43</td>
</tr>
<tr>
<td>Decreased mentality at admission</td>
<td>0.4303</td>
<td>0.55</td>
</tr>
<tr>
<td>Shock at admission</td>
<td>0.1010</td>
<td>0.91</td>
</tr>
<tr>
<td>WBC ≥ 12,000/mm³, at baseline</td>
<td>0.0003</td>
<td>2.01</td>
</tr>
<tr>
<td>Hb ≤ 9 mg/dL, at baseline</td>
<td>0.3089</td>
<td>0.70</td>
</tr>
<tr>
<td>Ha ≤ 135 mm³/L, at baseline</td>
<td>0.5526</td>
<td>1.11</td>
</tr>
<tr>
<td>ALT ≥ 200 U/L, at baseline</td>
<td>0.3277</td>
<td>1.64</td>
</tr>
<tr>
<td>IsCtRP ≥ 200 mg/L, at baseline</td>
<td>0.0054</td>
<td>1.23</td>
</tr>
<tr>
<td>PCT ≥ 5 ng/mL, at baseline</td>
<td>0.0004</td>
<td>1.48</td>
</tr>
<tr>
<td>Number of abscess, single vs multiple</td>
<td>0.6800</td>
<td>1.80</td>
</tr>
<tr>
<td>Maximal abscess diameter (cm)</td>
<td>0.0006</td>
<td>0.53</td>
</tr>
<tr>
<td>PCT elevation during admission</td>
<td>0.0008</td>
<td>2.46</td>
</tr>
<tr>
<td>PCT elevation within 2 days of admission</td>
<td>0.0011</td>
<td>0.62</td>
</tr>
<tr>
<td>Culture positive (blood or pus)</td>
<td>0.0007</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Table 2. Factors associated with 30-day mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 65 years, yrs &lt; 65</td>
<td>0.0495</td>
<td>1.53</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.6190</td>
<td>0.90</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.3639</td>
<td>1.87</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.1075</td>
<td>1.77</td>
</tr>
<tr>
<td>DM</td>
<td>0.2140</td>
<td>0.01</td>
</tr>
<tr>
<td>Myopathy</td>
<td>0.3345</td>
<td>0.14</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0.9230</td>
<td>1.02</td>
</tr>
<tr>
<td>Pneumonia abscess history</td>
<td>0.9092</td>
<td>1.00</td>
</tr>
<tr>
<td>Significant alcohol consumption</td>
<td>0.9093</td>
<td>1.00</td>
</tr>
<tr>
<td>Decreased mentality at admission</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Shock at admission</td>
<td>0.9093</td>
<td>0.00</td>
</tr>
<tr>
<td>WBC ≥ 12,000/mm³, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Hb ≤ 9 mg/dL, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Ha ≤ 135 mm³/L, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>ALT ≥ 200 U/L, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>IsCtRP ≥ 200 mg/L, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>PCT ≥ 5 ng/mL, at baseline</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Number of abscess, single vs multiple</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Maximal abscess diameter (cm)</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>PCT elevation during admission</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>PCT elevation within 2 days of admission</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
<tr>
<td>Culture positive (blood or pus)</td>
<td>0.9237</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Keywords: Liver abscess, Pyogenic, Hospitalization, Hospital Mortality

Comparative Analysis of Intrahepatic Infiltration of Activated T Cells and Macrophages between Autoimmune Hepatitis and Drug-Induced Liver Injury

Pil Soo Sung1,2, Hyun Yang1,2, Jae Jun Lee1,2, Kwon Yong Talk1,3, Hee Chul Nam1,3, Jeong Won Jang1,3, Si Hyun Bae1,2, Jong Young Choi1,3, Seung Kew Yoon1,3, Eun Sun Jung4, Sang Wook Choi1,3

1The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Eunpyeong St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; 3Division of...

Keywords: Liver abscess, Pyogenic, Hospitalization, Hospital Mortality
Aims: Pathogenesis of autoimmune hepatitis (AIH) involves genetic susceptibilities, molecular mimicry events, and dysfunction of immunoregulatory mechanisms. The major immune characteristic of AIH is the presence of a marked CD4 and CD8 T-cell infiltrate involved in hepatocellular damage. In this study, we aimed to identify the amount and pattern of immune cell infiltration in AIH, and to compare them with those of drug-induced liver injury (DILI).

Methods: From March 2016 to December 2018, 15 patients with AIH were prospectively enrolled in this study. For comparison, 22 patients with DILI in the same period were analyzed in the same way. Liver biopsy was performed, and immunohistochemical stain for CD3, CD68, CD20, and CD38 was done. Experienced pathologist confirmed the pathologic and immunohistochemical findings. For some patients, immune cells were harvested from fresh liver biopsy samples, and multicolor flow cytometry was used for the immunophenotyping of the infiltrated immune cells.

Results: First, we identified that activated CD8 and CD4 T cells were more infiltrated in the livers from patients with AIH than those from healthy controls by multicolor flow cytometry. Next, the frequency of infiltrated T cells, macrophages, and B cells were quantified by immunohistochemistry. The amounts of T cells, macrophages, and B cells infiltration had no associations with serum AST, ALT ALP or GGT in patients with AIH. Furthermore, serum levels of IgG and IgA were not correlated with the amounts of immune cells infiltrations, either. Next, we compared the infiltration of the immune cell subsets between patients with AIH and those with DILI. Baseline serum ALT was significantly higher in patients with AIH and those with DILI, but the levels of activated T cells (CD3+CD8+) infiltration were not significantly different between AIH and DILI. However, a larger number of macrophages were infiltrated in the livers in DILI than those in AIH, suggesting that drug-induced injury of hepatocytes triggers innate immunity more vigorously.

Conclusions: Both patients with AIH and DILI have activated T cells and macrophages infiltrated in the injured liver. Higher ALT and more macrophages infiltration in DILI suggest that drug-induced injury of hepatocytes might trigger innate immunity more vigorously than autoimmune-mediated mechanisms.

Keywords: Autoimmune hepatitis, Drug-induced liver injury, T cell, Macrophage
OP-042
Prevalence of Antimitochondrial Antibody and Primary Biliary Cholangitis in Korea: A Single Center Study
Yang Jae Yoo
Hepatology Center Bundang Jesaeng General Hospital

Aims: Primary biliary cholangitis (PBC), formerly known as primary biliary cirrhosis is classified as rare disease in South Korea. Anti mitochondrial antibody (AMA) is a signature antibody for PBC diagnosis. Ninety percent of PBC patients are AMA positive. The prevalence of AMA positivity in general population in South Korea is not well studied. We aimed to investigate the prevalence of AMA positivity in our hospital.

Methods: We retrospectively reviewed patients who were tested for AMA, from 2014 to 2018. All patients who had hepatitis B or C were excluded form analysis. Clinical data including age, sex, laboratory findings and image studies were also reviewed.

Results: Total of 1,120 patients were tested for AMA during this period. Among 1,120 patients tested, 40 patients were AMA positive. Among 190 with Alkaline phosphatase level higher than upper limit of normal (ULN), 11 were AMA positive. Among 664 with γ-Glutamyl Transeptidase level higher than ULN, 21 were AMA positive. Among 40 patients with AMA positive, 36 were female, mean age were 62 years old. Anti nuclear antibody was positive in 28 patients. Liver biopsy were performed in 19 patients. 14 were diagnosed as AIH-PBC overlap syndrome. 16 Patients had evidence of liver cirrhosis, and two have developed Hepatocellular carcinoma (HCC) during follow up.

Conclusions: Positive rate of AMA in our patients were higher than anticipated considering estimated prevalence of PBC in Korean population. Prognosis of PBC is good when treated early with UDCA. Considerably large number of PBC patients are presumed underdiagnosed. AMA should be actively tested when clinically suspected. Larger studies are needed to estimate true prevalence of AMA and PBC in Korea.

Keywords: Primary biliary cholangitis, Anti mitochondrial antibody, Prevalence, Korea

OP-043
Liver Transplantation for Patients with Pre-Existing Portal Vein Thrombosis: A Single-Center Experience
Tae-Seok Kim, Keun Soo Ahn, Yong Hoon Kim, Hyoung Tae Kim, Koo Jeong Kang
Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea

Aims: Portal vein thrombosis (PVT) is not uncommon in liver cirrhosis patients. In past, PVT had been considered as contraindication to liver transplantation (LT) because of technical challenges for adequate restoration of portal inflow followed by high morbidity and mortality. However, alternative options for PVT during LT have been introduced, and nowadays, PVT is no longer considered as absolute contraindication for LT. Herein, we introduce our experiences and outcomes of LT for patients with PVT.

Methods: Between Mar 2014 and June 2018, 65 patients underwent LT at our institution, and 13 (20%) of whom had PVT preoperatively. The characteristics and management of these patients were reviewed retrospectively and the outcomes were compared with that of non-PVT group.

Results: The type of PVT included Yerdel grade 1 in 7 patients (53.8%), grade 2 in 4 patients (30.8%), grade 3 in 1 patient (7.7%) and grade 4 in 1 patient (7.7%). For restoration of portal inflow, evasion thrombectomy was performed in 11 patients (84.6%), reno-portal bypass in 1 patient (7.7%) with grade 4 PVT, and SMV jump graft in 1 patient (7.7%) with grade 2 PVT. There was no portal vein-related morbidity except one patient who need portal vein stent because of sticture. The outcome after LT was comparable with that of patients without PVT.

Conclusions: Although it has a technical complexity in surgical procedure, LT is no longer contraindication for patient with PVT because of various alternative options and the outcome is comparable with the patient without PVT.

Keywords: Portal vein thrombosis, Liver transplantation, Ren-portal bypass, Jump graft
(28.5%) were in group 2, 23 (10.8%) were in group 3, and 12 (5.6%) were in group 4. There were no statistical differences in age and sex among 4 groups. But, body mass index (BMI), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were significantly different among 4 groups. Liver-to-spleen CT ROI values ratio (L/S ratio) on non-contrast CT was significantly correlated with graft steatosis with a correlation coefficient of 0.176 (P<0.001). MR spectroscopy also showed significant correlation with graft steatosis with a correlation coefficient of 0.289 (P<0.001).

Conclusions: Both L/S ratio and MR spectroscopy were able to estimate graft steatosis to some extent. And among them, MR spectroscopy was more relevant with histopathologic steatosis assessment.

**OP-045**

Neutrophil-to-Lymphocyte Ratio Predicts Acute Cellular Rejection in Living Donor Liver Transplantation

Boram LEE, YoungRok CHOI, Jai Young CHO, Ho-Seong HAN, Yoo-Seek YOON

Department of Surgery, Seoul National University Bundang Hospital, Seongnam, South Korea

Aims: The neutrophil-to-lymphocyte ratio (NLR) predicts poor prognosis in several conditions including transplantation. The aim of the study was to evaluate the effectiveness of NLR in prediction of ACR after living donor liver transplantation (LDLT).

Methods: This was a retrospective study of patients who underwent liver biopsy after LDLT from 2009 to 2017. The NLR was calculated 4 weeks before transplantation, at the time of transplantation, and immediately prior to liver biopsy. The correlations between NLR values and the incidence of ACR were investigated.

Results: Eighty-one patients were reviewed (ABO-compatible (ABOc) = 66, ABO-incompatible (ABOi) = 15). ACR occurred in 19 (28.8%) ABOc LDLT. ACR occurred within 1 month after transplantation in 15 (78.9%) ABOc LDLT. There was no significant difference 4 weeks before transplantation (ACR: no-ACR = 2.54 ± 1.15 : 3.68 ± 2.08, P=0.06) and transplantation (ACR: no-ACR = 20.53 ± 13.39 : 17.73 ± 8.74, P=0.06). However, NLR immediately prior to biopsy was significantly lower in the ACR group (ACR: no-ACR = 5.82 ± 3.42 : 28.66 ± 22.66, P<0.001). Liver function tests (LFT) in the ACR and no-ACR groups in ABOc LDLT were not significantly different. For prediction of NLR for ACR within 1 month in ABOc, the ROC revealed an AUC of 0.969. The NLR cut-off of 9.67 had a sensitivity 94.1% and specificity 86.7%.

Conclusions: NLR could be a non-invasive predictor of subclinical early ACR in ABO-compatible LDLT.

**OP-046**

Hepatitis B Vaccination and Entecavir Monotherapy Following Withdrawal of Hepatitis B Immunoglobulin (HBIG). An Alternative Approach to Prevention of Hepatitis B Reactivation after Liver Transplantation

Johann Faizal KHAN1,2, Youngdong YU2, Hye-Sung JO2, Kyung-Chul YOON2, Woo-Hyoung KANG2, Dong-Sik KIM2

1Hepatobiliary Surgery and Liver Transplantation, Hospital Selayang, Malaysia, 2Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Korea University Medical Center, Korea

Aims: Combination of HBIG with an oral nucleoside / nucleotide analog (Entecavir/Tenofovir) has been the mainstay of prevention of Hepatitis B reactivation after liver transplantation. HBIG is costly, inconvenient, and may contribute to development of mutant strains. There are no consensus guidelines regarding the role of Hepatitis B vaccination in prevention of Hepatitis B reactivation after liver transplantation.

Methods: 41 liver transplant recipients on Entecavir alone were given Hepatitis B vaccination once antibody titres were undetectable. HBIG was withdrawn from all patients. The response to a standard 3 dose regimen of Hepatitis B Vaccine was evaluated. Reactivation of Hepatitis B was defined as HBsAg positive titre.

Results: Mean age was 60.54 (44-74). 27 were DDLT, 14 were LDLT. Mean BMI was 23.56 (16.27-32.47). Mean MELD score and CTP score was 15.73 and 8.56 respectively 33 patients were transplanted for Hepatitis B related HCC and 8 were for Hepatitis B related hepatic decompensation. No recurrence or adverse events occurred. 34/36 (5 drop outs) patients had undetectable HBsAb titres. 9 patients had positive response to vaccination. 2 patients had persistent antibody titres (not vaccinated). 1 patient responded after a fourth dose. 2 patients had no response even after 4 doses and 1 no response after 6 doses. A significant positive response to vaccination was seen in patients receiving single immunosuppressive agent compared to a combination (P=0.048).

Conclusions: A standard 3 dose Hepatitis B Vaccination regime may confer additional immunity. Patients who are on single immunosuppressive agent are more likely to develop a positive response to vaccination.

**OP-047**

Living Liver Donor Surgical Complication: Single Center Experience with 512 Cases

Eun-Kyoun JWA, Dong-Lak CHOI, Joo-Dong KIM

Hepatobiliary Surgery, Daegu Catholic University Medical Center, Republic of Korea

Aims: Korea is the one of the most common country to do living donor liver transplantation. We were reached to 500th living donor liver transplantation in 2017. We review our donor
complication and find way to reduce the rate of morbidity. **Methods:** Institutional LT database was searched from 2005.05.08. to 2017.12.31. Their medical records and imaging studies were reviewed. **Results:** From 2005.05.08 we did first living donor hepatectomy, we did 512 living donor hepatectomy until 2017.12.31. Among them, 324 were male and 188 were female. Graft types were Right liver graft in 457 (89.3%), Left liver graft in 47 (9.2%), Left lateral section graft in 2 (0.4%) and Right posterior section graft in 6 (1.2%). Mean age of total donor was 30 years and Mean BMI was 22. Mean hospital days was 10days. All of the donors, surgical complication occurred in 32donors (6.3%). Minor complication was 10 cases(1.9%). Major complication was 24 case (4.7%). Between major complication, the most common complication was biliary complication (n=17) and the Other complications were small bowel obstruction operation (2), bleeding control (n=2), pleural effusion drainage (n=2), portal vein stent insertion (n=1). There are no mortality. There are re-operation case was just one case, which was immediate right hepatic artery bleeding. **Conclusions:** Our center’s complication was very low. But still biliary complication is the most common complication. When we meet abnormal biliary anatomy we must be careful and we try to reduced biliary complication.

**OP-048**

**Right Anterior Section Graft for Living-Donor Liver Transplantation**

Jonathan NAVARRO, Gi Hong CHOI, Myoung Soo KIM, Yoon Bin JUNG, Jae Geun LEE

Surgery, Yonsei University College of Medicine, Republic of Korea

**Aims:** In living-donor liver transplantation, the right lobe graft is commonly utilized to prevent small-for-size syndrome, despite the considerable donor morbidity. Conversely, the feasibility of the left lobe graft and the right posterior section graft in smaller-sized recipients is now commonly employed with comparable outcomes to right lobe grafts. The efficacy of the right anterior section graft has rarely been reported.

**Methods:** Here, we describe a 56-year-old man, with alcoholic liver cirrhosis, who successfully underwent living-donor liver transplantation using the right anterior section graft.

**Results:** Preoperatively, the right lobe of the donor occupied 76.2% of the total liver volume exposing the donor to a small residual liver volume. The right posterior section and left lobe volumes were insufficient, providing a graft-to-recipient weight ratio of 0.42% and 0.38%, respectively. However, the right anterior section could fulfill an acceptable GRWR of 0.83%. Clinical signs and symptoms and liver function improved following anterior section graft transplantation without complications.

**Conclusions:** The procurement of anterior section graft is technically feasible in selected patients, especially in high-volume liver centers.
BMPR2 Promotes Pancreatic Cancer Proliferation via the GRB2-Mediated PI3K-Akt-mTOR Pathway

Huahu GUO, Yazhou WANG, Zhengkui ZHANG, Mingzhe LI, Qi WANG, Kai ZHANG, Xiaodong TIAN, Yinmo YANG

General Surgery, Peking University First Hospital, China

Aims: Tumor microenvironment favors aberrant expression of tumor cells characterized by dysregulated release of cytokines, chemokines, and growth factors that the tumor exploits for survival and invasion. The crosstalk of bone morphogenetic proteins and its receptors between tumor and its surrounding stromal cells have been reported in breast cancer, but effects of the interaction in pancreatic cancer remain unclear.

Methods: The enrichment of BMP pathway gene set was anlaysis by GSEA software in three database of GEO. BMPR2 were reduced in PDAC cells via specific shRNA-mediated knockdown. Quantitative proteomic analysis was performed to explore the mechanism of BMPR2 regulation. The cell growth rate was accessed by CCK-8, FACS and colony formation assays. ChiP-sequence was performed to identify and characterize smad complex targets genes.

Results: Here we demonstrate that BMP pathway was hyperactivated in pancreatic cancer. BMPR2 was overexpressed in human pancreatic cancer specimens and associated with the prognosis of pancreatic cancer patient. Downregulated BMPR2 markedly inhibits the growth of pancreatic cancer cell lines Mia-PaCa-2 and PANC-1 in vitro and vivo. Mechanistically, disrupt the expression of BMPR2 suppresses the expression of GRB2 in a smad-independent manner, and then inactivates GRB2-associated signaling pathways, PI3K-Akt-mTOR pathway. In addition, LDN193189, a BMP pathway inhibitor, can also impair the expression of BMPR2 and inhibit the functions of pancreatic cancer cells by GRB2-mediated PI3K-Akt-mTOR pathway.

Conclusions: Thus, our results suggest that BMPR2 is an important mediator of pancreatic cancer cells and its surrounding microenvironment and offer insight into therapeutic applications for better survival of patients with this deadly disease.

Pre-Drainage and Post-Drainage Prognostic Nomograms to Predict Outcome of Percutaneous Drainage in the "Step-Up Approach" for Necrotizing Pancreatitis

Rajesh GUPTA1, Aditya KULKARNI1, Bakhavendra BABU1, Sunil SHENVI1, Rahul GUPTA2, Rohit NIMJE1, Gopal SHARMA1, Prateek VASWANI1, Sriman DEIVASIGAMANI1, Mandeep RANG1, Harjeet SINGH1, Vishal SHARMA1, M. Praveen KUMAR3, Deepak BHASIN4, Surinder RANA2

1Division of Surgical Gastroenterology, 2Department of Gastroenterology, 3Department of Radiodiagnosis, 4Department of Clinical Pharmacology, PGIMER Chandigarh, India

Aims: Percutaneous catheter drainage (PCD) with saline irrigation alone is effective in a large proportion of patients with pancreatic necrosis treated with the step-up approach. Early identification of patients who are likely to fail PCD helps in early referral and treatment.

Methods: Single-center retrospective cohort study using data from a prospectively maintained database. Patients with necrotizing pancreatitis undergoing PCD as initial intervention were included. Patients who did not respond underwent necrosec-
Comparison of the Prognostic Impact and Combination of Preoperative Inflammation-Based and/or Nutritional Markers and 18F-FDG-PETCT-Derived Markers of Tumor Metabolism in Patients with Bile Duct and Pancreatic Cancer

Min-Su Park
Surgery, Kyung Hee University, Republic of Korea

Aims: The aim of this study was to evaluate and compare the prognostic value of preoperative established inflammation-based and/or nutritional markers and 18F-FDG-PETCT-derived markers in patients with bile duct and pancreatic cancer.

Methods: This study retrospectively reviewed 80 patients who underwent R0 resection for bile duct and pancreatic cancer. C-reactive protein-to-albumin ratio (CAR), neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, Prognostic Nutritional Index (PNI), Glasgow Prognostic Score, were derived from routine blood tests. The maximum standardized uptake (SUVmax), peak standardized uptake (SUVpeak), metabolic tumour volume (MTV) and total lesion glycolysis (TLG) were measured.

Results: There was no association between 18F-FDG-PETCT measures of tumor metabolism and systemic inflammation. Among inflammation-based and/or nutritional markers and 18F-FDG-PETCT-derived markers, multivariate analyses demonstrated CAR, PNI, SUVmax, MTV and TLG as independent prognostic factors for OS, respectively.

Conclusions: The present study reports a direct association between 18F-FDG-PETCT-derived measures of tumor metabolism and systemic inflammation in patients with bile duct and pancreatic cancer.
The Significance of Early Virological Response in the Patients with Prolonged Antiviral Treatment for Chronic Hepatitis B

Sun Hong Yoo, Soon Woo Nam, Yoon Jung Kim, Sung Won Lee, Hae Lim Lee, Jeong Won Jung, Si Hyun Bae, Jong Young Choi, Sun Hong Yoo, Soon Woo Nam, Yoon Jung Kim, Sung Won Lee, Seung Kew Yoon, Jung Hyun Kwon

Internal Medicine, The Catholic University of Korea, Korea

Aims: Due to the potent oral antiviral agents for chronic hepatitis B (CHB), prolonged therapy could expect not only complete viral suppression but also HBsAg loss. Several reports issues whether the suboptimal response under oral antiviral therapy was associated with a higher risk of HCC. However, there remains uncertain about the impact of early virological response on serological response including HBeAg loss and HBsAg loss in the patients whose long-term therapy is inevitable.

Methods: A total of 4,011 consecutive patients who were treated with entecavir (n=1,956) or tenofovir (n=1,421) at three St. Mary’s Hospital of Catholic University between 2007 and 2016 were investigated. Early virological response is defined as HBV DNA <20 IU/ml at week 48 of therapy. The response rates of complete virologic response and with partial virologic response (1.1% vs. 0.2%, P=0.657).

Results: Median follow-up period was 55.9 months (6.2-99.8 months). The patients with HBeAg positive were 2,022 (50.4%) and early virological response was achieved in 1,394 patients (68.9%). During follow-up, cumulative rate of HBAg loss was 40.1%. HBeAg loss was a higher rate in patients with early virological response than with partial virological response (45.5% vs. 28.3%, P<0.001). HBsAg loss was achieved in 17 of 2,022 patients (0.8%). Achievement of HBsAg loss was much favor in complete virologic response group than partial virologic response group (1.1% vs. 0.2%, P=0.023). In the patients with HBeAg negative, early virological response was achieved in 89.9% (1,219 of 1,355 patients). In this group, cumulative rate of HBsAg loss was not different between the patients with early virologic response and with partial virologic response (1.1% vs. 1.5%, P=0.657).

Conclusions: Our results demonstrated that early full virological suppression is associated with a higher chance of HBeAg loss and finally HBsAg loss in HBeAg positive patients with prolonged antiviral therapy. However, its role is unclear in the HBeAg negative patients.

Keywords: Chronic hepatitis B, Virological response, HBeAg loss, HBsAg loss

No Resistance to Tenofovir Alafenamide (TAF) Detected through 144 Weeks of Treatment in Patients with Chronic Hepatitis B (CHB)

Ki Tae Yoon1, Young-Suk Lim2, Yang Liu3, Bandita Parhy2, Silvia Chang1, Ross Martin2, Becket Feierbach2, Hongmei Mo1, Anuj Gaggar1, John F Flaherty1, Henry LY Chan4

1Department of Internal Medicine, College of Medicine, Pusan National University, Pusan National University Yangsan Hospital, Yangsan, Korea; 2Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 3Gilead Sciences, Foster City, CA, United States; 4Institute of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Aims: Cumulative resistance analyses were performed through Week 144 for 2 Phase 3 studies (GS-US-320-0108, GS-US-320-0110) evaluating TAF or tenofovir disoproxil fumarate (TDF) for the treatment of CHB in HBeAg+ and HBeAg- treatment-naïve or treatment-experienced adults.

Methods: Patients were randomized 2:1 to receive TAF or TDF double-blind (DB) treatment for 144 weeks, and were then switched to open-label (OL) TAF. HBV pol/RT deep sequencing was conducted for any patient with ≥24 weeks of treatment and HBV DNA ≥69 IU/ml at Week 144 or at early discontinuation. Illumina Mi-Seq deep sequencing was conducted and sequence changes at the consensus sequence level (15%) were reported. In vitro phenotypic analysis using recombinant HBV in HepG2 cells was performed for: VB patients who were adherent to study drug, those with conserved site substitutions, or when polymorphic substitutions emerged in >1 patient.

Results: 1298 patients were randomized and treated with TAF (n=866) or TDF (n=432). Through Week 144, 9.9% (TAF, 10.4%; TDF DB, 11.9%) of enrolled patients qualified for sequencing at their last evaluable visit; Of these 128 patients, 63 had no sequence change from baseline, 22 were unable to sequence due to lower viral load, 31 had polymorphic site substitutions, and 12 had conserved site substitutions. Cumulatively, 70 patients qualified for phenotypic analysis and no isolates showed reduction in susceptibility to TAF or tenofovir (TAF: n=54, mean fold change EC50 0.99, range 0.32-1.68, tenofovir: n=16, mean fold change EC50 0.92, range 0.33-1.45).

Conclusions: No substitutions associated with resistance to TAF were detected through 144 weeks of treatment.

Keywords: TAF, Resistance, 144 weeks, CHB
Low-Level Viremia and Cirrhotic Complications in Chronic Hepatitis B Patients with Good Adherence to Entecavir

Dahye Kim1, Seung Bum Lee1, Jae Ho Park1, Byung Gyu Kim1, Seok Won Jung1, In Du Jeong1, Sung-Jo Bang1, Jung Woo Shin1, Bo Ryung Park2, Eun Ji Park2, and Neung Hwa Park1,2

1Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea; 2Biomedical Research Center, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea

Aims: Low-level viremia (LLV; <2,000 IU/mL) to nucleos(t)ide analog treatment was presented as possible cause of hepatocellular carcinoma (HCC) development in patients with chronic hepatitis B (CHB). However, detailed information on adherence was lacking. This study aimed to evaluate the effect of LLV on HCC development, as well as on mortality and cirrhotic complications among patients with good adherence to entecavir (ETV) treatment in real-world clinical settings.

Methods: We performed a 10-year retrospective observational analysis of data from 894 consecutive adult patients with treatment-naive CHB undergoing ETV treatment. LLV was defined by either persistent or intermittent episodes of <2,000 IU/mL detectable hepatitis B virus DNA during the follow-up period. Good adherence to medication was defined as a cumulative adherence ≥90% per study period.

Results: In the entire cohort (n=894) that did not consider adherence, cumulative incidence of HCC was significantly lower in the maintained virologic response (MVR) group than in the LLV group (log rank P=0.017). Multivariate analysis for the HCC incidence showed that LLV was an independent prognostic factor in addition to other traditional risk factors in the entire cohort. The good adherence group comprised 617 patients (69.0%). No significant difference was found between the MVR and LLV groups in terms of the incidence of liver-related death or transplantation, HCC, and hepatic decompensation in the good adherence group according to univariate and multivariate analyses.

Conclusions: In treatment-naive CHB patients with good adherence to ETV treatment in real-world clinical settings, LLV during treatment was not a predictive factor for HCC and cirrhotic complications, even if cirrhosis.

Keywords: Adherence, Hepatitis B virus, Hepatocellular carcinoma, Low-level viremia

Tenovir Disoproxil Fumarate on the Risk of Hepatocellular Carcinoma in Chronic Hepatitis B Patients with Failure to Preceding Treatments

Gi-Ae Kim1, Young-Suk Lim2

1Department of Internal Medicine, Kyung Hee University School of Medicine, Republic of Korea; 2Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Republic of Korea

Aims: Tenovir disoproxil fumarate (TDF)-monotherapy is recommended for the treatment of chronic hepatitis B (CHB) patients who are refractory to other drugs. Yet, little data are available for the effectiveness of TDF-monotherapy compared with TDF-based combination therapy on the risk of hepatocellular carcinoma (HCC) and death/transplantation.

Methods: This historical cohort study included 1,163 CHB patients who initiated TDF rescue therapy after persistent viremia and genotypic resistance mutations from the failure of preceding treatments between January 2012 and December 2015 at Asan Medical Center in Korea. The risks of HCC and death/transplantation of TDF-monotherapy (n=848) groups were compared with those of TDF-based combotherapy (n=315) groups.

Results: During 5.1 years of overall follow-up period, 60 (5.2%) patients developed HCC, and 23 (2.0%) died or received liver transplantation. In the 295 propensity score-matched pairs, compared with TDF-combotherapy, TDF-monotherapy showed no significantly high risks of HCC (1.27/100 person-year [PY] vs. 1.10/100 PY; HR 1.29, 95% CI 0.62−2.67, P=0.66) and death/transplant (0.55/100 PY vs. 0.57/100 PY; HR 1.63, 95% CI 0.53−4.98, P=0.39). In the 101 propensity score-matched pairs of cirrhosis subcohort, TDF-monotherapy was associated with a similar risk of HCC and death/transplant compared with TDF-combotherapy (HR 1.29, 95% CI 0.62−2.67, P=0.50 and HR 1.03, 95% CI 0.21−5.15, P=0.97). The findings were consistently identified through inverse probability treatment weighting and competing risks analyses.

Conclusions: In CHB patients with failure to preceding treatments, TDF-monotherapy showed no higher risks of HCC and death/transplantation compared with TDF-combotherapy. These findings suggest that TDF monotherapy can be an effective rescue treatment option for CHB patients with failure to preceding treatments.

Keywords: Hepatitis B virus, Liver cancer, Nucleos(t)ide analogue, Resistance
**Development of a Mathematical Modeling of HBsAg Kinetics during Long-Term Antiviral Treatment: A Pilot Study**

Hwi Young Kim¹, Tae Soo Jang², Hee-Dae Kwon², Joo Ho Lee³

¹Ewha Womans University College of Medicine, Department of Internal Medicine, Seoul, Korea; ²Inha University, Department of Mathematics, Incheon, Korea; ³CHA Bundang Medical Center, Department of Internal Medicine, Seongnam, Korea

**Aims:** The kinetics of serum hepatitis B surface antigen (HBsAg) levels during nucleos(t)ide analog (NA) treatment needs to be elucidated for the prediction of off-treatment durability of response in patients with chronic hepatitis B (CHB). The aim was to develop a novel method of mathematical modeling for HBsAg kinetics under long-term NA treatment.

**Methods:** In this pilot study, we reviewed viral decay patterns and HBsAg kinetics in 184 CHB patients from a tertiary hospital in Korea who were treated with entecavir or tenofovir as their initial NAs, without evidence of antiviral resistance. HBsAg and immune effectors were added as new compartments in the model equations for hepatitis B viral dynamics. Parameter estimation was performed using the non-linear least square minimization method and non-linear Kalman filter algorithm.

**Results:** Mean age was 52.1±10.9 years, and 112 patients (60.9%) were male. Patients received either entecavir (93, 50.5%) or tenofovir (91, 49.5%). Median follow-up duration was 72.5 months. At baseline, 112 patients (60.9%) were HBeAg-positive. Baseline liver stiffness by transient elastography was 6.9 kPa (median; interquartile range [IQR], 4.6-11.1), and alanine aminotransferase (ALT) was 81.0 IU/L (IQR, 39.3-161.8). Baseline HBV DNA and HBsAg titers were 6.26 Log10IU/mL (IQR, 5.34-7.54) and 2420.50 IU/mL (IQR, 1083.25-5342.12), respectively. The model equations for viral and HBsAg dynamics during antiviral treatment were developed as follows, considering i) both cytolytic and non-cytolytic clearance of infected cells, and ii) cccDNA and integrated HBV DNA in the host genome as dual sources of HBsAg:

\[
\begin{align*}
\frac{dT_1}{dt} &= S - d_1 * T_1 - (1 - \eta) b * V * T_1 \\
\frac{dT_2}{dt} &= \alpha * f * I * E - d_2 * T_2 - (1 - \eta) b * V * T_2 + m_2 * T_2 \\
di/dt &= ((1 - \eta) b * V (T_1 + T_2) + m_1 - d_1 - d_2 - \alpha * l * E \\
dV/dt &= (1 - \epsilon) p * d_1 * I - c * V \\
deEdt &= S_0 + b_0 * E / (c + k_0) - d_0 * E \\
sAg &= \gamma * T_2 / (T_2 + k_2) + \delta * I / (l + k_2)
\end{align*}
\]

*(NOTE. T, target cell; I, infected cells; V, virus; E, immune effectors; sAg, HBsAg; d, death rate; \(\eta\), treatment efficacy of inhibiting de novo infection; f, de novo infection rate of T; \(\epsilon\), calibration coefficient of \(\alpha\) for T; m, mitotic production rate of I; \(\alpha\), E-induced clearance rate of I; \(\epsilon\), treatment efficacy of inhibiting viral production; p, viral production rate by I; c, clearance rate of free virions; S0, production rate of E; b0, maximum birth rate for E; k0, Michaelis-Menten type half saturation constant for E.)*

Figure 1 and 2 demonstrate sample visualization of the HBsAg kinetics with fitted curves using the model equations.

**Conclusions:** Our novel mathematical model for hepatitis B viral dynamics showed promising results in terms of long-term fitting of HBsAg kinetics. These results need further validation in various clinical settings including discontinuation of NAs.

**Keywords:** Hepatitis B, Viral kinetics, HBsAg, Long-term treatment

---

**ALT Normalization after Entecavir and Tenofovir Correlated with Reduction of Development for HCC**

Sehwa Kim, Sung Won Chang, Ha Seok Lee, Min-jin Lee, Young-Sun Lee, Sang Jun Suh, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yeon, Soon Ho Um, Kwan Soo Byun

Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea

**Aims:** Recently, the use of potent antiviral agents has made it possible to effectively reduce liver disease related events such as hepatic encephalopathy, variceal bleeding, ascites, and HCC in patients with chronic hepatitis B. The aim of this study was to determine whether there is a relationship between normalized ALT resulting from the use of antiviral agents and the occurrence of liver disease related events.

**Methods:** From 2007 to 2018, we studied 427 patients treated...
with entecavir or tenofovir at Korea University Guro Medical Center. The patients divided into ALT normal group and ALT abnormal group after 1 year of antiviral treatment. The ALT normal level is 34 for men, 30 for women in the KASL standard, and 35 for men and 25 for women in the AASLD standard. Liver related disease included HCC, hepatic encephalopathy, variceal bleeding, and ascites.

**Results:** The baseline characteristics of 427 patients median age was 50 (IQR 42–57), median value of AST was 78 (IQR 47–135 IU/L), ALT was 88 (IQR 45–178 IU/L), HBV DNA was 2,190,000 (IQR 170,000–36,815,316IU), and AFP was 7.05(IQR 3.325–26.025 ng/ml). 67% of all patients were male and 33% were female. 61.4% of patients used entecavir and 46.4% of patients used tenofovir. The people who used both drugs sequentially were 7.5%. Patients with HBeAg-positive were 54.8% and patients with anti-HBe Ab positive were 50.8%. Overall survival in ALT abnormal group was lower than ALT normal group after 1 year of antiviral treatment without statistical significance (Log rank test, P=0.201 in the KASL standard and P=0.265 in the AASLD standard). The cumulative incidence of HCC in normal ALT group was significantly lower than abnormal ALT group (Log rank test, P<0.001 in both the KASL and AASLD standard). The incidence of Liver disease related events in the two group was not significant (Log rank test, P=0.333 in the KASL and P=0.428 in AASLD standard).

**Conclusions:** ALT normalization after 1 year of entecavir and tenofovir treatment is correlated with reduction of development for HCC, but not overall survival and development of liver disease related events. Patients who failed to normalize ALT after 1 year of entecavir and tenofovir treatment should be observed more carefully for development of HCC.

**Keywords:** Chronic hepatitis B, ALT, Hepatocellular carcinoma

---

**Aims:** to assess portal hypertension using Doppler ultrasound in patients with cirrhosis before and after Atovastatin administration.

**Methods:** This study was conducted in Thai Nguyen National Hospital included 56 patients with cirrhosis and portal hypertension (hepatic venous pressure gradient- HVPG ≥ 12 mm Hg) who were dived into 2 groups: 28 patients with cirrhosis who were received 20 mg of Atovastatin daily for 2 weeks and then 40 mg daily for another 2 weeks, and control group included 28 patients with cirrhosis who did not receive Atovastatin. All patients underwent full clinical examination, laboratory investigations, and abdominal Doppler ultrasound at baseline and after 30 days to evaluate portal vein diameter (PVD), portal vein velocity (PVV), portal hypertension index (PHI), HVPG.

**Results:** PHI decreased significantly in group after Atovastatin administration for 30 days (a decrease of 8.1% from baseline, P<0.05). HVPG significantly decreases were observed in patients who were received Atovastatin (a decrease of 8.5% from baseline, P<0.05) and in those who were not (a decrease of 4.8% from baseline, P<0.05). No significant adverse effects were detected.

**Conclusions:** Atovastatin is safe and effective in lowering portal hypertension. Atovastatin decreased HVPG and improved liver perfusion in patients with cirrhosis. The beneficial effects of Atovastatin should be confirmed in many clinical trials for portal hypertension.

**Keywords:** Portal Hypertension, Atovastatin, Cirrhosis, Effects
Conclusions: Low-dose propranolol (40-120 mg/day) as a secondary prophylaxis for variceal re-bleeding decreased overall mortality and varix rebleeding recurrence in patients with tense ascites.

Keywords: Propranolol, Ascites, Mortality

OP-063
Endoscopic Variceal Obturation versus Retrograde Transvenous Obliteration for Fundal Variceal Bleeding

Hyun Gil Goh, Han Ah Lee, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Sang Jun Suh, Young Kul Jung, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yeon, Kwan Soo Byun, Soon Ho Um
Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Aims: Although both endoscopic variceal obturation (EVO) and retrograde transvenous obliteration (RTO) are recognized as effective in treatment of fundal varices in patients with liver cirrhosis, the studies comparing the therapeutic effect of EVO and RTO are very limited.

Methods: Patients with fundal variceal bleeding were enrolled, and patients with previous treatment of fundal varices were excluded.

Results: One-hundred twenty-three patients with fundal variceal bleeding were included. Age was 61.4±12.2 years and 88 patients (71.5%) were men. Alcoholic liver disease was most frequent underlying liver disease (63 patients, 51.2%). Type of varices was GOV2 and IGV1 in 60 (48.8%) and 63 (51.2%) patients, respectively. Eighty-seven patients (71.5%) were men. Alcoholic liver disease was most frequent underlying liver disease (63 patients, 51.2%). Type of varices was GOV2 and IGV1 in 60 (48.8%) and 63 (51.2%) patients, respectively.

GV rebleeding rates differed significantly according to the type of varices (P=0.022), while, GV rebleeding rates did not differ between EVO and RTO groups (P=0.107). On multivariate analysis, only type of varices was independent predictor for GV rebleeding (HR, 3.291; 95% Confidence interval, 1.059-10.227; P=0.040).

Conclusions: Both EVO and RTO are effective for preventing GV rebleeding in patients with fundal variceal bleeding. Type of varices was independent predictor for GV rebleeding in these patients.

Keywords: Endoscopic variceal obturation, Retrograde transvenous obliteration, Fundal varices, Bleeding

Effect of Acute Kidney Injury on Long-Term Outcomes of Spontaneous Bacterial Peritonitis in Cirrhotics Using ICA-AKI Criteria

Won Sohn1, Jung Hee Kim2, Ju-Yeon Cho3
1Department of Internal Medicine, Kangbuk Samsung Hospital, Seoul, Korea; 2Department of Internal Medicine, Hallym University Hangang Sacred Heart Hospital, Seoul, Korea; 3Department of Internal Medicine, Chosun University Hospital, Gwang-Ju, Korea

Aims: Spontaneous bacterial peritonitis (SBP), a crucial complication of liver cirrhosis, is associated with high mortality. Acute kidney injury (AKI) is an important risk factor for the prognosis in cirrhosis. Recently, a new AKI criteria (International Club of Ascites, ICA-AKI) has been introduced in patients with cirrhosis. This study aimed to investigate the effect of AKI on long-term mortality of SBP in cirrhosis using ICA-AKI criteria.

Methods: A total of 157 cirrhotic patients with a first episode of SBP between January 2007 and December 2016 from three medical centers in Korea were analyzed. We investigated the long-term mortality with related risk factors of SBP in cirrhosis including the ICA-AKI criteria. The ICA-AKI stage at SBP diagnosis is as follows: stage 0, no increase of serum creatinine (SCr) or increase of SCr <0.3 mg/dl; stage 1, increase of SCr ≥0.3 mg/dl or SCr ≥1.5 - 2 times from baseline; stage 2, increase of SCr ≥2 - 3 times from baseline; stage 3, increase of SCr ≥3 times from baseline, or SCr ≥4.0 mg/dl with an acute increase of ≥0.3 mg/dl, or initiation of renal replacement therapy. Stage progression was defined as a progression of AKI to a higher stage.

Results: The mean age was 58.6 years. The etiology of liver cirrhosis was alcohol (n=73), hepatitis B virus (n=70), hepatitis C virus (n=9), and others (n=5). At the diagnosis of SBP, 106 patients were Child-Pugh class C (67%), the mean level of MELD score was 20.6, and the mean SCR level was 1.7 mg/dl. The ICA-AKI stage was stage 0 in 91 (58%), stage 1 in 33 (21%), stage 2 in 19 (12%), and stage 3 in 14 patients (9%). Stage
Severity Changes of Cirrhotic Patients during Seven Years Period in South Korea: A Multicenter Retrospective Study from 2008 to 2014

Jeong Han Kim, Eileen L. Yoon1, Chung Hwan Jun2, Jae Hyun Yoon3, Byung Seok Kim4, Jeong Eun Song5, Ki Tae Suk6, Moon Young Kim7, Seong Hee Kang8

Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Korea, 1Department of Internal Medicine, Inje University Sanggye Paik Hospital, Seoul, Korea, 2Department of Internal Medicine, Chonnam National University Hospital, Gwangju, Korea, 3Department of Internal Medicine, Daegu Catholic University School of Medicine, Daegu, Korea, 4Department of Internal Medicine, Daegu Catholic University School of Medicine, Gyeongsangbuk-do, Korea, 5Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Korea, 6Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

Aims: Clinical implications including disease severity of cirrhotic patients have been changed since oral antiviral agents for hepatitis B were introduced. On the other hands, alcoholic cirrhosis is still not well controlled and direct acting antiviral agents for hepatitis C are recently introduced. Therefore, we can expect improvement of severity will be observed more prominently in hepatitis B endemic area such as Korea. We aimed to investigate change of clinical severity in cirrhotic patients of Korea.

Methods: Medical records of 6,369 cirrhotic patients visited six tertiary university hospital in Korea from 2008 to 2014 were retrospectively reviewed. Clinical status of cirrhotic patients in each year was analyzed according to etiology, Child-Pugh score, decompensation, MELD score and mortality.

Results: Total 9,852 visit records were reviewed. Most common etiologies were hepatitis B and alcohol (38.6% and 39.7% each in 2008, and 35.1% and 39.0% each in 2014). Prevalence of decompensated cirrhosis did not decrease significantly from 45.2% in 2008 to 41.2% in 2014. Admission rate decreased from 56.8% in 2008 to 42.5% in 2014. Mean Child-Pugh score did not changed significantly from 6.6 to 6.4, but mean MELD score slightly reduced from 11.8 in 2008 to 10.9 in 2014. Overall mortality decreased from 8.9% in 2008 to 4.7% in 2014 and liver-related mortality also decreased from 7.8% to 3.1%. Among complications, variceal bleeding incidence reduced most significantly from 12.3% in 2008 to 7.8% in 2014. However, hepatocellular carcinoma (HCC) development rate did not decreased (9.8% in 2008 and 8.2% in 2014).

Conclusions: AKI and its progression are significant risk factors for mortality in cirrhotic patients with SBP. The new ICA-AKI criteria may be a useful tool to evaluate the prognosis of cirrhotic patients with SBP.

Keywords: Liver cirrhosis, Acute kidney injury, Albumin

Clinical Features and Prognosis of the Patients with Chronic Liver Disease Hospitalized with Variceal Bleeding

Jung Hwan Yu1, Young-Joo Jin1, Jongbeom Shin1, Jin-Woo Lee1, Young Kul Jung2, Hyung Joon Yim2, Jin Mo Yang2, Do Seon Song2, Young Seok Kim2, Sang Gyune Kim2, Dong Joon Kim2, Ki Tae Suk3, Eileen Yoon4, Sang Soo Lee4, Chang Wook Kim4, Hee Yeon Kim4, Jae Young Jang4, On Behalf of the Korean Acute-on-Chronic Liver Failure (KACLIF) Study Group

1Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, Incheon, South Korea, 2Division of Gastroenterology and Hepatology, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, South Korea, 3Department of Internal Medicine, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea, Suwon, South Korea, 4Department of Internal Medicine, Soonchunhyang University Hospital Bucheon, Bucheon, South Korea, 5Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, South Korea, 6Division of Gastroenterology and Hepatology, Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, South Korea, 7Department of Internal Medicine, Changwon Gyeongsang National University Hospital, Changwon, South Korea, 8Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea, 9Department of Internal Medicine, Soonchunhyang University Hospital, Seoul, Korea

Aims: Variceal bleeding is a critical acute deterioration causes in
the patient with cirrhosis. The aim of our study is to investigate the risk factor associated with mortality in the patients hospitalized with variceal bleeding and to evaluate the prognosis according to the presence of acute-on-chronic liver failure (ACLF).

**Methods:** This was a retrospective study conducted in patients from the Korean acute-on-chronic liver failure (KACLF) study cohort, including 474 consecutive patients who were hospitalized with variceal bleeding from January 2013 to December 2013 in 21 hospitals. ACLF was defined by EASL-CLIF consortium (CLIF-C).

**Results:** Among a total of 474 patients, 61 patients were diagnosed with ACLF according to the CLIF-C. The cumulative overall survival rates (OS) of the patients with varix bleeding at 30 and 90 days became significantly lower, according to the ACLF grade (p-value<0.001). The combination of virus and alcohol, as a cause of underlying liver disease, represented poor prognosis of the patients with varix bleeding than other causes. In multivariate variable analysis, the significant predictive factor of OS of the patients hospitalized with varix bleeding was white blood cell (Hazard ratio, HR 1.01, p=0.029), c-reactive protein (HR 1.09, p=0.013), and CLIF sequential organ failure assessment (SOFA) score (HR 1.49, p<0.001). The CLIF SOFA score also was a significant predictive factor of OS in patients with ACLF and varix bleeding (p-value<0.001). CLIF SOFA score showed the reliable area under the receiver operating characteristic curve (AUROC) for the prediction of mortality at 30 (0.895, CI 0.829-0.962) and 90 days (0.896, CI 0.842-0.951).

**Conclusions:** In patients hospitalized with variceal bleeding, the presence of ACLF showed a poor prognosis, according to CLIF-SOFA score. Furthermore, CLIF-SOFA model represented reliable score for mortality prediction in patients with variceal bleeding.

**Keywords:** Chronic liver disease, Variceal bleeding

---


**OP-067**

**NAFLD**

**Nonalcoholic Fatty Liver Disease and the Incidence of Myocardial Infarction: A Cohort Study**

Jieun Na1, Dong Hyun Sinn1, Danhee Kang2,†, Yoosoo Chang3, Seungho Ryu4, Soo Jin Cho5, Seung Woon Paik5, Young Bin Song6, Roberto Pastor-Barriuso7, Eliseo Guallar6,7, Juhee Cho5,†, Geum-Youn Gwak6,†

1Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; 2Department of Clinical Research Design and Evaluation, SAHST, Sungkyunkwan University, Seoul, South Korea; 3Center for Total Health Studies, Kangbuk Samsung Hospital, Seoul, South Korea; 4Center for Health Promotion, Samsung Medical Center, Seoul, South Korea; 5National Center for Epidemiology, Instituto de Salud Carlos III, and Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain; 6Center for Clinical Epidemiology, Samsung Medical Center, Sungkyunkwan University, Seoul, South Korea; 7Departments of Epidemiology and Medicine, and Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, USA.

†Contributed equally to this study; †Correspondence

**Aims:** Nonalcoholic fatty liver disease (NAFLD) is a multisystem disease associated with an increased risk of cardiovascular disease (CVD), diabetes, and chronic kidney disease. Indeed, CVD is the most common cause of death in NAFLD patients. In our study, we assessed whether the presence and severity of NAFLD was associated with the future development of myocardial infarction in a large cohort of asymptomatic adults without previous history of CVD.

**Methods:** A total of 111,492 adult men and women 40 years with no history of cardiovascular disease, liver disease or cancer at baseline who participated in a regular health screening exam between 2003 and 2013 were analyzed for incident myocardial infarction during follow-up. The main exposure was the presence of NAFLD at baseline. Fatty liver was diagnosed by ultrasonography, and NAFLD severity was assessed by the NAFLD fibrosis score (NFS).

**Results:** During 725,706.9 person-years of follow-up, 183 participants developed myocardial infarction (incidence rate 0.3 cases per 1,000 person-years). The age, sex, and year of visit-adjusted hazard ratio (HR) for incident myocardial infarction comparing participants with NAFLD to those without it was 2.14 (95% CI 1.59, 2.89). This association remained significant in fully-adjusted models (HR 1.54; 95% CI 1.11, 2.14). Compared to participants without NAFLD, the fully-adjusted HR for incident myocardial infarction in participants with low NFS (< -1.455) and with intermediate to high NFS (≥ -1.455) were 1.70 (1.22, 2.36) and 1.86 (1.22, 2.84), respectively.

**Conclusions:** In this large cohort study, NAFLD was associated with an increased incidence of myocardial infarction independently of established risk factors. In addition, this association was similar in participants with and without evidence of more advanced NAFLD as indicated by the NFS score. NAFLD patients may need to be carefully monitored and managed early to prevent myocardial infarction.
Aims: Body size-metabolic phenotype may help predict whether or not individuals with nonalcoholic fatty liver disease (NAFLD) develop advanced liver disease. We studied the association of body size-metabolic phenotype with nonalcoholic steatohepatitis (NASH) and significant fibrosis.

Methods: Our cross-sectional study included 559 subjects (mean age of 53 years; women 51%) with biopsy-proven NAFLD. Clinical, genetic, and histological characteristic features of NAFLD were evaluated. The metabolically unhealthy phenotype was defined by the presence of two or more metabolic components, while body size was categorized based on body mass index: obese (≥ 25 kg/m²) or non-obese (< 25 kg/m²). Body size-metabolic phenotypes were divided into four study groups: (1) metabolically-healthy/non-obese (MHO), (2) metabolically unhealthy/non-obese (MUNO), (3) metabolically-healthy/obese (MHO), and (4) metabolically unhealthy/obese (MUO).

Results: MHO and MUNO groups demonstrated comparable levels of insulin resistance, adipose tissue insulin resistance indexes, and visceral adipose tissue (VAT) areas. The VAT area was significantly higher in the MUO group versus MHO group. However, the VAT to subcutaneous adipose tissue (SAT) ratio was highest in the MUNO group. There was no difference in histology between the MUNO, MHO, and MUO groups. Multivariate analyses adjusted for age, sex, smoking status, PNPLA3, TM6SF2, and VAT/SAT areas demonstrated an independent and dose dependent relationship between the body size-metabolic phenotype and NASH or significant fibrosis.

Conclusions: The MUNO group displayed similar degree of hepatic histological severity compared to their MHO counterparts. Metabolic milieu beyond obesity may play a pathogenic role in MUNO individuals who develop NASH with significant hepatic fibrosis.

Keywords: Hepatic steatosis, Non-obese, Body mass index, Metabolic syndrome

**Development of Machine Learning Model to Predict the 7-Year Risk of the Non-Alcoholic Fatty Liver Disease (NAFLD) among General Korean Population: A Nationwide Population-Based Study**

Youn I Choi, Yun Soo Kim, Oh Sang Kwon, Ju Hyun Kim, Seung Kak Shin, and Dong Kyun Park

Division of Hepatology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Korea

Aims: Even though early diagnosis and prognosis of NAFLD have become a necessity in clinical setting, there is no reliable methods to risk stratify for the risk of NAFLD. The aim of this study was to develop and validate a machine learning (ML) model to predict the 7-year risk of the risk of newly developed NAFLD among Korean general population using life style factors and anthropometric characteristics at baseline.

Methods: We used the data from the Korean health examinee (HEXA) study (baseline: 2004-2013, follow up: 2012-2017), which consists of the data on the life style factors (diet pattern, exercise, alcohol, smoking, stress index), and anthropometric indices (body mass index, waist circumference, fat mass, and muscle mass). After exclusion of the excessive alcohol ingestion, total of 40,745 participants who were free of NAFLD at baseline were finally enrolled and divided into test sets and training sets. ML algorithms includes support vector machine, random forest, artificial neural network, XGBoost, and ensemble methods. Area under receive operating curves (AUROC) of each methods were compared.

Results: During follow up period, incidental 5,232 cases of NAFLD cases were developed. ML model of Ensemble method for prediction of 7-year risk of NAFLD yielded AUCs of 0.85 (95% CI (95% CI 0.80 to 0.90) using lifestyle factors and anthropometric indices. XGBoosts model showed AUROC of 0.82 (95% CI 0.80 to 0.85).

Figure 1. AUROC curves of ML(machine learning) based prediction model for the risk of NAFLD (non-alcoholic liver disease).

Conclusions: ML based prediction model can be used to risk stratify 7-year risk of NAFLD among general Korean population, enable physicians to close follow up based on patients level estimation through ML algorithm.

Keywords: Machine-learning, NAFLD, Life style, Anthropometric

**Prevalence and Incidence of Tamoxifen-Related Non-alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis**

Cheon Beom Lee1, Jeong-Ju Yoo1*, Sang Gyune Kim1, Young Seok Kim2, Soung Won Jeong3, Jae Young Jang4, Sae Hwan Lee5, Hong Soo Kim5, Baek Gyu Jun2, Young Don Kim1, Gab Jin Cheon1

1Department of Internal Medicine, Soonchunhyang University School of Medicine, Bucheon, Korea; 2Department of Internal Medicine, Soon-
Background: It is well known that tamoxifen treatment is associated with an increased risk of developing nonalcoholic fatty liver disease (NAFLD). We conducted a systematic review and meta-analysis to evaluate the incidence of NAFLD using tamoxifen in breast cancer patients.

Methods: We searched PubMed, EMBASE, and the Cochrane Library from database inception to December, 2018, for studies reporting incidence of NAFLD using tamoxifen. Cross-sectional, cohort and randomized controlled trials with >25 participants were included. The lists of authors and abstracts from the search were reviewed by two investigators to determine the manuscripts for full text review. Event rates were calculated using a random-effects model.

Results: Twenty studies including 9796 patients met our inclusion criteria. The overall prevalence of obesity of tamoxifen induced NAFLD was 40.9% from 11 cross-sectional studies. The overall incidence of NAFLD was 71.0/1000 patient per years in tamoxifen group and 23.7/1000 patient per years in non-tamoxifen group from 1 randomized control trial and 8 cohort studies. The risk of NAFLD was much higher in tamoxifen group (incidence rate ratio 2.77, 95% CI 1.87-4.08, I²=69%).

Conclusion: Use of tamoxifen is associated with increased risk of incidence and prevalence of NAFLD. Therefore, long-term use of tamoxifen requires clinical attention and regular liver imaging follow-up is required.

Keywords: Tamoxifen, Nonalcoholic fatty liver disease, Incidence, Prevalence
**OP-072**

Updated Study on Action Mechanisms of Cereblon as a Novel Prognostic Biomarker for Hepatocellular Carcinoma

Shin Hwang¹, Kyung Jin Lee², Gi-Won Song¹, Yun-Gyu Kim²

¹Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; ²Department of Convergence Medicine, Asan Medical Center, Seoul Korea

**Aims:** Cereblon (CRBN) is a 50 kDa cytosolic protein that is known as an important player in various cellular functions in multiple myeloma, but little is known about the biological significance of CRBN in hepatocellular carcinoma (HCC). We presented the discovery process of CRBN as a new prognostic biomarker of HCC and developed prognostic prediction models of HCC using CRBN.

**Methods:** Laboratory study was focused on assessment of CRBN expression status and its regulatory mechanisms in vitro and in vivo studies. Post-resection prognosis of 212 patients with HCC of 2–5 cm was assessed according to CRBN expression.

**Results:** CRBN was highly expressed in HCC cell lines and patient-derived HCC samples, and very highly expressed in metastatic HCC. CRBN depletion decreased HCC cell motility and induced down-regulation of MMP-9 and MMP-2, whereas overexpression of CRBN increased migratory ability of HCC cells and expression of hTERT, HKR3, and cell cycle-related factors. Clinical study revealed that high CRBN expression showed higher tumor recurrence rate (P=0.027) and lower patient survival rate (P=0.015) than low CRBN expression. The prognostic impact of CRBN on HCC recurrence was greater than that of microvascular invasion (hazard ratio 1.97 vs. 1.46). Prognostic prediction models combining CRBN and other risk factors enhanced the prognostic prediction power (Harrel’s concordance index >0.63).

**Conclusions:** CRBN is associated with aggressive tumor biology and has a high prognostic impact in HCC. Tumor aggressiveness was artificially changed according to the expression status of CRBN in vivo mouse model, which is the world-first finding in the field of HCC biomarker so far. We believe that CRBN is a new reliable prognostic biomarker of HCC.

**Keywords:** Biomarker, Cereblon, Prognosis, Prediction

**OP-074**

Circulating Exosomal microRNA-125b Inhibits Metastasis in Hepatocellular Carcinoma

Hye Seon Kim¹,², Jin Seoub Kim¹,², Wonhee Hur¹,², Hee Chul Nam¹,³, Pil Soo Sung¹,³, Si Hyun Bae¹,³, Jong Young Choi¹,³, Seung Kew Yoon¹,², Jeong Won Jang¹,²

¹Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; ²The Catholic University Liver Research Center, Seoul, Republic of Korea

**Aims:** Exosomes are 30-100 nm-sized vesicles that are released from many cell types into the body fluids. Exosomal miRNAs have recently emerged as potentially promising biomarkers in...
cancers and play an important role in cell to cell communication. The aim of this study is to investigate exosomal miRNAs contributing to extrahepatic metastasis from hepatocellular carcinoma (HCC).

**Methods:** Microarray-based miRNA profiling was performed to explore potential markers on the whole blood samples from patients with various liver diseases. Exosomes were extracted using exoquick and five miRNAs tested in sera of 47 healthy controls and 241 patients with and without metastasis. Then, target gene prediction was performed using TargetScan. Targets by miRNAs and epithelial-mesenchymal transition (EMT)-related protein expressions were assessed by Western blot. Biological functions of selected exosomal miRNAs in metastasis were investigated with a series of in vitro experiments including cell migration assay.

**Results:** Microarray-based miRNA profiling revealed 10 miRNAs with differential expressions, of which five exosomal miRNAs were further evaluated regarding metastasis. Transmission electron microscope and immunoblotting for exosomal markers confirmed the isolation of circulating exosomes from the patients. Among the selected miRNAs, exosomal miR-125b correlated with patient outcome, with increasing expression trends with tumor stage progression but followed by a significant drop with extrahepatic metastasis. Low exosomal miR-125b expression was associated with poor survival in patients as well as early metastases. For patients with serial serum samples before and after metastasis, exosomal miR-125b levels decreased upon metastasis. Transfection of HCC cells with miR-125b mimics downregulated SMAD2 and MMP2 known to regulate cancer metastasis. Moreover, miR-125b mimics inhibited migration ability of HCC cells.

**Conclusions:** Exosomal miR-125b has an anti-metastatic role by inhibiting cell migration and regulating EMT in HCC. Our findings suggest that exosomal miR-125b could be a potential biomarker and novel therapeutic target for metastasis from HCC.

**Keywords:** Exosome, Biomarker, Hepatocellular carcinoma, Metastasis

---

**Gut Microbes May Enhance the Efficacy of Immuno-therapy in the Murine Metastatic Liver Cancer Model**


1Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; 2Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea

**Background/Aims:** Primary and metastatic liver cancers are the leading causes of cancer-related death. Commensal bacteria play an important role in anti-tumor immunity, and then liver is continually exposed to gut microbes. However, the role of gut microbes in immune surveillance of liver tumors is still poorly understood. We conducted a study to evaluate the anti-tumor effects of vancomycin in combination with cytokine-induced killer (CIK) cells and programmed cell death 1 (PD-1) antibody in the metastatic liver cancer model.

**Methods:** A20 lymphoma cells (1X10^6) were injected intravenously into the BALB/c mice. Mice were randomly divided into 8 groups of eight mice and received the following treatments: 1) vehicle control, 2) CIK cells (5X10^6/mouse, i.v.), 3) PD-1 antibody (250 µg/mouse, i.p.), 4) CIK cells (5X10^6/mouse, i.v.) plus PD-1 antibody (250 µg/mouse, i.p.), 5) vancomycin (500 mg/kg, PO), 6) vancomycin (500 mg/kg, PO) plus CIK cells (5X10^6/mouse, i.v.), 7) vancomycin (500 mg/kg, PO) plus PD-1 antibody 250 µg/mouse, i.v.) and 8) all of three regimen for 2 weeks. The mice were euthanized at the termination of the experiments and liver samples were subjected to histological and immunohistochemical examination.

**Results:** The vancomycin group showed significantly higher liver weight and nodule counts than other groups compared with control. Conversely, CIK cell group and vancomycin plus PD-1 antibody group showed significantly lower liver weight and nodule counts among those (Table 1).

**Conclusions:** Gut microbes can be used as a pharmabiotics to...
TEAD2 as a Novel Prognostic Factor for Hepatocellular Carcinoma

Jong Seok Ju, Woo Sun Rou, Hyuk Soo Eun, Seok Hyun Kim, Byung Seok Lee
Department of Internal Medicine, Chungnam National University Hospital, Korea

Aims: TEA domain transcription factors (TEADs) have an essential role in tumorigenesis. However, there is little data about TEAD2 expression in hepatocellular carcinoma (HCC). We investigated the expression of TEA domain transcription factor 2 (TEAD2) in hepatocellular carcinoma (HCC) and whether it is correlated with patient prognosis in HCC.

Methods: We obtained mRNA expression data for Hippo pathway genes from 50 normal control and 377 patients with HCC from The Cancer Genome Atlas. We performed gene set enrichment, GeneNeighbors, ClassNeighbors, and survival analyses based on gene expression. We also performed real-time polymerase chain reaction and survival analysis using samples and clinical data from 46 patients with HCC.

Results: TEAD2 and VGLL4 mRNA expression was significantly higher in HCC than in controls; TEAD2 mRNA expression was higher in advanced (TNM stage III/IV) than in early stages (TNM stage I/II). Survival analysis revealed that higher mRNA expression of TEAD2 and VGLL4 was correlated with poor overall survival (P=0.0067 and 0.051, respectively). Clinical analysis revealed an association between higher mRNA expression of TEAD2 and poor recurrence-free survival (P=0.056). In gene set enrichment analysis, patients with higher TEAD2 and VGLL4 mRNA expression showed high epithelial-mesenchymal transition and angiogenesis-related gene expression.

Conclusions: Increased TEAD2 mRNA expression suggests the poor prognosis of patients with HCC. TEAD2 shows potential as a prognostic factor for HCC and novel therapeutic target.

Keywords: TEAD2, Hepatocellular carcinoma, Prognosis

Hsa_circ_0005986 as a Prognostic Biomarker in Hepatocellular Carcinoma

Se Young Jang1, Gyeongbha Kim2, Soo Young Park2, Young-Oh Kweon1, Yu Rim Lee2, Jongwon Seo1, Young Seok Han1, Jaeryung Han1, Heon Tak Ha2, Jae Min Chun2, Eunhye Lee2, Sumin Im3, Jae Kyung Seo2, Jung Gil Park2, Hye Won Lee2, Won Young Tak1, and Keun Hur2

1Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, South Korea; 2Department of Biochemistry and Cell Biology, Cell and Matrix Research Institute, School of Medicine, Kyungpook National University, Daegu, South Korea; 3Department of Surgery, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, South Korea; 4Department of Internal Medicine, College of Medicine, Yewang University, Daegu, South Korea; 5Department of Pathology, Keimyung University School of Medicine, Daegu, South Korea

Aims: Circular RNAs (circRNAs), a class of endogenous RNAs, have been found to interact with microRNAs (miRNAs) or other molecules and regulate gene expression at the transcriptional or posttranscriptional level. Circular RNAs have drawn attention to become potential biomarkers for cancers due to resistance to RNAses. The aim of the study is to analyze the expression of hsa_circ_5986 in hepatocellular carcinoma (HCC) and to investigate its clinical significance.

Methods: We analyzed clinical tissue samples from 162 patients who diagnosed as HCC at Kyungpook National University Hospital. RNAs were extracted from tissue samples according to the Trizol instructions. Circular RNA-specific primers were designed on the junction site, not linear RNA. Circular RNA expression levels were evaluated by quantitative real-time PCR. The association of hsa_circ_5986 expression with clinicopathological features and the survival were statistically analyzed.

Results: The mean age of the patients was 60 years (range: 18–88 years), and the majority were male (n=139, 85.8%). The Child-Turcotte-Pugh (CTP) classes were class A for 138 (85.2%) patients and class B for 22 (13.6%) patients. Seventy-three cases of HCC were stage I or II and 89 cases were stage III or IV, according to the TNM staging AJCC UICC 8th edition. We revealed that the expression level of hsa_circ_0005986 in hepatocellular carcinoma was decreased according to the cancer stage (P<0.01). In addition, the higher expression of hsa_circ_0005986 was associated with better overall survival (P<0.01, figure A) and progression-free survival (P=0.05, figure B).

Conclusions: Hsa_circ_0005986 can be a potential prognostic biomarker for predicting survival in HCC patients.

Keywords: Circular RNA, Hepatocellular carcinoma, Survival, Biomarker

A. Overall Survival rate according to the hsa_circ_5986 level

![Figure A](image-url)
Prognostic Value of Alpha-Fetoprotein in Patients Who Achieved Complete Response to Transarterial Chemoembolization for Hepatocellular Carcinoma

Jae Seung Lee¹, Wonseok Kang², Dong-Hyun Sinn³, Moon Seok Cho¹, Geum-Yoon Gwak¹, Yong-Han Paik¹, Joon Hyeok Lee¹, Kwang Cheol Koh⁴, Seung Woon Paik⁴, Hwi Young Kim⁵, Tae Hun Kim⁶, Kwon Yoo⁶, Yeonjung Ha⁶, Young Mi Hong⁸, Ki Tae Yoon⁹, Mong Cho¹, Jung Gil Park⁹, Nae-Yun Heo⁹, Young Mi Hong⁹, Ki Tae Yoon⁹, Mong Cho¹, Jung Gil Park⁹, Min Kyu Kang⁹, Soo Young Park³, Young Oh Kweon¹, Won Young Tak³, Se Young Jang³, Beom Kyung Kim¹,², Jun Yong Park³,², Do Young Kim³,², Sang Hoon Ahn³,², Kwang-Hyub Han³,², Seung Up Kim¹,²: The Korean TACE Study Group

¹Department of Internal Medicine, Yonsei University College of Medicine; ²Yonsei Liver Center, Severance Hospital; ³Department of Medicine, Samsung Medical Center; Sungkyunkwan University School of Medicine; ⁴Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul; ⁵Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam; ⁶Department of Gastroenterology, Ajou University School of Medicine, Suwon; ⁷Department of Internal Medicine, Inje University Haeundae Paik Hospital; ⁸Liver Center, Pusan National University Yangsan Hospital, Busan; ⁹Department of Internal Medicine, Yeungnam University Medical Centre, Daegu; ¹⁰Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea

Aims: The prognostic values of alpha-fetoprotein (AFP) in patients with hepatocellular carcinoma (HCC) are well-known. We investigated whether AFP is prognostic in patients with HCC who achieved radiological complete response (R-CR) after trans-arterial chemoembolization (TACE).

Methods: Between 2005 and 2018, 917 patients with HCC (588 treatment-naïve [TN-HCC] and 322 with recurrent HCC after curative resection [R-HCC]) who achieved R-CR after TACE (index date), based on the modified RECIST criteria, were recruited. AFP response was defined as the percentage of baseline AFP and AFP at R-CR.

Table 1. Multivariate analysis for progression-free survival after achieving CR

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCLC B/C vs. 0/A</td>
<td>0.025</td>
<td>1.298 (1.034-1.630)</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>0.001</td>
<td>1.387 (1.152-1.670)</td>
</tr>
<tr>
<td>Baseline AFP &gt; 20 ng/mL</td>
<td>0.597</td>
<td>1.055 (0.866-1.285)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.035</td>
<td>1.281 (1.017-1.562)</td>
</tr>
<tr>
<td>Albumin at CR</td>
<td>0.053</td>
<td>0.858 (0.735-1.002)</td>
</tr>
</tbody>
</table>

Naïve HCC

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCLC B/C vs. 0/A</td>
<td>0.031</td>
<td>1.387 (1.039-1.870)</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>0.430</td>
<td>1.105 (0.862-1.416)</td>
</tr>
<tr>
<td>Baseline AFP &gt; 20 ng/mL</td>
<td>0.416</td>
<td>1.110 (0.863-1.429)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.043</td>
<td>1.349 (1.010-1.802)</td>
</tr>
<tr>
<td>Albumin at CR</td>
<td>0.077</td>
<td>0.840 (0.692-1.019)</td>
</tr>
</tbody>
</table>

Recurrent HCC

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCLC B/C vs. 0/A</td>
<td>0.371</td>
<td>1.175 (0.825-1.675)</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>&lt;0.001</td>
<td>1.892 (1.411-2.537)</td>
</tr>
<tr>
<td>Baseline AFP &gt; 20 ng/mL</td>
<td>0.759</td>
<td>1.052 (0.759-1.458)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.540</td>
<td>1.128 (0.768-1.656)</td>
</tr>
<tr>
<td>Albumin at CR</td>
<td>0.383</td>
<td>0.885 (0.673-1.164)</td>
</tr>
</tbody>
</table>

Table 2. Multivariate analysis for overall survival after achieving CR

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 70</td>
<td>0.004</td>
<td>1.443 (1.123-1.854)</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>0.002</td>
<td>1.405 (1.137-1.737)</td>
</tr>
<tr>
<td>Baseline AFP &gt; 20 ng/mL</td>
<td>0.007</td>
<td>1.467 (1.112-1.956)</td>
</tr>
<tr>
<td>Bilirubin at CR</td>
<td>&lt;0.001</td>
<td>1.401 (1.220-1.608)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.666</td>
<td>0.940 (0.709-1.246)</td>
</tr>
<tr>
<td>Progression free survival</td>
<td>&lt;0.001</td>
<td>0.977 (0.971-0.982)</td>
</tr>
</tbody>
</table>

Naïve HCC

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 70</td>
<td>0.036</td>
<td>1.375 (1.021-1.853)</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>0.006</td>
<td>1.423 (1.107-1.829)</td>
</tr>
<tr>
<td>Baseline INR</td>
<td>0.029</td>
<td>5.052 (1.175-21.715)</td>
</tr>
<tr>
<td>Baseline AFP &gt; 20 ng/mL</td>
<td>0.001</td>
<td>1.738 (1.249-2.419)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.113</td>
<td>0.764 (0.548-1.060)</td>
</tr>
<tr>
<td>Progression free survival</td>
<td>&lt;0.001</td>
<td>0.980 (0.974-0.986)</td>
</tr>
</tbody>
</table>

Recurrent HCC

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple tumors</td>
<td>0.082</td>
<td>1.436 (0.956-2.157)</td>
</tr>
<tr>
<td>BCLC B/C vs. 0/A</td>
<td>0.439</td>
<td>1.214 (0.743-1.985)</td>
</tr>
<tr>
<td>Baseline bilirubin</td>
<td>&lt;0.001</td>
<td>1.420 (1.180-1.709)</td>
</tr>
<tr>
<td>AFP at CR &gt; 20 ng/mL</td>
<td>0.115</td>
<td>1.408 (0.921-2.154)</td>
</tr>
<tr>
<td>AFP response (%)</td>
<td>0.044</td>
<td>1.003 (1.000-1.005)</td>
</tr>
<tr>
<td>Progression free survival</td>
<td>&lt;0.001</td>
<td>0.963 (0.950-0.977)</td>
</tr>
</tbody>
</table>
respectively. During the follow-up period, 390 (66.3%) in TN-HCC and 253 (78.6%) in R-HCC experienced recurrence. In addition, 304 (51.7%) in TN-HCC and 125 (38.8%) in R-HCC died. The median progression-free survival (PFS) in TN-HCC and R-HCC groups was 17.1 and 15.5 months, respectively, whereas the median overall survival (OS) was 56.4 vs. 90.4 months, respectively. In TN-HCC group, AFP at R-CR > 20 ng/mL (hazard ratio [HR]=1.349) and BCLC stage B and C (HR=1.387) independently predicted the shorter PFS (all P<0.05), whereas only multiple tumors independently predicted the shorter PFS in R-HCC group (HR=1.892, P<0.001). In TN-HCC group, baseline AFP > 20 ng/mL (not at R-CR) independently predicted shorter OS (HR=1.738), together with age > 70 years (HR=1.375), multiple tumors (HR=1.423), prothrombin time at baseline (HR=5.052) and shorter PFS (HR=0.980) (all P<0.05). In R-HCC group, AFP response independently predicted shorter OS (HR=1.003), together with higher total bilirubin level (HR=1.450) and shorter PFS (HR=0.963) (all P<0.05).

Conclusions: AFP values at R-CR and at baseline were independently predictive of recurrence and mortality in treatment-naive patients after TACE, respectively. Thus, AFP should be used for more detailed risk stratification even after achieving R-CR after TACE.

Keywords: Hepatocellular carcinoma, Tumor marker, Recurrence, Overall survival

OP-079

Undetectable Viral DNA after Curative Surgery Predicts Favorable Survivals in Patients with Hepatitis B-Related Hepatocellular Carcinoma

Pil Soo Sung1,2, Jeong Won Jang2,3,4, Hyun Yang2,3, Kwon Yong Tak2,3, Hee Chul Nam1,2, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,2, Sang Wook Choi1, Young Kyoun You, Dong Goo Kim1, Sang Wook Choi1

1Department of Internal Medicine, Eunpyeong St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2The Catholic University Liver Research Center, Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 3Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 4Department of Surgery, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

Aims: Recent studies showed increased hepatocellular carcinoma (HCC) recurrence after curative resection in patients with a high serum level of hepatitis B virus (HBV)-DNA at the time of surgery. However, the relationship between tumor recurrence and antiviral response to therapy is still unclear. In this study, we aimed to correlate postoperative viral DNA levels with posthepatectomy long-term survivals in patients with HBV-related HCC.

Methods: A retrospective study was conducted on patients who underwent liver resection between Jan 2003 to Dec 2017 at Seoul St. Mary’s Hospital. The HBV-DNA titer was determined between month 6 and 12 after surgery, as well as long-term tumor recurrence and overall survivals were determined.

Results: Of 320 patients who underwent liver resection and whose baseline and follow-up HBV DNA levels were determined, 225 patients received antiviral treatment. At a median follow-up of 42.1 months, 125 patients (39%) had developed HCC recurrence and 70 patients (22%) had died or underwent salvage liver transplantation. The median time to recurrence was 27.2 months. Among the enrolled patients, 251 (78%) showed undetectable HBV DNA level, 34 (11%) showed low levels of HBV DNA detection (<1000 copies/mL), and 35 (11%) showed high levels of serum HBV DNA (≥1000 copies/mL). There was no significant difference between the two groups of patients who received antiviral treatment or not for either transplantation-free or disease-free survival. Furthermore, baseline HBV DNA level (high, ≥10000 copies/mL; low, <10000 copies/mL) was not associated with postoperative survival outcomes. On the other hand, after comparing survival outcomes between patients by their postoperative serum HBV DNA level, we confirmed that undetectable HBV DNA was a significant protective factor of both disease-free survival (P=0.013) and transplantation-free survival (P=0.002). On multivariate analyses, undetectable HBV DNA was still a significant factor of both disease-free survival (HR = 0.646, 95% CI, 0.438-0.955, P=0.028) and transplantation-free survival (HR = 0.393, 95% CI, 0.237-0.654, P<0.001).

Conclusions: Undetectable viral DNA after curative surgery predicts favorable survivals in patients with HBV-related HCC.

Keywords: Hepatocellular carcinoma, Hepatitis B virus, Antiviral treatment, Recurrence

OP-080

Prognosis and Survival Outcomes According to Body Mass Index in Hepatocellular Carcinoma Patients: An Analysis of a Nationwide Cancer Registry Database

Boram Cha1, Jung Hwan Yu*, Young Ju Suh1, Bo-Hye Song1, Young-Joo Jin1, Jin-Woo Lee1

1Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, Incheon, South Korea; 2Department of Biomedical sciences, College of Medicine, Inha University, Incheon, South Korea

*Corresponding Author

Aims: Body mass index (BMI) is a value derived from the weight and height of individual, and is known to be closely related to the prognosis and mortality of various disease. The aims of our study is to evaluated the differences of post-treatment overall survival (OS) according to BMI in the patients with hepatocellular carcinoma (HCC), and to determine the meaning of BMI in these patients.

Methods: The archived records of 10,578 HCC patients registered at the Korean Central Cancer Registry from 2008 through
2014 were retrospectively analyzed. In this registry, we selected Barcelona Clinic Liver Cancer (BCLC) 0, A, or B staged HCC patients (n=4,977). We compared normal weight (BMI 18.5-24.9 kg/m², n=1,790) and overweight (BMI 25-29.9 kg/m², n=1,790) patients after propensity score matching (PSM), and analysed the difference of OSs of these patients according to the treatment method.

Results: Among a total of 4,977 HCC patients, 151(3.0%), 3,014 (60.6%), 1,607 (32.3%), and 205 (4.1%) patients had BMI of underweight, normal, overweight, and obesity, respectively. HCC patients showed good prognosis in the order of overweight, normal, obesity, and underweight. However, comparing normal and overweight in HCC patients after PSM, there was no significant difference in survival rate between two groups (P=0.153). In separate analyses of males and females, the overweight had better prognosis than the normal body weight in male (P=0.014), but there was no significant difference in the OS between two groups in females (P=0.156). Overweight patients showed better OS in Transarterial Chemo-embolization (TACE) treatment (P=0.039) compared to normal body weight, but not in surgical resection (P=0.618), radiofrequency ablation (P=0.553), or sorafenib (P=0.241).

Conclusions: In patients with HCC of BCLC 0-8, overweight patients showed good prognosis, but there was no significant difference between overweight and normal body weight after PSM. However, unlike females, males showed better prognosis in the case of overweight, especially TACE treated patients. Our results carefully suggest that the meaning of normal BMI may be different between males and females in the patients with HCC. Keywords: Gender difference, Treatment in overweight HCC patients

Availability of Tumor Markers in Patients with Pre-treatment State of Hepatocellular Carcinoma

Saerom Kang, Seongwoo Nam, Hyeokchoon Kwon, Jongkyung Choi, Joowon Chung, Jung Shin, Sieun Kim

Department of Internal medicine, National Medical Center, Korea

Aims: To get information about differential diagnosis and clinical assessment, we evaluated quantitative changes of tumor markers (AFP, PIVKA-II) according to size, morphologic changes & clinical courses of tumor.

Methods: Medical records of 566 patients with hepatocellular carcinoma (HCC) were reviewed from 2009, April to 2019, March. 168 patients were excluded due to past anticancer management of other hospital, unconfirmed state, unavailability of both tumor marker within 6 months. Total 398 patients were enrolled. Age of cancer diagnosis, etiologic factor, metastasis or portal vein invasion, tumor size, morphology (single or multinodular, infiltrative, mass form), AFP & PIVKA-II were checked at time of HCC diagnosis. Size was classified as under 3 cm, 3-5 cm and over 5 cm. AFP & PIVKA-II were classified as under normal limit, normal limit~100, 100~1000, over 1000. PIVKA/AFP ratio is calculated for assessment.

Results: Each results were described as followed tables. Under 3 cm, both and each tumor marker’s availability for diagnosis were only 40~50%. But according to tumor size above 3 cm, positive predictive value of tumor markers were increased. Especially PIVKA-II were more useful in larger size (> 5 cm). If we used both marker in larger size HCC (> 5 cm), only 2.5% showed normal tumor marker ranges. AFP levels were not depended on tumor morphology, but PIVKA-II levels were changed to morphology. Infiltrative form showed highest PIVKA-II, and multinodular form showed lowest PIVKA-II. So PIVKA/AFP ratio (≥ 5 & 100) showed differences as infiltrative (77%, 43%), mass (66%, 28%), and multinodular (59%, 17%) forms.

Validation of AJCC 8th Staging System in Patients with Resected Hepatocellular Carcinoma

Sun Young Yim¹, Yoo Jin Lee², Tae Hyung Kim³, Young Sun Lee¹, Sang Jun Suh, Na Yeon Han, Yeon Seok Seo, Ji Hoon Kim, Hyung Joon Yim, Dong Sik Kim, Soon Ho Um

¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, ²Department of Pathology, ³Department of Radiology, ⁴Department of Surgery, Korea University Medical Center, Korea

Aims: The American Joint Committee on Cancer (AJCC) 8th edition staging manual introduced several significant changes to the staging system for hepatocellular carcinoma (HCC). Our study aimed to validate the latest staging system and compare the performance to the previous 7th edition.

Methods: We retrospectively reviewed database of 698 patients with pathologically confirmed stage I-II HCC between year 2003 and 2016 from three institutes. Overall and cancer-specific survival (OS, CSS) analysis were performed using Kaplan-Meier method and compared using log-rank tests. The Harrell concordance index (c index) and Akaike information criterion (AIC) were calculated to compare prognostic powers.
Results: A total 698 patients who had undergone hepatic resection were available for the analysis. The cohort were comprised of T1a (22.5%), T1b (38.4%), T2 (30.1%) T3 (4.2%) T4 (4.9%) stages according to AJCC 8th staging system while T1 (58.3%), T2 (32.7%), T3a (4.2%) T3b (2.9%) T4 (2%) stages according to AJCC 7th staging system. When the AJCC 8th staging system was applied for OS, p-values of pairwise comparisons among all T stages differed significantly (P<0.005) except for T3 and T4 (P=0.137). The AIC value of OS 8th edition staging system were lower than 7th edition (2493.85 and 2500.19, respectively) while c-indices were higher (0.63 and 0.66, respectively) (P=0.005). The AJCC 8th system also performed better for CSS, the AIC value for the 8th edition was 1638.27 while it was 1651.96 for 7th edition and the c-indices were 0.7 and 0.65, respectively (P<0.001).

Conclusions: The latest staging system provided more accurate prognostic information than the previous edition. However, prognostic power of the new staging system for discrimination of T3 and T4 stage should be further validated in a larger cohort.

Keywords: AJCC, Hepatocellular carcinoma, Survival, Prediction

OP-083

HCV Eradication Using Direct-Acting Antivirals Improve Treatment Outcomes in Patients with HCV-Related HCC Treated with TACE: A Multi-Center Retrospective Cohort Study

Seung Up Kim¹, Eun Ju Cho², Soo Young Park³, Young Mi Hong³, Soon Sun Kim⁴, Hwi Young Kim⁴, Nae-Yun Heo⁵, Jung Gil Park⁶, Beom Kyung Kim⁷, Jun Yong Park⁷, Do Young Kim⁸, Sang Hoon Aha⁹, Kwang-Hyub Han⁹, Jeong-Hoon Lee¹⁰, Su Jong Yu¹⁰, Yoon Jun Kim¹⁰, Jung-Hwan Yoon¹¹, Won Young Tak¹², Young Oh Kweon¹², KI Tae Yoon¹², Mong Cho¹², Jee Youn Cheong¹², Seung Ha Park¹²; The Korean TACE Study Group

¹Department of Internal Medicine, Yonsei University College of Medicine, Yonsei Liver Center, Seoul, Korea; ²Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; ³Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea; ⁴Department of Internal Medicine, Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea; ⁵Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea; ⁶Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Republic of Korea; ⁷Departments of Internal Medicine, Inje University College of Medicine, Busan, Korea; ⁸Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Korea

Aims: Direct-acting antiviral (DAA) treatment effectively eradicate chronic hepatitis C virus (HCV) infection. This multicenter, retrospective, cohort study investigated whether HCV eradication using DAA treatment improve treatment outcomes in patients with HCV-related hepatocellular carcinoma (HCC) treated with transarterial chemoembolization (TACE).

Methods: Between 2006 and 2017, patients with HCV-related HCC who achieved sustained virological response (SVR) and treated with TACE within 12 months were recruited. The study population was stratified into two groups: 1) no antiviral treatment (AVT) (n=297 [88.9%], Control group), 2) SVR by pegylated interferon-based AVT (n=10 [3.0%], PR group), and 3) SVR by DAA (n=27 [8.1%], DAA group).

Results: The median age of the study population (244 men and 90 women) was 68.2 years. A total of 297 (88.9%), 10 (3.0%), and 27 (8.1%) patients were stratified into Control, PR, and DAA groups, respectively. During the follow-up period, 251 (75.1%) patients experienced progressive diseases (PD), whereas 230 (68.9) patients were dead. On multivariate analysis, DAA group was independently associated with a reduced risk of mortality (hazard ratio [HR]=0.510, 95% confidence interval [CI] 0.284-0.917, P=0.024) when compared to Control group (reference), whereas cirrhosis (HR=2.787), higher alpha-fetoprotein level (HR=1.000), and maximal tumor size (HR=1.140) were independently associated with an increased risk of PD (all P<0.05). The progression-free survival (PFS) of DAA group was significantly higher than that of Control group (P=0.021 by log-rank test), but similar to that of PR group (P=0.158 by log-rank test). On multivariate analysis, DAA group was independently associated with a reduced risk of mortality (HR=0.350, 95% CI 0.129-0.948, P=0.039) when compared to Control group (reference), whereas older age (HR=1.030), larger maximal tumor size (HR=1.066), multiple tumor (HR=1.619), segmental portal vein thrombosis (HR=2.620), cirrhosis (HR=1.553), and higher alpha-fetoprotein level (HR=1.000) were independently associated with an increased risk of mortality (all P<0.05). The overall survival of DAA group was significantly higher than that of Control group (P=0.006 by log-rank test), but similar to that of PR group (P=0.212 by log-rank test).

Conclusions: DAA treatment prolongs PFS and overall survival in patients with HCV-related HCC treated with TACE.

Keywords: Transarterial chemoembolization, direct-acting antiviral, Hepatitis C, Outcome
**OP-084**

The Study about Immunologic Markers Predicting Efficacy of Locoregional Therapy for Hepatocellular Carcinoma

Sang Youn Hwang, Seon Mi Lee, Jung Woo Im, Ki Jeong Jeon

Dongnam Institute of Radiological & Medical Sciences

**Aims:** We aimed to investigate changing pattern of immunologic factors after locoregional therapy (LRT) (radiotherapy and transarterial chemoembolization and radiofrequency ablation) for hepatocellular carcinoma and discover predictive marker of response of LRT.

**Methods:** Eligible HCC patients were recruited in Dongnam Institute of Radiological & Medical Sciences from July 2017 to December 2017. We performed blood sampling of three times (baseline, 1 day, 1 week, 4 weeks after LRT) and analyzed immunologic markers as followings; CD4+, CD8+, regulatory T cell (Treg), monocyte and granulocyte myeloid derived suppressor cell (mo-MDSC & g-MDSC) in all enrolled patients. Response assessment using both RECIST and modified RECIST criteria were performed after 1 month & 3 months after initial LRT.

**Results:** Thirteen patients were enrolled in the study. Eleven patients were male, two patients were female. The median age was 66 years (range, 48-78) and all patients were in ECOG performance status 0-1. Ten patients had Child A cirrhosis and 5 patients were in BCLC A stage, 6 patients in BCLC B, 2 patients in BCLC C. The median value of AFP is 40.2 ng/mL (range, 2.6-4100), that of PIVKA is 79 mAUL/mL (range 12-695). The median size of tumor were 2.0 cm (range, 0.8-11.2). Nine patients had multiple tumor. The level (%) of mo-MDSC at 1 day after LRT was significantly increased than baseline (7.09 ± 5.85 versus 3.51 ± 3.17, p value = 0.032). The tendency was showed that the level of CD4+, CD8+, CD4+/CD8+ ratio were maximized at 1 week after LRT and those of g-MDSC were maximized at 1 day after LRT. At 1 months after LRT, 4 patients had progressive disease (PD) and 8 patients had complete response (CR). At 3 months after LRT, 10 patients had PD (2 lung metastasis, 8 intrahepatic new lesions) and 3 patients had CR. The level (%) of Treg at 1 day after LRT was significantly increased in patients with CR than PD in 1 months response assessment (7.53 ± 1.41 versus 4.76 ± 0.86, p value = 0.001) and that of Treg and mo-MDSC were significantly increased in patients with CR than lung metastasis in 3 months response assessment (Treg; 6.37 ± 0.31 versus 4.49 ± 0.78, p value = 0.014, mo-MDSC; 3.57 ± 1.67 versus 0.44 ± 0.01, p value = 0.043). The level (%) of baseline CD8+ T cell was significantly increased in patients with CR than PD in 3 months response assessment (31.86 ± 7.34 versus 19.71 ± 7.09, p value = 0.012).

**Conclusions:** Our study suggests that our investigation about maximal immunogenic period after LRT may be meaningful in the era of immunotherapy and the immunologic markers may be predictive tool of treatment response of LRT of HCC. Further well controlled, large scaled study to prove survival benefit using our markers is recommended.

**Keywords:** Hepatocellular carcinoma, Locoregional therapy, Immunologic marker

---

**OP-085**

Development of a New Nomogram Including Neutrophil-to-Lymphocyte Ratio to Predict Survival in Patients with Hepatocellular Carcinoma Undergoing Transarterial Chemoembolization

Hye Kyung Hyun1, Young Eun Chon2, Hana Park2, Yeonjung Ha2, Mi Na Kim1, Beom Kyung Kim1, Joo Ho Lee2, Seung Up Kim1, Do Young Kim2, Sang Hoon Ahn2, Seong Gyu Hwang2, Kwang-Hyub Han2, Kyu Sung Rim2, and Jun Yong Park2

1Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 2CHA Bundang Liver Center, CHA Bundang Hospital, Seongnam, Korea; 3Yonsei Liver Center; Severance Hospital, Seoul, Korea

**Aims:** The neutrophil-to-lymphocyte ratio (NLR) has recently been reported to predict the prognosis of hepatocellular carcinoma (HCC). We explored whether NLR predicted the survival

**Results:** Thirteen patients were enrolled in the study. Eleven patients were male, two patients were female. The median age was 66 years (range, 48-78) and all patients were in ECOG performance status 0-1. Ten patients had Child A cirrhosis and 5 patients were in BCLC A stage, 6 patients in BCLC B, 2 patients in BCLC C. The median value of AFP is 40.2 ng/mL (range, 2.6-4100), that of PIVKA is 79 mAUL/mL (range 12-695). The median size of tumor were 2.0 cm (range, 0.8-11.2). Nine patients had multiple tumor. The level (%) of mo-MDSC at 1 day after LRT was significantly increased than baseline (7.09 ± 5.85 versus 3.51 ± 3.17, p value = 0.032). The tendency was showed that the level of CD4+, CD8+, CD4+/CD8+ ratio were maximized at 1 week after LRT and those of g-MDSC were maximized at 1 day after LRT. At 1 months after LRT, 4 patients had progressive disease (PD) and 8 patients had complete response (CR). At 3 months after LRT, 10 patients had PD (2 lung metastasis, 8 intrahepatic new lesions) and 3 patients had CR. The level (%) of Treg at 1 day after LRT was significantly increased in patients with CR than PD in 1 months response assessment (7.53 ± 1.41 versus 4.76 ± 0.86, p value = 0.001) and that of Treg and mo-MDSC were significantly increased in patients with CR than lung metastasis in 3 months response assessment (Treg; 6.37 ± 0.31 versus 4.49 ± 0.78, p value = 0.014, mo-MDSC; 3.57 ± 1.67 versus 0.44 ± 0.01, p value = 0.043). The level (%) of baseline CD8+ T cell was significantly increased in patients with CR than PD in 3 months response assessment (31.86 ± 7.34 versus 19.71 ± 7.09, p value = 0.012).

**Conclusions:** Our study suggests that our investigation about maximal immunogenic period after LRT may be meaningful in the era of immunotherapy and the immunologic markers may be predictive tool of treatment response of LRT of HCC. Further well controlled, large scaled study to prove survival benefit using our markers is recommended.

**Keywords:** Hepatocellular carcinoma, Locoregional therapy, Immunologic marker
of patients with HCC undergoing transarterial chemoembolization (TACE), and developed a predictive model.

**Methods:** In total, 1,697 patients with HCC undergoing TACE as first-line therapy at two university hospitals were enrolled (derivation set n=921, internal validation set n=395, external validation set n=381). The tumor Size, tumor Number, AFP level, Vascular invasion, Child-Pugh score, Objective Response after TACE, and NLR were used as predictors of overall survival (OS) via multivariate Cox's regression model, were incorporated into a 14-point risk prediction model (SNAVCORN score).

**Results:** The time-dependent areas under the receiver-operating characteristic curves for OS at 1, 3, and 5 years predicted by the SNAVCORN score were 0.812, 0.734, and 0.700 in the derivation set. Patients were stratified into three risk groups by ABCRN score (low, 0–4; intermediate, 5–9; high, 10–14). Compared with the low-risk group, the intermediate-risk [HR 3.10, P<0.001] and high-risk (HR 7.37, P<0.001) groups exhibited significantly greater mortality.

**Conclusions:** The prognostic performance of the SNAVCORN score including NLR in patients with HCC treated with TACE was remarkable, much better than those of the conventional scores. The SNAVCORN score will guide future HCC treatment decisions.

Table 2. Prognostic factors for overall survival and risk score calculation in the derivation cohort (n=921)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Uni</th>
<th>Multi</th>
<th>SNAVCORN Risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh Score</td>
<td>0.03</td>
<td></td>
<td>3.710 (1.865-7.411)</td>
</tr>
<tr>
<td>NLR</td>
<td>0.03</td>
<td></td>
<td>0.817 (0.698-0.960)</td>
</tr>
<tr>
<td>MRI</td>
<td>0.03</td>
<td></td>
<td>1.030 (0.646-1.679)</td>
</tr>
</tbody>
</table>

**Keywords:** Hepatocellular carcinoma, Transarterial chemoembolization, Neutrophil-to-lymphocyte ratio, Risk-prediction model

---

**OP-087**

Effectiveness of Dose Reduction of Sorafenib on HCC Treatment: A Real Life Multicenter Data Analysis

Kwon Yong Tak, Jeong Won Jang, Pil Soo Sung, Hee Chul Nam, Jong Young Choi, Seung Kew Yoon, Jin Mo Yang, Chang Wook Kim1, Hee Yeon Kim1, Seung Won Lee2, Hae Rim Lee3, U Im Chang3, Do Seon Song3, Jung Hyun Kwon4, Sun Hong Yoo5, Sang Wook Choi5, Myeong Jun Song5, Seok Hwan Kim6

Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, 1Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, The Catholic University of Korea, Uijeongbu, Korea, 2Department of Internal Medicine, Bucheon St. Mary’s Hospital, The Catholic University of Korea, Uijeongbu, Korea, 3Department of Internal Medicine, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea, Siwon, Korea, 4Department of Internal Medicine, Incheon St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea,

**Aims:** Nivolumab is an immune checkpoint inhibitor approved for the second-line therapy for advanced HCC. The aim of this study is to describe our experience with nivolumab in patients who have progressed on or been intolerant of prior sorafenib.

**Methods:** Forty-two patients with advanced HCC receiving nivolumab (3mg/kg intravenously every 2 weeks) were enrolled between October 2017 and November 2018. Assessment of response was based on the Immune-Modified Response Evaluation Criteria in Solid Tumors (iRECIST) and RECIST version 1.1 every 8 weeks.

**Results:** The median age of patients was 61 years. Portal vein invasion and extrahepatic spread was present in 38% and 76%, respectively. The median duration of nivolumab treatment was 76 days. Six out of 42 patients are on treatment, while 36 patients stopped treatment because of disease progression, serious toxicity, treatment refusal and discontinuance after achieving a complete response (CR). For evaluating tumor response, one showed CR; 7 (16.7%) partial response; 9 (21.4%) stable response; 1 immune unconfirmed progression and 24 (57.1%) immune confirmed progression. Three patients were continued to receive nivolumab after first response of progression due to a possibility of pseudo-progression and finally confirmed as progressed disease. Median duration of response was 80 days. The 3- and 6-month disease control rate were 47.0% and 23.5%, respectively. Median OS was 242 days and median progression free survival (PFS) was 108 days. Survival rate and PFS rate at 6 months were 55.6% and 29.0%, respectively. Common adverse reactions included abdominal discomfort (29%), skin eruption or pruritus (24%), general weakness (14%), fatigue (10%). The grade 3 adverse events included hepatotoxicity, azotemia, hematocrit, hyperbilirubinemia, hypercalcemia, and pneumonitis.

**Conclusions:** In real life practice of a single center, nivolumab as an above second-line therapy appears to have meaningful efficacy and acceptable tolerability in patients with advanced HCC. Further follow-up studies are warranted.

**Keywords:** Advanced HCC, Nivolumab

---

**OP-086**

Outcome and Safety of Second or Third-Line Nivolumab Treatment in Real Life: A Single Center Experience

Soo Jeong Koh, Ji Hee Park, Joong-Won Park1, Bo Hyun Kim, Ju Hee Lee, Young Hwan Koh, Chang-Min Kim

Center for Liver Cancer and Pancreatobiliary Cancer, National Cancer Center Goyang, Republic of Korea

**Aims:** Nivolumab is an immune checkpoint inhibitor approved...
Aims: Currently, there is a lack of general agreement on sorafenib dosing. This study is a large real-life cohort study aiming to evaluate whether sorafenib dosing would affect patient outcomes.

Methods: A total of 782 patients treated with sorafenib between 2008 and 2017 were evaluated for sorafenib dosing. Sorafenib dose was recorded daily during admission by counting number of remaining pills and questionnaires during regular follow up for out-patients. Clinical outcome measures were analyzed according to dose modification. Primary outcomes were overall survival and time to progression.

Results: Median survival of patients was 5.2 months. In multivariate analysis, dose reduction had significant benefit on overall survival (P=0.019) and progression-free survival (P=0.034). In subgroup analysis, there were no significant difference in overall and progression-free survival between the 800-to-600 mg group and the 800-to-400mg group. Both hand-foot syndrome (P=0.049) and drug discontinuation due to adverse events (P=0.003) were more frequent in the 800-to-600 vs. 800-to-400 mg group. Dose reduction to 200 mg significantly reduced overall survival (P=0.014) and progression-free survival (P=0.025). Dose reduction significantly increased both medication duration (P<0.001) and cumulative dose (P<0.001). In subgroup analysis, the 800-to-400 mg group had significantly longer duration (P<0.001) and higher cumulative dose (P=0.02) than the 800 mg-maintained group. The benefits from dose reduction persisted in subgroup analysis of good responders.

Conclusions: In HCC patients treated with sorafenib, appropriate dose reduction may lead to longer overall and progression-free survival by increasing adherence coupled with higher cumulative dose. Based on our data, dose reduction of sorafenib from 800 mg to 400 mg rather than 600 mg is suggested. Dose reduction to 200 mg is not recommended.

Keywords: Sorafenib, Hepatocellular carcinoma, Dose reduction

OP-088

Serum Exosomal microRNA-10b-5p as a Potential Biomarker of Early Stage Hepatocellular Carcinoma

Hyo Jung Cho1, Jung Woo Eun2, Baek Geum Ok1, Chul Won Seo1,2, Hye Ri Ahn1, Young-Iwan Ahn1, Jinhee Jung1, Soon Sun Kim1, Sung Won Cho1, and Jae Youn Cheong1

Department of Gastroenterology, Ajou University School of Medicine, Suwon, South Korea; Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, South Korea

Aims: There is no reliable serum biomarker for screening early Hepatocellular carcinoma (HCC). Exosomal microRNA has been highlighted as promising cancer biomarker. This study aimed to find reliable serum biomarker of early HCC by using small RNA sequencing of HCC cell derived exosome (HEX).

Methods: Exosomes from human HCC cell lines (Hep3B and Huh-7) and immortalized normal hepatocyte cell line (THLE-2) were isolated and small RNAs were extracted. Differentially expressed exosomal microRNAs between HEX and normal hepatocyte were screened by using Illumina Hiseq2000 deep sequencing. To select potential candidate of biomarker among the overexpressed microRNAs in HEX, TCGA data was analyzed. For validation of clinical usefulness of the exosomal microRNAs, RT-PCR was performed in the independent liver disease cohort including 18 normal control, 19 chronic hepatitis B (CHB) patients, 20 liver cirrhosis (LC) patients, 20 early stage HCC (modified UICC stage I), 19 advanced HCC patients (modified UICC stage III or IV).

Results: A total of 49 overexpressed exosomal microRNA in HEX more than 1.5 folds compared to normal hepatocyte were identified. TCGA data was analyzed to select the candidate microRNAs among the 49 microRNAs. In the analysis of TCGA data, microRNA-10b-5p, microRNA-18a-5p, microRNA-215-5p, and microRNA-940 were identified as significantly overexpressed microRNAs in HCC tissue, and they also associated with HCC patient's prognosis. RT-PCRs of the 4 microRNAs were performed in the independent cohort for validation of clinical usefulness of the candidate biomarkers. As a result, serum exosomal microRNA-10b-5p was significantly overexpressed in early and advanced HCC patients compared to the patients with CHB or LC (Fig.1). In the comparison of area under the curve (AUC) between hepatocellular carcinoma (HCC) groups (early and advanced HCC) and control groups (normal control and CHB), the AUC of serum exosomal microRNA-10b-5p was significantly higher in early and advanced HCC patients compared to control groups (Fig.2).
Multicenter Retrospective Analysis of the Efficacy of Regorafenib after Progression on Sorafenib with Hepatocellular Carcinoma

Ha Seok Lee¹*, Sung Won Chang¹, Min Jin Lee¹, Sehwa Kim¹, Young-Sun Lee¹, Young Kuk Jung¹, Sang Jun Sul¹, Ji Hoon Kim¹, Yeon Seok Seo¹, Hyung Joon Yim¹, Jong Eun Yeon¹, Kwan Soo Byun¹, SB Cho², SY Hwang³, HW Lee⁴, Young Chang⁵, Jae Young Jang⁶

Department of Internal Medicine, Korea University College of Medicine, Chonnam National University Hwasun Hospital, Dongnam Inst. of Radiological Medical Sciences, Gangnam Severance Hospital, Soonchunhyang University, Republic of Korea

Introduction: Regorafenib has been proved as 2nd line systemic therapy for hepatocellular carcinoma (HCC) patients with progression after sorafenib through 3 phase trial improving survival compared to placebo. Nevertheless, real-world data are needed to assess clinical outcomes in the practice. We analyzed the real-world data to assess clinical outcomes in the practice.

Methods: This study was a multicenter, non-comparative, retrospective cohort study. Between July 2017 and May 2019 in seven Korean institutions (Korea University College of Medicine, Chonnam National University Hwasun Hospital, Korea Cancer Center Hospital, Gangnam Severance Hospital, Soonchunhyang University Hospital), patients with HCC who had evidence of disease progression on sorafenib were eligible for inclusion in this study. A total of 133 Patients who received at least one dose of regorafenib were included in this analysis. Tumor response was assessed according to modified RECIST criteria. Kaplan-Meier method and Cox regression were used for survival analysis.

Results: Their median age was 60 years, and most patients (n=112, 84.2%) were male. Hepatitis B virus (n=91, 68.4%) infection was the most common etiology of HCC. Except for 2 patients (1.5%) with Child-Pugh B (n=1) and C (n=1), all patients were classified as Child-Pugh A at the time of initiation of regorafenib. 113 patients (84.9%) had extrahepatic metastasis, with the most common metastatic site being the lungs (n=77, 57.8%), followed by the bones (n=32, 24%), adrenal glands (n=11, 8.2%) and vascular invasion (n=56, 42.1%). We assessed a best response for 112 patients with at least one follow up imaging studies. Three patients (2.6%) achieved CR, and 11 patients (9.8%) achieved PR. Objective response rate was 12%. SD and PD were the best responses in 25 (22.3%), and 71 (63.3%) patients, respectively. The disease control rate was was 32.1%. The median overall survival (OS) was 10.03 months, and the median progression-free survival (PFS) was 2.7 months. Four out of 8 variables were indentified statistically significant in univariate logistic regression analysis for OS and PFS. These 4 significant variables entered multivariate logistic regression analysis. As a result, There was an association with increased overall survival risk if the Child-pugh score was higher than 5 [OR (95% CI)=3.638 (1.797-7.361), P=0.000] or AFP was higher than 400 [OR (95% CI)=3.750 (1.797-7.361), P=0.001] and decreased OS risk if the Sorafenib TTP was above the median (3.7 mo) [OR (95% CI)=0.395 (0.195-0.803), P=0.01]. The risk of PFS decreases when Sorafenib TTP was above the median (3.7 mo) [OR (95% CI)=0.571 (0.376-0.869), P=0.009] and increases when HCC extent was more than half of liver [OR (95% CI)=1.683 (1.068-2.653), P=0.025].

Conclusions: Regorafenib was effective in patients with advanced HCC who progressed on first-line sorafenib in real-life setting consistent with the efficacy of the previous controlled clinical trial. TTP on first-line sorafenib, Child pugh score, AFP and HCC extent were independent predictor of the prognosis for regorafenib.

Keywords: Hepatocellular carcinoma, Exosome, MicroRNA, Sequencing

Figure 1. Kaplan-Meier curves for OS and PFS

Keywords: Hepatocellular carcinoma, Regorafenib, Sorafenib

Appraisal of Transarterial Chemoembolization Refractoriness in Patients with Hepatocellular Carcinoma

Jonggi Choi, Danbi Lee, Ju Hyun Shim, Kang Mo Kim, Young Suk Lim, Yung Sang Lee, and Han Chu Lee

Department of Gastroenterology, Asan Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Aims: In real-world practice, transarterial chemoembolization (TACE) has been widely used for treating hepatocellular carcinoma (HCC) beyond, as well as within, guideline recommen-

(AUROC) for early HCC diagnosis, exosomal microRNA-10b-5p (AUROC=0.992) shows significantly higher diagnostic accuracy compared to AFP (AUROC=0.695). (P=0.0002) (Fig.2)

Conclusions: Serum exosomal microRNA-10b-5p is promising biomarker to detect early HCC.

Keywords: Hepatocellular carcinoma, Exosome, MicroRNA, Sequencing

Validation of Prognostic Impact of ADV Score for Resection of Hepatocellular Carcinoma: An Analysis Using Nationwide Korea Liver Cancer Registry Database

Yohan Park¹, Shin Hwang²

¹Department of Surgery, Busan Baik Hospital, Inje University College of Medicine, Busan, Korea; ²Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Aims: We validated the prognostic power of ADV score (alpha-fetoprotein-des-γ-carboxyprothrombin (DCP)-tumor volume score: (AFP (ng/ml) x DCP [PIVKA-II] (mAU/mL) x tumor volume (mL): expressed in log10) for predicting risk of hepatocellular carcinoma (HCC) recurrence after hepatic resection (HR).

Methods: This study included 1526 patients who underwent HR for solitary HCC between 2008 and 2012 and followed up until December 2016. They were registered to the Korean cancer registry database. We selected the only patients who underwent HR as the first treatment of HCC.

Results: During follow-up, 349 patients (22.8%) died due to HCC recurrence. Distribution of ADV scores were < 2log in 25 (1.6%), 2-3log in 175 (11.4%), 3-4log in 318 (20.8%), 4-5log in 309 (20.2%), 5-6log in 240 (15.7%), 6-7log in 156 (10.2%), 7-8log in 113 (7.4%), 8-9log in 93 (6.1%) and >9log in 97 (6.4%). Patient survival rate was closely correlated with ADV score (P<0.001). 5-year patient survival rate was around 90% in ADV score of 2log, 85% in ADV score of 4log, 75% in ADV score of 6log, 60% in ADV score of 8log and 50% in ADV score of >8log (P<0.001). These ADV score-dependent prognostic stratification was quite well matched with the previously reported results from single center and multicenter studies.

Conclusions: Our results using a high-volume HCC cohort confirmed that ADV score is an integrated surrogate prognostic biomarker which can be reasonably applicable to the patients undergoing HR for HCC.

Keywords: Cohort, ADV score, Tumor marker, Resection

OP-091

Better Prediction of Outcomes by Response Evaluation Using the Modified RECIST Compared with the RECIST 1.1 in Patients with HCC Treated with Yttrium-90 Radioembolization

Hong Jun Choi¹, Jae Seung Lee², Beom Kyung Kim, Jun Yong Park, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, Yong Eun Chung, Song-Ee Baek, Mi-Suk Park, Myeong-Jin Kim, Hyungjin Rhee², and Seung Up Kim²

Yonsei University College of Medicine

Background/Aims: The response evaluation criteria in solid tumours 1.1 (RECIST 1.1) have been commonly used for response evaluation of solid tumours including hepatocellular carcinoma (HCC). Because of the importance of the remaining ‘viable cancer tissue’ of HCC, the modified RECIST (mRECIST) have been adopted for HCC response evaluation. However, few studies have investigated which response evaluation method is better for predicting the treatment outcomes of HCC. Thus, we compared the performance of the RECIST 1.1 and mRECIST for predicting survival rates in patients with HCC treated with transarterial radioembolisation (TARE) using Yttrium-90 (90Y).

Methods: Between 2012 and 2017, 102 patients with unresectable intrahepatic HCC treated with TARE were reviewed retrospectively. The RECIST 1.1 and mRECIST were used to evaluate the treatment responsiveness of HCC to TARE at 1, 3 and 6 months after TARE. A responder was defined as the sum of either a complete or partial response by each method.

Results: The median age of the study patients (92 males and 19 females) was 64.1 years. The median alpha-fetoprotein and des-gamma-carboxyprothrombinin levels were 42.0 ng/mL and 1693.5 mAU/mL, respectively. The median maximal tumor size was 8.3 cm, and multiple tumours were observed in 41 (36.3%) patients. During the follow-up period (median 20.7 months), 21 patients (20.6%) died, with a median survival of 32.5 months. Using the mRECIST, the treatment responders at 1, 3 and 6 months following TARE showed significantly better survival rates compared with the non-responders (hazard ratio [HR]=5.736, log-rank P=0.008 at 1 month; HR=3.145, P=0.022 at 3 months, and HR=2.887, P=0.061 at 6 months). In contrast, using the RECIST 1.1, the treatment responders at 1, 3 and 6
Preoperative Transcatheter Arterial Chemoembolization for Surgical Resection of Huge Hepatocellular Carcinoma (≥ 10 cm): A Multicenter Propensity Matching Analysis

Chao Li1, Lei LIANG1, Ming-Da WANG1, Han WU1, Jiong-Jie YU1, Timothy M. PAWLIK2, Wan-Guang ZHANG1, Yao-Ming ZHANG1, Ya-Hao ZHOU1, Wei-Min GU1, Hong WANG1, Ting-Hao CHEN1, Jun HAN1, Hao XING1, Zhen-Li LI1, Wan Yee LAU1, Meng-Chao WU1, Feng SHEN1, Tian YANG2

1Department of Hepatic Surgery, Shanghai Eastern Hepatobiliary Surgery Hospital, China; 2Department of Surgery, Ohio State University, Wexner Medical Center, Columbus, USA.

Aims: We sought to evaluate the impact of preoperative TACE with perioperative outcomes, long-term overall survival (OS) and recurrence-free survival (RFS) after liver resection of huge HCCs (≥ 10 cm).

Methods: Using a multicenter database, consecutive patients who underwent curative-intent resection for huge HCC with- out macrovascular invasion between 2004 and 2014 were identified. The association between preoperative TACE with perioperative outcomes, long-term overall survival (OS) and recurrence-free survival (RFS) was assessed before and after propensity score matching (PSM).

Results: Among the 377 enrolled patients, 88 patients (23.3%) received preoperative TACE. The incidence of perioperative mortality and morbidity was comparable among patients who did and did not undergo preoperative TACE (3.4% vs. 2.4%, P=0.704, and 33.0% vs. 31.1%, P=0.749, respectively). PSM analysis created 84 matched pairs of patients. In examining the entire cohort as well as the PSM cohort, median OS (overall cohort: 32.8 vs. 22.3 months, P=0.035, and PSM only: 32.8 vs. 18.1 months, P=0.023, respectively) and RFS (12.9 vs. 6.4 months, P=0.016, and 12.9 vs. 4.1 months, P=0.009, respectively) were better among patients who underwent preoperative TACE versus patients who did not. After adjustment for other confounding factors on multivariable analyses, preoperative TACE remained independently associated with a favorable OS and RFS after resection of huge HCC.

Conclusions: Preoperative TACE did not increase perioperative morbidity or mortality, yet was associated with an improved OS and RFS after liver resection of huge HCC.

Optimal Timing of Radiotherapy for Incomplete Transarterial Chemoembolization in BCLC Stage B Hepatocellular Carcinoma

Hwa Kyung Byun, Nalee Kim, Jinsil Seong

Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Aims: Efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE) has been documented through many reports. However, optimal timing of RT still remains unanswered. This study was to investigate the optimal time to start RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC).

Methods: During 2001-2016, 112 patients with BCLC-B HCC were treated with RT for 116 lesions after incomplete TACE. Through the medical records review, the time-interval between the last TACE and the start of RT was examined. The optimal cut-off of time-interval to maximize the difference in local failure-free rate (LFFR) was determined using the maximally selected rank statistics.

Results: In total patients, the median overall survival was 17.9 months. The median age was 59 years (range, 34–83 years), the median tumor size was 6 cm (range, 1–20 cm), and the median number of the tumor was 1 (range, 1–9). The median number of TACE on the target lesion before RT was 2 (range, 1–7). We found 5 weeks as the optimal cut-off value of time interval, which we classified patients groups as consolidation RT (cRT) for earlier than 5 weeks and salvage RT (sRT) for later than 5 weeks. Of 116 lesions, 69 lesions (59.5%) and 47 lesions (40.5%) underwent cRT and sRT, respectively. The median tumor size was larger in the cRT group (7.2 cm vs. 5.3 cm; P=.045). In the cRT group, the 1-year and 2-year LFFRs were 94.6% and 79.5%, respectively, and in the sRT group, those were 70.6% and 50.7%, respectively (P=.005). In multivariate analysis, cRT independently predicts favorable LFFR (hazard ratio, 4.15; 95% confidence interval, 1.56–10.86; P=.005).

Conclusions: We found optimal timing of RT for incomplete TACE as within 5 weeks after TACE. Early application of RT within 5 weeks after TACE was associated with better local control.
Validation of ADV Score as a Quantifiable Prognostic Biomarker for Hepatocellular Carcinoma Recurrence after Liver Transplantation

Shin Hwang, Yong-Kyu Chung, Chul-Soo Ahn, Ki-Hun Kim, Deok-Bog Moon, Tae-Yong Ha, Gi-Won Song, Dong-Hwan Jung, Gil-Chun Park, Young-In Yoon, Sung-Gyu Lee
Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Aims: We assessed the prognostic power of ADV score (alpha-fetoprotein-DCP-tumor volume: score (AFP (ng/ml) x DCP [PIVKA-II] (mAu/mL) x tumor volume (mL): expressed in log_{10}) for predicting risk of hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT). In patients with multiple tumors, total tumor volume was calculated as the volume of the largest tumor multiplied by tumor number.

Methods: This study include 668 recipients who underwent LT for HCC between 2007 and 2013 and followed up until 2018. Patients showing complete pathological response after pretransplant locoregional treatment were excluded. Tumor recurrence rate and patient survival rate were assessed according to ADV score.

Results: During follow-up, 151 patients (22.6%) showed HCC recurrence and 147 patients (22.0%) died due to HCC recurrence. Distribution of ADV scores were < 2log in 38 (5.7%), 2-3log in 115 (17.2%), 3-4log in 188 (28.1%), 4-5log in149 (22.3%), 5-6log in 85 (12.7%), 6-7log in 56 (8.4%), 7-8log in 19 (2.8%) and >8log in 18 (2.6%). Tumor recurrence rate and patient survival rate were closely correlated with ADV score (P<0.001). 5-year patient survival rate was around 85% in ADV score of 3log, 75% in ADV score of 5log, 50% in ADV score of 7log and 20% in ADV score of 8log (P<0.001). These ADV score-dependent prognostic stratification was well maintained in subgroup analyses with pretransplant locoregional treatment group and multiple tumor group (P<0.001).

Conclusions: Our results suggest that ADV score is an integrated surrogate prognostic biomarker which can be reasonably applicable to LT recipients with HCC.

Keywords: Recurrence, Tumor marker, Hepatocellular carcinoma, Biomarker

Incidence and Risk Factors for Herpes Zoster after Adult Liver Transplantation

Seohhee Lee, Sangjin Kim, Jongwook Oh, Young Jae Jeong, Jinsoo Rhu, Kyung Sik Kim, Jisoo Lee, Gyu-sung Choi, Jong Man Kim, Jae-Won Joh
Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: Herpes zoster (HZ) is caused by reactivation of the varicella zoster virus, which occurs frequently in liver transplant recipients with impaired cellular immunity. The purpose of this study was to evaluate the incidence and risk factors for HZ after adult liver transplantation (LT).

Methods: In our institution, 993 patients underwent adult LT from January 1997 to December 2013. We retrospectively analyzed the incidence rate of HZ and risk factors for HZ after LT.

Results: Of 993 LT recipients, 101 (10.2%) were diagnosed with HZ. The incidence of HZ at 1, 3, 5, and 10 years was 6.6%, 9.1%, 10.0%, and 11.9%, respectively. Therefore, we observed that the incidence of HZ after LT was 16.3 per 1,000 personyears. Older age (≥50 years) at LT and mycophenolate mofetil (MMF) exposure were independent risk factors of HZ infection after adult LT.

Conclusions: Patients older than 50 years or with MMF exposure are considered to be at high risk for HZ. Therefore, adult liver recipients with such factors should not be given strong immunosuppression treatments.

Keywords: Herpes zoster, Liver transplantation

Dextroplantation of Left Liver Graft in Infants

Nam-Joon YI, Suk Kyun HONG, Jeong-Moo LEE, Jae-Hyung CHO, Kwang-Woong LEE, Kyung-Suk SUH
Surgery, Seoul National University College of Medicine, Republic of Korea

Aims: The position of the left side liver graft is important which could lead complications of the hepatic vein (HV) and portal vein (PV) especially in small children using variants of left lateral section (vLLS) graft. The purpose of this study was to evaluate the outcome of novel technique of implantation to the right side (dextroplantation) of vLLS in infants.

Methods: From 2015 to 2016, 8 consecutive infants underwent dextroplantation using a vLLS graft (Group D). The graft was implanted to right side of the recipient after 90 degree counter clockwise rotation; graft left HV was anastomosed to IVC using the
OP-098

Effect of Everolimus on Hepatocellular Carcinoma Recurrence after Liver Transplantation
Dong Jin JOO, Jae Geun LEE, Dae Hoon HAN, Gi Hong CHOI, Jin Sub CHOI, Myoung Soo KIM, Soon Il KIM
Department of Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: This study was retrospectively conducted to reveal the effect of everolimus (EVR) particularly in the HCC patients who underwent liver transplantation (LT).

Methods: Total 311 HCC patients underwent LT during the study period. We divided the patients into two groups; TAC group and EVR group. TAC group maintained their TAC blood level around 5-8 ng/mL. EVR blood level was around 3-5 ng/mL with low dose TAC < 5 ng/mL. We compared the oncologic outcomes.

Results: Seventy-seven recipients (24.8%) had tumors above Milan criteria (MC) before LT. The number of EVR group was 114 (36.7%), TAC group was 197 (63.3%). More LDLTs were performed in EVR group (78.1%) than TAC group (65.0%; \( P=0.015 \)). EVR group included more patients with above MC than TAC group (32.5% vs 10.3%, \( P=0.020 \)). However, HCC recurrence happened more in TAC group than in EVR group (19.3% vs 9.6%, \( P=0.025 \)). EVR group showed better outcomes both in recurrence-free survival and overall patient survival rates (\( P=0.029 \) and \( P<0.001 \), respectively). EVR group within MC showed better recurrence-free survival than TAC group, but there was no significant difference between two groups who had tumors beyond MC. However, in the overall patient survival rates, EVR group showed better outcomes than TAC group regardless of their tumor status. In the Cox regression analysis, EVR was an independent factor decreasing risk of HCC recurrence after LT (HR: 0.352, \( P=0.003 \)).

Conclusions: EVR-based immune suppression showed better oncologic outcomes after LT for HCC patients and was an independent factor decreasing the risk of HCC recurrence.

OP-099

Minimal Invasive Living Donor Right Hepatectomy: An Experience of Consecutive 114 Cases by a Single Surgeon
Sang Hyun KANG, Dong Hwan JUNG, Hwui Dong CHO, Shin HWANG, Ki Hun KIM, Chul Soo AHN, Tae Yong HA, Gi Won SONG, Gil Chun PARK, Young In YOON, Jae Hyun KWON, Yong Kyu CHUNG, Su Min HA, I Ji JUNG, Jin Uk CHOI, Sung Gyu LEE, Deok-Bog MOON
Division of Hepatobiliary Surgery and Liver Transplantation, Asan Medical Center, Republic of Korea

Aims: Because the donor is not performed operation under pathologic condition, it is important to consider the quality of life such as cosmetic effect. The aim of this study was to evaluate the safety and feasibility of minimal invasive living donor right hepatectomy.

Methods: All consecutive cases of minimal invasive living donor right hepatectomy between January 2014 and March 2018 in a tertiary referral hospital were enrolled in this retrospective cohort study. All surgical procedures were performed by one surgeon. All patients underwent subcostal incision and incision length was applied flexibly according to the weight of the graft (9-12 cm). The group was analysed in terms of donor demographics, preoperative data, postoperative outcomes.

Results: The mean age of the donors was 27.4 ± 6.7 years, the gender ratio for men and women was 18:96. The mean operative time was 402.5 ± 78.8 minutes and mean postoperative hospital stay was 10.1 ± 1.7 days. The number of complications was 6 cases (5.3%) and among them, the Clavien-Dindo classification III or higher complication was 2 (1.8%). There were no mortality cases.

Conclusions: Minimal invasive living donor right hepatectomy was a safe and feasible procedure for donors. It showed an acceptable incidence of complications. The authors suggest that minimal invasive living donor right hepatectomy could be a reasonable operative option for donors in terms of cosmetic effect.

OP-100

The Protective Effect of Antioxidants against Hepatic Ischemia Reperfusion Injury in Rat
Min-Su Park
Department of Surgery, Kyung Hee University, Korea

Aims: Hepatic ischemia reperfusion (I/R) injury is a major complication of liver surgery, including hepatic surgery, liver transplantation, and trauma. Antioxidants including citric acid, cassia tora and hesperidin reduces oxidative stress and inflammation during hypoxia and reoxygenation. Our objective was to investigate the protective effect of antioxidants against hepatic I/R injury in rat.

Methods: We fed Sprague-Dawley rats citric acid, cassia tora
Factors Predicting Cholestasis in Post Right Lobe Donor Hepatectomy in the Era of Standardized Donor Selection Protocols: Analysis of 340 Donors over 19 Months

Naganathan SELVAKUMAR, Subash GUPTA
Liver Transplantation and HPB Surgery, Max Superspeciality Hospital, India

Aims: Despite over 10000 LDLTs completed worldwide the Right lobe donation continues to carry high risk donation status. Of all the reported donor mortalities post-operative liver failure secondary to small remnant is still the highest. Hence we analyzed the factors which leads to post donor hepatectomy cholestasis (PDHC).

Methods: Retrospective analysis of 340 donors during the time period of 06-02-2017 to 12-09-2018 was done. Our group has experience of 2800 LDLTs with zero donor mortality. Data analysis was done based on two cut off values of Total bilirubin (TB) one based on the median of Peak bilirubin (PB) of the study cohort and another based on 5 mg % which is universally accepted as the cut off for defining post-operative liver failure and small for size syndrome.

Results: On analysis 2.3 mg % was found to be the median PB. With 2.3 mg% cut off Day -1 TB, Day -5 TB, POD to normal TB, Peak INR, % of liver remnant were statistically significant @ P<0.05. On analysis with 5.0 mg % cut off Male gender, BMI, Blood Group-O, Area of middle hepatic vein congestion, Day -3 INR, peak INR, Day -1 TB, Day -5 TB, POD to Normal TB and Hospital Stay were statistically significant @ P<0.05.

Conclusions: High risk for PDHC includes Males, High BMI, Blood Group “O” and high middle hepatic vein congestion area. Peak INR and POD -3 INR were significantly higher in this group. They tend to have significantly higher TB on POD-1, POD-3 and PB along with prolonged hospital stay.

Oncologic Outcome of Two Stage Hepatectomy in Patients with Bilobar Multiple Colorectal Liver Metastases

Jin Hong Lim¹, Sung Whan Cha², Dai Hoon Han², Gi Hong Choi², Dong Sup Yoon², Jin Sub Choi¹
Department of Surgery, ¹Yonsei University College of Medicine, Gangnam Severance Hospital, ²Yonsei University College of Medicine, Severance Hospital

Aims: Two stage hepatectomy has been widely performed for last decades as the paradigm of definition of resectability has shifted. There are many studies that advocate the efficacy of two stage hepatectomy, but rare reports that practically compare the oncologic outcome between surgical group and non-surgical group.

Methods: From January 2010 to November 2018, 51 patients were planned for 2 stage hepatectomy and 43 patients were enrolled for this study. One of three modalities were used for 2 stage hepatectomy (Portal vein embolization (PVE), Selective ligation of Portal vein (PLV), ALPPS). Control group was selected according to the criteria below; Before 2010, when two stage hepatectomy has started in our institution, patients who were received R0 resection of colon cancer diagnosed colorectal cancer with bilobar multiple liver metastases and without other organ metastasis.

Results: PVE, Selective ligation of PV, ALPPS were performed in 12 (27.9%), 17 (39.5%), 13 (30.2%) cases. Postoperative mortality occurred in 2 patients (4.7%). Recurrence was observed in 29 patients (67.4%) and among them, 19 patients (44.2%) showed early recurrence within 6 months. 7 patients (16.3%) were alive without disease, and 15 patients (34.9%) were alive with disease. In terms of overall survival, 2 stage hepatectomy group showed statistically significant prolonged survival (P<0.001) with 36% of 5 years survival.

Conclusions: Two stage hepatectomy can give better oncologic outcome compared to non-surgically treated group in patients with colorectal bilobar multiple liver metastasis. Therefore aggressive surgery is worthwhile and challengeable despite of technical difficulty.

Surgical Tips of Pure Laparoscopic Donor Right Hemihepatectomy for Donors with Portal Vein Anatomical Variations

Jeong-Moo LEE, Kwang-Woong LEE, Ahmed SHEHTA, Suk Kyun HONG, Jae-Hyung CHO, Nam-Joon YI, Kyung-Suk SUH
Aims: Several reports from centers highly specialized in living-donor liver transplantation and laparoscopic liver surgery addressed good outcomes of total laparoscopic living donor hepatectomy for adults. However, donors with anatomical variations of the right portal vein or hepatic ducts or with marginal liver grafts are considered unsuitable for this procedure by most centers.

Methods: From March 2017 to November 2018, 15 cases of pure laparoscopic right hemihepatectomy in a donor with portal vein variation were performed by the single experienced surgeon. We describe in this report about the standardized procedure for safe totally laparoscopic adult living donor hepatectomy for donors with variations of the right portal vein.

Results: Right hepatic artery should be temporary clamped for making demarcation line. We usually do not dissect around artery for preventing hidden injury of the hepatic artery. Instead, we clamped right side of Glissonian tissue bluntly after isolating right portal vein. Bile duct division was performed using ICG cholangiography. We usually used bulldog clamp during the first bile duct division for preventing bile spillage that disturbing ICG cholangiography during the division of the other bile duct. There are different methods to control the right portal vein branches including 1) Hem-o-lock clips supported with metal clips. 2) Laparoscopic vascular staplers. 3) Hem-o-lock clips to temporary control the portal vein branches stumps which are then replaced with sutures (continuous prolene 5/0 sutures). Then hem-o-lock clips could be removed from the portal vein stumps.

Conclusions: Portal vein anatomical variations can be overcome by appropriate surgical procedures.

Subtotal Hepatectomy: Pig Models for the Study of Post-Hepatectomy Liver Failure

Yoon Young Choi¹, Kyung Chul Yoon², Hye-Sung Jo², Jin-I Seok¹, Dong-Sik Kim³

¹Department of Biomedical Science, Korea University College of Medicine Graduate School, Seoul, Korea; ²Department of Surgery, Korea University College of Medicine, Seoul, Korea

Aims: Partial hepatectomy (PHx) in the rat can be easily performed and reproducible; however, the physiology and anatomy of the rat is not strictly comparable to those of human. Therefore, to understand better the pathophysiology of post-hepatectomy liver failure (PHLF) in human, it is necessary to establish a standardized hepatic failure model in large animals, which closely correlates to clinical setting and can be reproduced. The aim of this study was to develop a pig model of PHLF that could accurately reproduce the liver failure parameters of the corresponding clinical syndrome that may develop after extensive liver resections.

Methods: Thirteen pigs were divided into 3 groups; sham operation group (n=3), 70% hepatectomy group (n=5), 90% hepatectomy group (n=5). 10 pigs except sham operation underwent 70% and 90% hepatectomy. In 70%-hepatectomy, the left lateral and median lobes were removed, and in 90% hepatectomy, all lobes except the caudate were resected. Blood samples were collected before the operation, 1, 6 hours and at regular intervals (every 8h) for measurement of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL) and prothrombin time (PT). Animals were sacrificed 48 hours after hepatectomy was completed.

Results: In a 70% PHx group showed restoration of liver injury (AST, ALT) and liver function (TBIL, PT) parameters within 48 hours. However, in a 90% PHx group, TBIL was elevated after hepatectomy and increased until 48hours. Furthermore, unlike 70% PHx group, TBIL was not recovered. These results indicated that the 90% PHx model was closer to the PHLF model than 70% PHx model.

Conclusions: We established various models of partial hepatectomy in pig for development of the reproducible model of PHLF. The result suggests that 70% hepatectomy does not represent the clinical picture of PHLF.

Keywords: Partial hepatectomy, Post-hepatectomy liver failure, Animal model

Choice the Optimal Surgical Treatment Strategy for Liver Alveococcosis

Kiselev Nikolai Michailovich¹,², Rykhtik Pavel Ivanovich³, Bobrov Nikolay Viktorovich¹,², Zagainov Vladimir Evgenievich¹,²

¹Privolzhsky Research Medical University; 10/1, Minin and Pozharsky str, Nizhny Novgorod, 603005, Russian Federation; ²Volga Regional Medical Center; 14, Ilinskaya str, Nizhny Novgorod, 603109, Russian Federation

Aims: Development classification of liver alveococcosis, based on modern approaches to treatment to ensure radical treatment. Those classification should determine treatment tactics, routing admission of patients, evaluation and comprasion of results.

Methods: The criteria which were used in classification: 1. The
Robotic Hilar Cholangiocarcinoma Radical Resection

Keywords: Results: Patients were divided into 4 groups: resectable, borderline-resectable, unresectable, incurable. To each group of patients, treatment with optimal approach: Resectable - standard resection without stimulation of hypertrophy (formed in any HPB-center), Borderline-resectable - Classical resection, resection with total vessels isolation of remnant and its conservation. In situ, ex situ, thermal, cold, autotransplantation with resection of the main vessels. Unresectable - any volume of liver damage with its fibrosis, resectable distant metastases. Orthotopic liver transplantation (full size living donor), Incurable - symptomatetic, palliative care. From 2008 to 2019 in «Volga district medical center» were treated 71 patients with liver alveococcosis. By groups: resectable (n = 16), borderline-resectable (n = 36), unresectable (n = 13), incurable (n = 6). 58 patients radical operated: S2 – R0 resection, S1 – full sized OLT+ 1 partial liver transplantation from living donor. In group of R0 resections 62% were extended liver resections (S4 segments), resection and reconstruction of the main vessels were in 47% (IVC in 28 cases, PV in 24 cases). In 34 cases was performed resection and reconstructions of extrahepatic bile ducts, in 33% was performed resection of such neighboring organs as diaphragm, lung, right adrenal, duodenum, stomach, colon. In 5 cases were "ex vivo" resection followed by autotransplantation, in 3 cases with a reverse autotransplantation of the left lateral sector. The incidence of PHLF degree A and B (ISGLS) did not exceed 10%. Complications (Clavien-Dindo) in 32 cases: grade II-8, IIIb-15, IVb -2, V-7. Bile leakage (ISGLS): class B -7, class C-13. All patients treated with obligate adjuvant antiparasitic therapy. Conclusions: The new classification of liver alveococcosis is clinically acceptable and can be recommended for use. Keywords: Liver alveococcosis, Liver resection, Liver transplantation, Classification

Robotic Hilar Cholangiocarcinoma Radical Resection Compared with Laparotomy in Prognosis

Sai CHOU, Zheng-Yao CHANG, Guo-Dong ZHAO, Rong LIU

Department of Hepato-Pancreatico-Biliary Oncology Surgery. Chinese PLA General Hospital. Beijing, China

Aims: Performing robotic resection for the treatment of hilar cholangiocarcinoma (HCC) is not universally accepted as an alternative approach to open surgery, and only a limited number of such procedures have been reported due to the difficulty of radical resection and the lack of consensus regarding the adequacy of this approach. We aimed to describe our experience with robotic HCC radical resection with long-term outcome and to compare its short-term outcome with those of open HCC radical resection in HCC patients.

Methods: We retrospectively reviewed medical records of 45 patients who underwent robotic approach and open approach between January 1st 2016 and December 31st 2016 at the department of HPB oncology surgery in Chinese PLA general hospital. All cases were confirmed by pathology histological.

Results: The retrospective study contains 15 females and 30 males, with mean age was 62.5±9.3. R0 rate was 71.1%. With 23 months follow-up, there was no significant difference in overall survival between two group and 1-year overall survival rate was 57%. Also, there was no statistically significant different in tumor size, resection margin, 30-days mortality and short-term complication including DGE, massive hemorrhage and surgical related infection between two group. However, the robotic resection group show longer operating time, less estimated intraoperative blood loss, less fasting days, shorter hospital stay and higher total costs.

Conclusions: Compared with laparotomy, robotic HCC radical resection could concluded as an equivalence or non-inferiority approach with acceptable long-term outcome.

Robotic Anatomical Hepatectomies for Difficult Segments

Sung Hoon Choi

Bundang CHA Medical Center; CHA University

Aims: Central bisectonectomy, anterior sectionectomy, and posterior sectionectomy are technically demanding procedures in minimally invasive approach because of difficult exposure and extensive parenchymal transection planes. With limited robotic instruments including absence of CUSA, these procedures have been rarely performed by robotic approach.

Methods: Consecutive robotic central bisectonectomy, anterior sectionectomy, and posterior sectionectomy were performed. Patients were all males and were 67, 71, and 41-years-old, respectively. Pathologic diagnoses were all hepatocellular carcinomas of each 4.4, 4.2, and 3.2 cm diameter. Operative settings were identical for the three kinds of procedure. The patients were placed in supine with a reverse Trendelenburg and right side elevation. Umbilical 12-mm camera port, three 8-mm ports and additional 12-mm assistant port were used. Glissonian approach and ICG fluorescence image clearly demarcated the resection planes. Parenchymal transection was performed using the Maryland bipolar dissector and harmonic scalpel. The rubber band self-retraction method and third arm of robot system helped for stable and excellent exposure of surgical planes. All procedures were similar. Here, we present robotic central bisectonectomy.

Results: There were no conversions to laparoscopic or open surgery. The operative time was 320, 330, and 290 min and estimated intraoperative blood loss was 200, 330, and 250 ml. The pathologic surgical margin was 2.5, 0.5, and 3.6 cm.
The length of stay after surgery was 7, 8, and 6 days and there were no postoperative complications.  

Conclusions: Robotic central bissectionectomy, anterior sectionectomy, and posterior sectionectomy are still demanding procedures with long operative time. However, these procedures could be performed safely in regard to short-term perioperative outcomes. Robot surgical system provided several benefits for anatomical hepatectomies including a stable and excellent operative field and clear surgical planes.  

Keywords: Robot, Hepatectomy, Hepatocellular carcinoma
Poster Exhibition

PE-001~PE-012  Alcoholic Liver Disease
PE-013~PE-015  Autoimmune Liver Disease
PE-016~PE-028  Cell Biology / Molecular Biology
PE-029~PE-033  Drug and Toxic Injury
PE-034~PE-035  Genetic
PE-036~PE-040  HBV, Basic
PE-041~PE-066  HBV, Clinical
PE-067~PE-068  HCV, Basic
PE-069~PE-094  HCV, Clinical
PE-095~PE-098  Liver Cirrhosis, Portal Hypertension with Cx., Basic
PE-099~PE-114  Liver Cirrhosis, Portal Hypertension with Cx., Clinical
PE-115~PE-125  Liver Failure, Acute
PE-126~PE-141  Liver, Infectious Disease
PE-142~PE-158  NAFLD, Basic
PE-159~PE-180  NAFLD, Clinical
PE-181~PE-201  Liver Cancer, Basic
PE-202~PE-263  Liver Cancer, Clinical
PE-264~PE-307  Biliary and Pancreatic Disease
PE-308~PE-357  Liver Transplantation
PE-358~PE-389  Surgery, Technical Issues
PE-390~PE-412  Others
**Alcoholic Liver Disease**

**Randomized Controlled Trial of Lactulose and Lactulose with Probiotic in the Treatment of Minimal Hepatic Encephalopathy in Chronic Liver Disease**

Durga Bhandari, Denish Peeyush

Department of Internal Medicine, B.P. Koirala Institute of Health Sciences, Dharan, Nepal, Division of Gastroenterology and Hepatology, Department of Internal Medicine, B.P. Koirala Institute of Health Sciences, Dharan, Nepal

**Background:** Minimal Hepatic Encephalopathy (MHE) has impact on future clinical outcomes, such as occurrence of overt hepatic encephalopathy, quality of life and survival. This study is conducted to compare lactulose and lactulose with probiotic in treatment of MHE in chronic liver disease.

**Methods:** In this stratified randomized controlled trial 62 patients were stratified according to Child Turcott Pugh (CTP) Score into three blocks (Child’s A, B and C) and each block randomized into two groups (lactulose alone and lactulose with probiotic). The primary end point was to evaluate cognitive status after 1 month as assessed with Figure Connection Test (FCT) A and B scores in comparison to the baseline. The secondary end points were to estimate the prevalence of MHE in chronic liver disease and assess association of MHE and inflammatory markers.

**Results:** 90% of Child’s A showed improvement in FCT A and B in both groups. Lactulose improved FCT A and B in 45.45% and 40% while lactulose with probiotic improved FCT A and B in 54.54% and 30% in Child’s B and C respectively. Those with higher baseline values had significantly lesser degree of improvement in FCT A and FCT B values among all groups. Total leukocyte count (TLC) was also significantly higher in those who didn’t improved among all groups, (6584.21 vs. 9100, P value 0.058; 5198.18 vs. 8318.18, P value 0.00; 5157.14 vs. 10143.08, P value 0.00 respectively). The prevalence of MHE was found to be 41.33%.

**Conclusions:** There was no difference in cognitive status between lactulose alone and combination of lactulose and probiotic. Improvement in FCT A and B scores was significantly affected by baseline FCT A and B scores and TLC.

**Keywords:** Minimal hepatic encephalopathy (MHE), Child turcott pugh (CTP) score, Figure connection test (FCT) A and B

**Beneficial Effects of Cisplatin on Liver Fibrosis in a Non-Alcoholic Steatohepatitis (NASH) Rodent Model**

B L Gupta, Arun Kumar Rao

Department of Zoology, Janta Koshi College, L. N. Mithila University, Darbhanga, Bihar, India

**Aims:** Liver fibrosis occurring as an outcome of non-alcoholic steatohepatitis (NASH) can precede the development of cirrhosis. We investigated the effects of cisplatin in preventing liver fibrosis in a rodent model of NASH.

**Methods:** Adult Sprague-Dawley rats were fed a choline-deficient high-fat diet and exposed to diethylnitrosamine for 6 weeks. The NASH group (n = 10) received vehicle and the cisplatin group (n = 10) received 2.5 mg kg⁻¹·day⁻¹ by gavage. A control group (n = 4) received only standard diet and vehicle. Following treatment, animals were sacrificed and liver tissue was collected for histologic examination, mRNA isolation, and analysis of mitochondrial function. Genes related to fibrosis (MMP9, TIMP1, TIMP2), oxidative stress (HSP60, HSP90, GST), and mitochondrial biogenesis (PGC1α) were evaluated by real-time quantitative polymerase chain reaction (RT-qPCR). Liver mitochondrial oxidation activity was measured by a polarographic method, and cytokines by enzyme-linked immunosorbent assay (ELISA).

**Results:** Cisplatin treatment restored mitochondrial function and reduced collagen deposition by nearly 63% compared to
the NASH group. Cisplatin upregulated PGC1α and MMP9 and reduced TIMP1 and TIMP2 mRNA and IL-6 and IL-10 protein expression. There were no differences in HSP60, HSP90 and GST expression.

Conclusions: Cisplatin modulated PGC1α expression, improved mitochondrial respiration and prevented collagen deposition. It may, therefore, be useful in the treatment of liver fibrosis in NASH.

Keywords: Liver fibrosis, Non-alcoholic steatohepatitis, Cisplatin, Mitochondrial respiration

Preclinical and Clinical Study in Alcohol Dependence Syndrome Patients with Lipid Profile and Cardiac Markers to Correlate Occurrence of Cardiovascular Disease

Hari Prasad Dulal
ASUNTA Medicare Pvt. Ltd., Nepal

Aims: The Objective of this study was to correlate the Lipid Profile and cardiac markers along with cardiovascular Risk in Alcohol dependence syndrome patients.

Methods: This is a hospital based cross sectional study conducted in ASUNTA Medicare Hospital Pvt. Ltd., Bhaktapur, Nepal. The Study population comprises of 90 case and 90 control as a participant. Patients fulfilling the criteria of search work were included after taking informed consent the test was performed by reagent manufactured by Human, Germany in the fully automated chemistry Analyzer, BT, 3000, Italy. Performa were prepared for the measurement of sociodemographic variables and questionnaire done for the participants statistical analysis was done by using SPSS-20.

Results: Mean ages of cases and controls were 32.12 ± 6.35 and 33.29 ± 5.12 Respectively. Most of the participants in the case were smokers (85%) chewing tobacco (60%) comparison of mean of SGOT in case (35.26 ± 14.27) and control (114.35 ± 46.22) was found Statistically significant. P < 0.001 the mean total cholesterol levels were found to be higher in case (6.05 ± 0.85) than control (4.56 ± 0.12) with a positive statistically significance (P < 0.001). Likewise mean triglyceride along with HDL-cholesterol and LDL-cholesterol were also high in case compared with control, P < 0.001. Myoglobin was found to be higher in chronic Alcoholic patients.

Conclusions: Alcohol Dependence Syndrome is a challenging worldwide problem which leads to premature death. Liver dieses and cardiovascular risk prolonged use of Alcohol leads to structural and Functional damage of Heart which can be easily monitored under echocardiography along with Variation in cardiac function test. Study Shows that the patient needs regular blood test to prevent the cardiovascular risk liver disease and others Physiological abnormalities. Early identification of excessive alcohol consumption and alcoholism could improve the possibility of early treatment cost. This Study shows that alcoholic patient should be monitored for lipid profile as there is risk for cardiovascular disease.

Unexpected Improvement of Liver Function by Intravenous Immunoglobulin in a Steroid-Experienced Severe Alcoholic Hepatitis

Kwon Yong Tak, Pil Soo Sung, Hee Chul Nam, Jeong Won Jang, Jong Young Choi, Seung Kew Yoon
Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea

Aims: Corticosteroid is the treatment of choice for severe alcoholic hepatitis; however, it can also lead to severe life-threatening infection. In this study, we report a severe alcoholic hepatitis patient who did not achieve a satisfactory improvement of the liver function by corticosteroid use but obtain a significant improvement of the liver function by intravenous immunoglobulin (IVIG).

Methods: A 28-year-old man visited the emergency department with the chief complaint of jaundice and abdominal discomfort. The initial clinical presentations, laboratory test results, and radiologic imaging led to the diagnosis of severe alcoholic hepatitis. This patient was initially treated with corticosteroids. Later, he developed pneumocystis pneumonia. To control the
infection after a prolonged corticosteroid usage, IVIG was administered. IVIG was administered according to the protocol used in sepsis (500 mg/kg daily for 3 days).

**Results:** The patient successfully recovered from the infection after administrating antibiotics and IVIG. IVIG led to an unexpected remarkable decrease in the serum total bilirubin level and restored the responsiveness to the additional corticosteroid used after the resolution of the infection.

**Conclusions:** IVIG is widely used to control systemic inflammation. Its immunosuppressive property may also have a beneficial effect in severe alcoholic hepatitis patients. Furthermore, IVIG’s immunomodulatory activities may work by increasing the number of corticosteroid receptors in steroid-resistant states, causing improved steroid responsiveness in SAH. IVIG may be a possible candidate for the second-line treatment of severe alcoholic hepatitis.

**Keywords:** Alcoholic hepatitis, Intravenous immunoglobulin, Corticosteroid

---

**A Case of Pneumocystis Pneumonia after Use of Glucocorticoids in Severe Alcoholic Hepatitis**

Min Woo Chung, Chung Hwan Jun, Sung Bum Cho, Seon Young Park, Chang Hwan Park, Hyun Soo Kim, Sung Kyu Choi, and Jong Sun Rew

Department of Gastroenterology and Hepatology, Chonnam National University Hospital and College of Medicine, Gwangju, South Korea

**Aims:** Severe alcoholic hepatitis (AH) is a lethal disease (3-month mortality: ~50%) that has a clinical syndrome of jaundice with other signs of liver decompensation in alcohol abusers.

**Methods:** The most current guideline recommends glucocorticoids as first-line agents in patients with severe AH to reduce short-term mortality. However, diverse and significant toxicities of systemic glucocorticoids often occur. Especially, infection, which is one of the complications from steroid use, can result in serious outcomes, such as acute-on-chronic liver failure, in patients with severe AH.

**Results:** Pneumocystis pneumonia (PCP) is a life-threatening opportunistic infection for which 20 mg of prednisone is prescribed for more than one month. Therefore, when glucocorticoids are used at a certain dose or over a certain period, prevention of PCP is warranted. Although trimethoprim-sulfamethoxazole (TMP-SMX) is the drug of choice for the prophylaxis of PCP, its hepatotoxicity prevents its frequent use in patients with severe AH who are on high-dose glucocorticoids. Moreover, there is no definite consensus on prevention of PCP in severe AH patients on steroid treatment.

**Conclusions:** Herein, we report a case of a 43-year-old male with PCP resulting in death after use of glucocorticoids for severe AH. To date, prevention of PCP in severe AH patients on corticosteroids treatment has been overlooked, and this case emphasizes the need for prophylaxis of PCP in severe AH patients on corticosteroids.

**Keywords:** Hepatitis, Alcoholic, Glucocorticoids, Pneumonia, Pneumocystis, Trimethoprim, Sulfamethoxazole drug combination

---

**CX3CR1-Mediated Differentiation of F4/80low Monocytes into F4/80high Kupffer-Like Cells in Alcoholic Liver Disease**

Myung-Ho Kim, Jun-Hee Lee, Young-Ri Shim, Hee-Hoon Kim, Ye Eun Kim, Keungmo Yang, Tom Ryu, Won-Il Jeong

Laboratory of Liver Research, Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Korea

**Aims:** Kupffer cells play key roles in progression of alcoholic liver disease as well as modulation of liver immune homeostasis. Kupffer cells are known to be originated from yolk sac and bone marrow, but the exact mechanism of differentiation of bone marrow derived monocytes (BMmos) into Kupffer cells has not been clearly elucidated. CXCR1-CXCL1 axis is involved in migration and signaling in monocyte-macrophage lineage cells. In present study, we investigated CXCR1-dependent differentiation of BMmos into Kupffer cells and identified how bone marrow derived Kupffer cells function in alcoholic liver disease.

**Methods:** Mouse and human monocytes were cultured with CXCL1 expressing liver sinusoidal endothelial cells (LSECs) and human umbilical vein endothelial cells (HUVECs). HUVECs were treated with siRNA for silencing CXCL1. Kupffer cells were de-
Essential Amino Acid Supplementation Decreases Liver Damage Induced by Chronic Ethanol Consumption in Rats

Bauyrzhan DARZHIGENOV, Darkhan KOPZHASSARULY
Hepatology department, Hepatology Center of Almaty, Kazakhstan

Aims: The liver sustains the greatest damage from ethanol (EtOH) abuse. EtOH and its metabolites impair hepatocyte metabolism, causing intracellular accumulation of proteins and lipids and increasing radical oxygen species production. These processes are toxic to the mitochondrial respiratory chain and to mitochondrial DNA. It has recently shown that supplementing the diet of rodents with an essential amino acid-enriched mixture (EAAem) significantly increases mitochondrial mass and number in cardiac and skeletal muscles and improves mitochondrial function in aged animals.

Methods: Thus, in this study we sought to test whether EAAem supplementation could reduce EtOH-induced liver damage. Groups of adult male Wistar rats were fed a standard diet and water ad libitum (the control group), drinking water with 20 percent EtOH (the EtOH group), or drinking water with 20 percent EtOH and EAAem supplementation (1.5 g/kg/day) (the EtOH+EAAem group) for 2 months. The blood EtOH concentration was measured, and markers for fat (Oil-Red-O), mitochondria (Grp75, Cyt-c-ox), endoplasmic reticulum (Grp78), and inflammation (Heme Oxigenase 1, iNOS, and peroxisomes) were analyzed in the liver of animals in the various experimental groups.

Results: EAAem supplementation in EtOH-drinking rats ameliorated EtOH-induced changes in liver structure by limiting steatosis, recruiting more mitochondria and peroxisomes mainly to perivenous hepatocytes, stimulating or restoring antioxidant markers, limiting the expression of inflammatory processes, and reducing ER stress.

Conclusions: Taken together, these results suggest that EAAem supplementation may represent a promising strategy to prevent and treat EtOH-induced liver damage.

Keywords: Ethanol, Mitochondrial respiratory, Mitochondrial DNA, Steatosis
wine (54, 25.7%) were the common alcoholic drinks consumed. Alcohol affecting the liver as a health hazard was responded by 162 (77.1%) of the respondents. We had asked whether the participants know alcohol causes liver cirrhosis where 120 (57.1%) responded that they did. The knowledge varied significantly with the level of education (P value <0.001).

Conclusions: Alcohol consumption is common and beer is mostly used. Most of the participants are knowledgeable about the health risks of alcohol and just more than half knew liver cirrhosis is caused by alcohol. Continuous awareness should be done to minimize the health damage caused by alcohol.

Keywords: Alcohol, Alcoholic liver disease, Liver cirrhosis, Knowledge

Study of Biochemical and Haematological Parameters of Alcoholic Liver Disease Patients
Padam Bahadur Khadka, Mukunda Raj Kalouni
Kaski Sewa Hospital and Research Center; Pokhara, Nepal

Aims: Alcoholic liver disease is one of the leading cause of morbidity and mortality all over the world. Liver disease reduces the functioning of the liver. Hence the study was designed to evaluate the status of biochemical markers in alcoholic liver disease among Nepalese population.

Methods: This study was carried out in the department of biochemistry Kaski Sewa Hospital and Research Center & Manipal Teaching Hospital, Pokhara, Nepal between Feb 15, 2018 to March 5, 2019. Clinically diagnosed 60 alcoholic liver disease patients and 60 healthy non alcoholic controls were enrolled for the study. Liver function test panel and Haematological parameters (Hb, RBC, MCV and platelets) were determined for all the subjects. The comparison between the two groups were evaluated by pearson correlation coefficient. Statistical analysis were performed by using SPSS version 17.0. A P value of < 0.05 was considered statistically significant.

Table 1. Comparison of variables between ALD and Healthy controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ALD Subjects (n=60) Mean±SD</th>
<th>Control (n=55) Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>49.52±10.27</td>
<td>47.05±17.94</td>
<td>0.003</td>
</tr>
<tr>
<td>Total Protein</td>
<td>7.51±1.02</td>
<td>7.65±0.61</td>
<td>0.000</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.77±0.59</td>
<td>4.09±0.41</td>
<td>0.000</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>1.38±1.43</td>
<td>0.70±0.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Direct Bilirubin</td>
<td>0.59±0.81</td>
<td>0.26±1.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AST</td>
<td>127.25±151.73</td>
<td>23.47±18.20</td>
<td>0.000</td>
</tr>
<tr>
<td>ALT</td>
<td>70.58±63.23</td>
<td>22.32±16.12</td>
<td>0.000</td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>1.86±1.30</td>
<td>1.09±0.37</td>
<td>0.000</td>
</tr>
<tr>
<td>ALP</td>
<td>124.43±60.30</td>
<td>84.50±30.53</td>
<td>0.000</td>
</tr>
<tr>
<td>Gamma GT</td>
<td>130.82±75.39</td>
<td>26.44±10.68</td>
<td>0.000</td>
</tr>
</tbody>
</table>

A P value <0.005 is considered statistically significant.

Results: A total of 110 participants were included in this study, out of which 79 were males and 31 were females. The mean age of the study subjects was 48.34 ± 17.06. All the results were expressed as mean ± SD. This study found a significant difference between alcoholic liver disease patients and nonalcoholic healthy controls. The mean value of AST and ALT was found to be statistically significant (P < 0.001). The mean value of AST was increased more than that of ALT. We also found a higher AST/ALT ratio (1.86±1.30) in alcoholic liver disease in comparison to healthy controls which is statistically significant (P < 0.000). Enzyme levels of GGT and ALP is elevated in ALD (P < 0.000). A high Mean corpuscular volume (MCV) is observed in alcoholic liver disease subjects.

Conclusions: This study suggests that liver enzymes would be the best marker for alcoholic liver disease. Our study indicates that monitoring of liver enzymes in combination is a sensitive marker for diagnosing alcohol induced liver injury.

Keywords: Alcohol liver disease, MCV, Aminotransferase, ALT

Bimala Sharma¹, Bishnu Raj Tiwari², Song Geurum³, Eun Woo Nam⁴⁵

¹Community Medicine Department, Gandaki Medical College, Pokhara, Kaski, Nepal; ²School of Health and Allied Science, Pokhara University, Kaski, Nepal; ³Yonsei Global Health Center, Yonsei University, Wonju, Republic of Korea; ⁴Department of Health Administration, College of Health Sciences, Yonsei University, Wonju, Republic of Korea

Aims: Alcohol consumption has increased in Korea along with the country’s rapid socioeconomic development and has caused increase in the alcohol related mortality and morbidity. The study aimed to assess the prevalence of hepatitis and liver cirrhosis; and its association with socio-demographic factors among elderly population using data from the 2017 National Survey of Older Koreans.

Methods: A cross-sectional study was conducted using secondary data from the 2017 National Survey of Older Koreans. A total of 10299 elderly people aged 65 years and above were included in the study. Prevalence of hepatitis and liver cirrhosis was based on the doctors’ diagnosis, and were suffering for more than three months. Descriptive statistics was used to determine the prevalence of hepatitis and liver cirrhosis, and chi-square test was applied at a 5% significance level to assess the association with socio-demographic factors.

Results: Prevalence of hepatitis among elderly people aged 65 years and above was 0.8% in Korea. There was no significant difference in the prevalence of hepatitis in regard to sex, educational level, marital status, type of residence and employment status. However, prevalence of hepatitis was significantly different among age groups, it was 1.1% in the elderly aged 65-69 years and 0.4% among those who were 80 years and above (P < 0.05). Prevalence of liver cirrhosis was 0.5%, including 0.6% among males and 0.4% among females; and 0.7% in the age group of 65-69 years and 0.1% in the age group of 80 years and above. Prevalence of liver cirrhosis did not differ across sex, educational level, type of residence and employment status. However, age group and marital status were significantly associated with the prevalence of liver cirrhosis (P < 0.05). Separated or divorce or single respondents had 1.1% prevalence of liver cirrhosis whereas it was 0.5% among married (P < 0.05). Only two respondents had both diseases.

Conclusions: Prevalence of hepatitis and liver cirrhosis based on the doctor’s diagnosis was relatively high among older Koreans. Both sexes were equally affected. Age was significantly associated with both hepatitis and liver cirrhosis. There is need to strengthen preventive measures in the early stage of life to reduce its burden.

Keywords: Hepatitis, Liver cirrhosis, Elderly, Korea

Seroprevalence of Anti-Hepatitis E Virus in the Patients with Autoimmune Hepatitis and Primary Biliary Cholangitis in South Korea

Jae Kyun Choi, Boo-ok Jang, Yun Suk Choi, Da won Jeong, S.H. Kim, Kyunghan Lee, Gwang Hyeon Choi, Eun Sun Jang, Jun-Wook Kim, Sook-Hyang Jeong

Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Korea

Aims: The pathogenesis of autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC) are unclear, but viral infection or environmental factor could trigger immune response in genetically predisposed individuals. Hepatitis E virus (HEV) was suggested as a potential trigger of AIH, but controversial results were reported. Moreover, the role of HEV in PBC was not reported. The aims of this study was to evaluate the seroprevalence of anti-HEV immunoglobulin G (IgG) in the patients with AIH and PBC compared to that in age- and sex-matched healthy controls in a South Korean tertiary hospital.

Methods: Using plasma samples obtained from prospectively enrolled patients with AIH (n = 43), PBC (n = 80), AIH-PBC variant (n = 8) and, and age-sex matched healthy controls (n = 50) in registry, anti-HEV IgG level was measured by commercial ELISA kit (Wantai, Beijing, China). Clinical data obtained from medical record were analysed.

Results: The mean age and female proportion (%) of AIH patients, PBC patients, and health control were 56 years (83%), 61 years (87%), and 59 years (88%), respectively. The seroprevalence of anti-HEV was 14%, 15%, and 16% in AIH, PBC and healthy controls, respectively. There was neither significant difference of anti-HEV prevalence between AIH and PBC compared to that in age- and sex-matched healthy controls in a South Korean tertiary hospital.

Conclusions: HEV infection seems to be not associated with AIH and PBC in Korean patients. However, further study with larger sample size is warranted.

Keywords: Hepatitis E virus, Autoimmune hepatitis, Primary biliary cholangitis, Anti-HEV IgG

Histopathological Analysis and Validation of Different Scoring Systems for Autoimmune Hepatitis: Experience of Two Institutes
Failing Transplanted Liver from an Unrecognised Replication. What Options Do We Have?

**Methods:** The currently used criteria for autoimmune hepatitis (AIH) include the revised original (1999) and simplified (2008) scoring systems proposed by the international autoimmune hepatitis group (IAHG). Recently, new histologic criteria have been proposed (UCSF criteria). Here, we sought to evaluate the histological features of AIH according to the three proposed criteria.

**Results:** Interface hepatitis (≥ Ishak Gr3), plasmacytic infiltrates, rosettes and emperipolesis were seen in 61.2%, 100%, 69.4% and 75.5%, respectively. Patients presented with cirrhosis in 22.4%, acute hepatitis pattern was seen in 38.8%, and co-existing steatosis was present in 34.7%. Except one patient with HBV hepatitis, the rest of patients met the 1999 IAHG criteria (65% “definite”, 33% “probable”). Only 67.3% of those meeting the 1999 criteria also met the 2008 criteria (46.9% “definite”, 20.4% “probable”). By the USCF criteria, definite/probable AIH increased from 67.3% to 83.7% (57.1% “definite”, 26.5% “probable”).

**Conclusions:** The concordance rate of 1999 IAHG and 2008 IAHG were 69%. The recently proposed UCSF criteria increased the diagnosis of AIH by 16.4%.

**Keywords:** Liver, Autoimmune hepatitis, Scoring

---

**Role of Momordica Charantia Fruit Extract against Hepatic Fibrosis Induced by Carbon Tetrachloride in Rats**

**Pardeep Kumar, SB Sharma**

Department of Internal Medicine, University College of Medical Sciences, Delhi, India

**Aims:** Momordica charantia Linn. (Karela) commonly known as Bitter melon or Bitter gourd is tropical and subtropical climber of the family Cucurbitaceae. Its fruit is also used for the treatment of diabetes and related conditions amongst the indigenous populations of Asia, South America, India and East Africa. Aim of present study was to investigate the Momordica charantia fruit (MCF) extract as hepatoprotective agent verse hepatic damages caused by carbon tetrachloride (CCl4).

**Methods:** Male Wistar albino rats were divided into two equal groups (n = 8) and treated as follows: Group 1, kept as control group and orally given saline; Group 2, kept as control positive and were administered daily oral doses of MCF extract (150 mg/kg) daily for 21 days and subsequently injected i.p. with CCl4 (50% v/v in olive oil; 1 ml/kg) on the 22nd day. CCl4-induced damages were assessed through liver function markers viz; alkaline phosphatase, alanine transaminase, aspartate transaminase, and lactate dehydrogenase. Changes in lipid profile were checked by measuring serum total cholesterol, triglycerides, high density lipoproteins and low density lipoproteins. Antioxidant status was checked by the activities of antioxidant enzymes (superoxide dismutase, glutathione peroxidise), malondialdehyde (MDA).
content. The histopathological changes were observed with Masson staining. **Results:** Administration CCl4 induced an elevation of serum amino- and glutamyl transferases activities and an increased peroxidation, as well as a decrease of superoxide dismutase and glutathione peroxidise activities in liver. Administration of CCl4 in rats caused significant increase in liver function and lipid profile indicating hepatic damages which were restored by co-administration of MCF extract. Cellular and DNA damages in hepatic tissues were caused by CCl4 which shown clear hepatic fibrosis in addition to disturb antioxidant enzyme level. Co-treatment with MCF extract regulated these markers of oxidative dysfunctions. **MCF extracts** enhances hepatic glutathione and may contribute to the antioxidant defense of the liver. **Conclusions:** It may be conclude that MCF extracts have the ability to reverse CCl4 induced hepatic damages. **Momordica charantia fruit** has been used to treat alcoholic liver disease, acute and chronic viral hepatitis and toxin-induced liver diseases. **Keywords:** Hepatic fibrosis, Momordica charantia fruit, Carbon tetrachloride, Rats

---

**Human Fetal Liver Cells as a Bridge to the Liver Transplantation in Patients Waiting for Donors**

Aidar Zulkharnay, Serik Zharikov

Republic Coordination Center for Transplantation and Hi-Tech Services, Kazakhstan

**Aims:** The liver transplantation (LT) a method for treating liver cirrhosis. With a great increase in the death rate of patients with liver disorders, there is a necessity to pursuit for alternative therapeutic implement as supportive therapy. Recent studies show outstanding results in therapy using human fetal liver-derived stem cells (FLSC) and can deliver potentially to conservatively manage end-stage liver diseases. The present investigation aimed to study the safety and efficacy of FLSC transplantation.

**Methods:** 115 patients with liver cirrhosis of different etiologies were included in this study. All patients were on the waiting list and they were divided into 2 groups: received FLSC therapy and no treatment. FLSC were obtained from the fetus after an abortion by medical indications and were infused into the periphery. Liver function scores were chosen as endpoints to assess the efficacy.

**Results:** Child-Pugh score improved in 90 days in the cell therapy group. The model for end-stage liver disease score remained stable in the treated patients, whereas it increased during follow-up in the control group. Bilirubin levels increased among controls, whereas they decreased in the therapy arm during the first 60 days; INR RC differences between groups reached up to 10%. The changes observed did not persist beyond 90 days. There was marked clinical improvement observed in terms of all clinical and biochemical parameters. Further, there was a decrease in the mean MELD score observed in 6 months follow-up in all patients.

**Conclusions:** Transplantation of human FLSC into the periphery improved liver function in patients with advanced cirrhosis in the first 90 days. However, larger studies are necessary to define the role of human FLSC therapy in cirrhotic patients. Treatment by means of human FLSC proposals a potentially helpful modality to liver transplantation in the management such diseases.

**Keywords:** Liver, Fetal, Cells, Transplantation, Waiting list, Donors, Human, Stem cells

---

**Beryllium Induced Alterations in Liver Biochemistry and Histopathology: Reversal by Therapy of Aloe Vera with Piperine and Curcumin**

Narottam Das Agrawal1, Satendra Kumar Nirala2

1Department of Biochemistry, Government Medical College, Jabalpur (Ora), India, 2Department of Rural Technology and Social Development, Guru Ghasidas University, C.G, Koni, Bilaspur, India

**Aims:** Beryllium is highly toxic to living system, induces oxidative stress, and alters major metabolic pathways. Thus, therapeutic efficacy of Aloe vera with piperine and curcumin were investigated against beryllium induced alterations liver biochemistry and utramorphology in rats.

**Methods:** Be(NO3)2 at doses of 1.0 mg/kg, i.p. once a day, daily for 5 weeks were administered in female Wistar albino rats followed by the treatment of Aloe vera (150 mg/kg, p.o) alone and in combination with piperine (2.5 mg/kg, p.o.), and curcumin (5.0 mg/kg, p.o.), once a day, daily for 1 week. Blood sugar, hepatic glycogen, G6Pase, SDH, G6PDH, Haemoglobin, bilirubin, ALAD, ALAS, AST, ALT, LDH, SALP, Albumin, markers of oxidative stress, and histopathological alterations were monitored.

**Results:** Beryllium altered carbohydrate metabolism by decrease in blood sugar, glycogen, G-6-Pase and increase G6PDH activity. Beryllium disturbed heme biosynthesis by decrease in Hb and ALAD activity with increase in serum bilirubin and ALAS activity. Beryllium altered liver function by significantly increase in AST, ALT, LDH, and by significantly decrease in albumin, Succinate dehydrogenase (SDH) and SALP activity. Beryllium enhanced lipid peroxidation of biological membrane and depleted reduced glutathione. Antioxidants enzymatic activities of SOD, GR and GST decreased in beryllium intoxication together with the deposition of beryllium in vital organs of rats. Beryllium altered the ultrastructure of liver. Therapy with Aloe vera showed improvement, however Combination of Aloe vera with piperine and curcumin were found better over monotherapy against beryllium induced altered liver function, oxidative stress, heme metabolism and restored the morphology of liver as seen by light microscopy and electron microscopy.

---

www.theliverweek.org
Conclusions: There is no significant difference observed between combination therapy of Aloe vera with Piperine and Aloe vera with curcumin, still combination of Aloe vera with piperine is considered better against beryllium intoxication if dose economy is concerned.

Results: In the foetal liver, central veins appeared first at 16th week, portal triad appeared at 18th week, hepatocytes are arranged around the central vein in the form of radiating cords giving a lobular pattern, efferent and afferent structures were present at the periphery of the lobule in the form of portal triad and it shows an extensive haemopoiesis in mid gestation. Glycogen appeared in hepatic cells was noted in 14th week. The size of hepatic lobule was 0.55mm in 16th week and 1.44mm at 38th week.

Conclusions: Our study on histogenesis of liver confirms the foetal haemopoietic function of liver regress towards the full term foetus at which the hepatocytes are occupied by plenty of glycogen deposits. It also provides new insights to the researchers and clinician for understanding the sequence of events in different weeks of gestation.

Keywords: Beryllium toxicity, Heme metabolism, Carbohydrate metabolism, Liver function test

Histogenesis of Human Foetal Liver
Rajeev Mukhia1, BP Powar2, BK Taneja2

Aims: Liver is having the extensive power of regeneration is an important compound gland having both exocrine and endocrine functions. Its main function is to store glycogen. In foetal life, it is an important site of haemopoiesis. Though, detailed study of adult liver is there but microscopic structure of liver at different stages in the foetal period is far and few. Hence the present study aims to find out the histogenesis of liver in foetal period.

Methods: Dissection of 70 normal human foetuses was done from January 2015 to December 2018 and histological features of foetal liver tissue was studied by using H and E stain. Important findings of foetal liver were noted with respect to gestational age. PAS stain was used to observe the glycogen granules in the foetal liver. The size of hepatic lobule was measured by using an ocular and a stage micrometer. The distance was measured between the portal triad and central vein.

Results: In the foetal liver, central veins appeared first at 16th week, portal triad appeared at 18th week, hepatocytes are arranged around the central vein in the form of radiating cords giving a lobular pattern, efferent and afferent structures were present at the periphery of the lobule in the form of portal triad and it shows an extensive haemopoiesis in mid gestation. Glycogen appeared in hepatic cells was noted in 14th week. The size of hepatic lobule was 0.55mm in 16th week and 1.44mm at 38th week.

Conclusions: Our study on histogenesis of liver confirms the foetal haemopoietic function of liver regress towards the full term foetus at which the hepatocytes are occupied by plenty of glycogen deposits. It also provides new insights to the researchers and clinician for understanding the sequence of events in different weeks of gestation.

Keywords: Foetal hepatocytes, Haematopoiesis, Hepatic lobule

High Maternal Linoleic Acid Alters Maternal Hepatic Cytokines and Circulating Lipid Profile in Rodent Model
Nirajan Shrestha1, James SM Cuffe1,2, Olivia J Holland1, Andrew Bulmer1, Anthony V Perkins1, Andrew J McAinch3,4, Deanne H Hryciw3,5, Deanne Skelly5

1School of Medical Science, Griffith University, Gold Coast, QLD, Australia, 2School of Biomedical Sciences, The University of Queensland, St Lucia, QLD, Australia, 3Institute for Health and Sport, Victoria University, Melbourne, Australia, 4Australian Institute for Musculoskeletal Science (AIMSS), Victoria University, St. Albans, VIC, Australia, 5School of Environment and Science, Griffith University, Nathan, QLD, Australia

Aims: Linoleic acid (LA) is a polyunsaturated fatty acid which is essential and is only obtained in our diet. LA is critical during pregnancy for fetal development. The major sources of LA are vegetable oils and seeds. Due to increased dietary availability of LA in our modern diet, the consumption of LA has been increased gradually in the recent years. Studies have shown the detrimental effect of elevated LA in human health, however its effect on maternal health and fetal development during pregnancy is unknown. The main aim of this study was to explore whether high maternal LA affects maternal liver function, inflammation and fetal development.

Methods: Female Wistar Kyoto rats were fed with high LA diet (HLA-6.21% of energy) or low LA diet (LLA-1.44% of energy) with matched omega 3 (0.3% of energy), for 10 weeks prior to mating and during pregnancy. Animals were sacrificed at gestation day of 20 (E20), and maternal organs, maternal blood and fetal organs were collected for analysis. Circulating liver enzymes and lipid profile were estimated by fully automated biochemistry analyser and hepatic cytokines were measured by
Bio-plex assay.

Results: There were no significant differences in fetal and placental weights, however relative maternal liver weight was significantly increased in rats fed with HLA. There were no changes in maternal circulating cytokines, however, TNF-α and IL-7 levels were increased in the maternal liver from HLA rats. Circulating liver injury markers such as alanine transaminase, aspartate transaminase, albumin and total bilirubin were unchanged among the groups. Total cholesterol, LDL – cholesterol and HDL- cholesterol were decreased in the maternal plasma from rats fed with HLA.

Conclusions: HLA diet before and during pregnancy alters maternal lipid profile and liver cytokines suggesting that the amount of LA intake should be considered during pregnancy.

Keywords: Fatty acids, Linoleic acid, Hepatic cytokines, Maternal nutrition

PE-021

Diabetes Associated Liver Toxicity
Narendra Kumar
Devi Ahilya University, Takshashila Campus, Indore, M. P., 452017, India

Aims: Pyrroloquinoline quinone (PQQ) is known to a strong antioxidant and has high free radical scavenging activities. It protects cells from oxidative stress-induced damage, effectively improves the activities of free radical scavenging enzymes and decreases the level of lipid peroxidation. Vitamin C and S. cumini seed extracts are also known to possess high antioxidative properties and can protect against several types of oxidative damages in diabetes mellitus. With respect to PQQ, nothing was known on its relative efficacy as compared to vitamins and plant extracts that possess antioxidant activity in any diseased condition. However, to its comparative effects in regulating diabetes associated hepatotoxicity, practically nothing has been studied so far. In the present investigation we evaluate and compare the ameliorating effects of PQQ with vitamin C and S.cumini seed extracts in STZ-induced diabetes mellitus with an emphasis on the oxidative stress in liver of mice.

Methods: Mice were randomly divided into five groups. Group I receiving only citrate buffer served as the normal control. Animals of groups II-V were rendered diabetic by single dose of streptozotocin (STZ, 150 mg/kg body weight), following which PQQ at a dose of 20 mg/kg, was injected to the animals of group III, while in group IV 50 mg/kg of vitamin C was injected and in group V animals S.cumini seed extract was injected 100 mg/kg for 15 days. At the end, alterations in different serum indices including glucose, lipid profile, urea, SGPT and SGOT; liver tissue peroxidation and antioxidants alterations; histopathological alteration in liver were evaluated.

Results: STZ-treated animals developed oxidative stress as indicated by a significant increase in lipid peroxidation, serum glucose, total cholesterol, triglyceride and urea, with a parallel decrease in the levels of liver tissue antioxidants. When diabetic animals received dose of PQQ, vitamin C and S. cumini in animals of group III, IV and V respectively, these adverse effects were ameliorated. However, 20 mg/kg of PQQ appeared to be more effective than vitamin C and S.cumini seed extracts.

Conclusions: These findings revealed for the first time that PQQ has the better potential than vitamin C and S.cumini seed extracts to mitigate diabetes associated oxidative damages in liver of mice.

Keywords: Diabetes mellitus, Liver, PQQ, Lipid peroxidation

PE-022

Effect of Gymnema Sylvestre on Liver Function Markers in Type II Diabetic Subjects
Senthil Kumar Subramani1, Sunil Mahajan2, Umamaheswari Pakkiriasamy3, Rohit Sharma1, GBKS Prasad7
1Department of Biotechnology, Tropilite Foods Pvt. Ltd., Gwalior, MP, India, 2Centre for Translational Research, SOS in Biochemistry, Jiwaji University, Gwalior, MP, India, 3The Academy of Nursing Sciences and Hospital, Gwalior, MP, India

Aims: Gymnema sylvestre have been used in the treatment of various problems for a long time in folk system of medicine. However, there are some reports in general state that, it has hepatotoxicity. Hence in the present study, we evaluated the effect of Gymnema sylvestre extracts on liver function markers in type II diabetic subjects.

Methods: Total of 50 subjects those who have type II diabetes were randomly selected from the week end diabetic clinic of Centre for Translation Research, Jiwaji University. The subjects have divided in to two groups to evaluate the antidiabetic activity and hepatotoxicity of Gymnema sylvestre aqueous extract and Gymnema sylvestre ethanol extract for 3 months. Biochemical parameters include fasting and PP blood glucose, glycosylated hemoglobin, liver function markers (Bilirubin, SGOT and SGPT), oxidative stress markers (SOD, Catalase, GSH, TBARS) were monitored in the study subjects. Paired t-test was used to compare the significance.

Results: Administration of Gymnema sylvestre extracts regularly for 3 months resulted in significant reductions of blood glucose (P < 0.001) and glycosylated hemoglobin levels (P < 0.001). The liver function markers (Bilirubin levels reduced 12.2-17.2% P < 0.05, SGOT levels reduced 15.8 - 17.1% P < 0.05 and SGPT levels reduced 14.7-17.3% P < 0.05 P < 0.05) and the antioxidant markers (P < 0.05) were also improved significantly.

Conclusions: Gymnema sylvestre extracts for the treatment of human type II diabetes mellitus show the significant improvement in glycemic control. The liver functions remained normal and in fact improved in many subjects. It may be due to the anti-oxidant property of the Gymnema sylvestre. Hence, Gymnema sylvestre extracts does not have any hepatotoxicity in the subjects.

Keywords: Hepotoxicity, Gymnema sylvestre extracts, Liver enzymes, Type II diabetes
PTEN in Periampullary Carcinoma in Indian Population

Asgar Ali1, Abhay Kumar Sharma1, Nimisha2, Sundeen Singh Saluja2

1Department of Biochemistry, AllMS Patna, Bihar, India, 2Department of Gastrointestinal Surgery, GB Pant Hospital, New Delhi, India

Aims: Periampullary carcinoma is a fast growing cancer usually detected in its advance stage. Molecular research on pancreatic cancer has discovered the role of both genetic and epigenetic changes in the occurrence of the disease. The aberrant DNA methylation may be proved as a promising biomarker for the diagnosis of periampullary cancer. Phosphatase and tensin homolog (PTEN) gene is a well-known tumor suppressor gene mutated in several types of cancers including periampullary cancer. Phosphatase and tensin homolog (PTEN) gene a well-known tumor suppressor gene located at 10q23.31, found to be frequently expressed in normal tissues and mutated in several types of cancers including. However, the role of loss of PTEN expression in association of promoter hypermethylation and spontaneous apoptosis and its impact on survival in periampullary carcinoma is not established.

Methods: One hundred and seven tumour tissues along with their nonadjacent tissues as normal from patients’ undergone pancreaticoduodenectomy for periampullary carcinoma were analysed for the mutational, expression, hypermethylation and apoptotic status of PTEN gene. Molecular profiling was performed by next generation sequencing, protein expression by immunohistochemistry, the methylation status by methylation specific PCR and Programmed cell death (apoptosis) by terminal deoxynucleotidyltransferase biotin–dUTP nick end labelling (TUNEL) assay. The changes were correlated with clinicopathological characteristics, overall survival (OS) and recurrence free survival (RFS).

Results: Total 107 specimens (77 men, 30 women) were evaluated, 41(38) had well differentiated while 66 (62) had moderately or poorly differentiated tumors. Patient in their early stage T1 are having better survival as compared to stage T2 T3 and T4 with the significant p- value 0.017 while patients with positive lymph nodes showing poor survival in comparative with the patients with negative lymph nodes with P = 0.047. Further, those who not receiving adjuvant CTRT were shown to have better survival with highly significant P = 0.00. In-addition, patients with ampullary tumor were shown to have better survival than tumors of common bile duct, duodenum and head of pancreas with high significant P = 0.00. However, cases with recurrence were shown to have poor survival as compare to patients with no recurrence P = 0.00. The correlation of molecular parameters with clinicopathological characteristics showed significantly more loss of expression in ampullary tumours (P = 0.06) while significantly more hypermethylation (P = 0.08) and loss of apoptosis (P = 0.06) in patients with age >50years.

Conclusions: The loss of expression of PTEN gene is seen in ampullary subgroup of periampullary tumours. The promoter hypermethylation of PTEN gene and spontaneous apoptosis suppression in significantly more in older patients. PTEN gene loss did not have less impact on survival.

Keywords: Pten gene, Periampullary carcinoma, Methylation, Gene silencing

Optimal Time and Condition of Hypoxic Preconditioning to Maximize Mesenchymal Stem Cell Function

Waqar Khalid Saeed1, Dae Won Jun2

1Nihtar Medical College and Hospital, Multan, Pakistan, 2Department of Internal Medicine Hanyang University, Seoul, South Korea

Aims: There are several reports that hypoxic preconditioning can enhance stem cell function. But the optimal time and condition of hypoxia of stem cell as well as its effect on function are still unclear. We investigated the characteristics of stem cells obtained from various hypoxic culture conditions (0.5–5% O2) and normal oxygen culture conditions (21% O2) to find out optimal culture conditions.

Methods: Cell viability and morphology were measured by MTT assay and trypan blue incorporation and cell number count assay in combination with normal and hypoxic culture conditions. In addition, the expression of major transcription factors, intracellular proteins, and paracrine factor of mesenchymal stem cells was confirmed by western blot and multiplex assay in various hypoxic culture conditions.

Results: Cell viability of hypoxic condition (0.5–5% O2, and 24–48hr) slightly increased compared to normoxia, but there were significant differences. HIF-1α, a typical marker of hypoxia, increased in 0.5% and 1% O2 at 48 hours. We performed the whole cytokine array and compared the expression levels at each condition by selecting the factors which increased in hypoxic culture. Most of the factors that increased in hypoxic cultures were known to be important factors in neuronal cell growth and regeneration. The expression levels of angiogenin, IGF-BP-2, MCP-1, IL-2Ra, VEGF-A and PDGF-BB were increased in hypoxia compared to normoxia. Cell proliferation was highest in 48h hypoxia (0.5% and 2% O2 concentration).

Conclusions: PDGF-BB, IGFBP-6, VEGF-A, NT-3 and angiogenin at 48 hours were increased in hypoxia (0.5% and 2% O2).

Keywords: Stem cells, Hypoxia, Paracrine effect

TRP2, a Prodrug of BMP7 Suppresses Hepatic Fibrosis in Mice Induced by the Treatment with Carbon Tetrachloride

Kyoungjoo Cho1, Nam Hee Kim2, Hyejeong Park1, Hyuk Moon1, Hyun Sil Kim3, Jong In Yook1, Kwang-Hyub Han1,2, Sang Hoon Ahn1,2, Simon W. Ro3, Seung Up Kim1,2

1Yonsei Liver Center, Severance Hospital, 2Department of Internal Medicine Hanyang University, Seoul, South Korea, 3Department of Internal Medicine Hanyang University, Seoul, South Korea

Aims: There are several reports that hypoxic preconditioning can enhance stem cell function. But the optimal time and condition of hypoxia of stem cell as well as its effect on function are still unclear. We investigated the characteristics of stem cells obtained from various hypoxic culture conditions (0.5–5% O2) and normal oxygen culture conditions (21% O2) to find out optimal culture conditions.

Methods: Cell viability and morphology were measured by MTT assay and trypan blue incorporation and cell number count assay in combination with normal and hypoxic culture conditions. In addition, the expression of major transcription factors, intracellular proteins, and paracrine factor of mesenchymal stem cells was confirmed by western blot and multiplex assay in various hypoxic culture conditions.

Results: Cell viability of hypoxic condition (0.5–5% O2, and 24–48hr) slightly increased compared to normoxia, but there were significant differences. HIF-1α, a typical marker of hypoxia, increased in 0.5% and 1% O2 at 48 hours. We performed the whole cytokine array and compared the expression levels at each condition by selecting the factors which increased in hypoxic culture. Most of the factors that increased in hypoxic cultures were known to be important factors in neuronal cell growth and regeneration. The expression levels of angiogenin, IGF-BP-2, MCP-1, IL-2Ra, VEGF-A and PDGF-BB were increased in hypoxia compared to normoxia. Cell proliferation was highest in 48h hypoxia (0.5% and 2% O2 concentration).

Conclusions: PDGF-BB, IGFBP-6, VEGF-A, NT-3 and angiogenin at 48 hours were increased in hypoxia (0.5% and 2% O2).

Keywords: Stem cells, Hypoxia, Paracrine effect
**Development of Doxorubicin-Incorporated Phenylboronic Acid Nanoassembly and Evaluation of Anti-Cancer Effect in Hepatocellular Carcinoma**

Byung-Yoon Kang¹, Sung Min Kim², Wonhee Hur¹, Won Jong Kim¹, Seung Kew Yoon*¹

¹The Catholic University Liver Research Center & WHO Collaborating Center of Viral Hepatitis, College of Medicine, The Catholic University of Korea, Seoul, Korea, ²Department of Chemistry, Pohang University of Science and Technology (POSTECH), Pohang 37673, Korea

**Aims:** Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third highest cause of cancer-related death. Various therapeutic approaches have been proposed in an attempt to prolong survival of advanced HCC patients using different anti-cancer drugs or delivery systems. In this study, we investigated the ways to maximize the efficiency of delivery of anti-cancer drugs in HCC.

**Methods:** In vitro cytotoxicity of the nanocomplex with PBA conjugated doxorubicin (Dox), Dox and Phenylboronic acid (PBA) alone in various HCC cells was assayed by MTT assay. Using the xenograft and orthotopic model, the anti-cancer effect of nanocomplex was evaluated by measuring the tumor size and MR imaging. Serum AFP, ALT and creatinine levels were measured in those mice.

**Results:** The cytotoxicity of the nanocomplex increased dependent on its concentration. At low concentrations, nanocomplex showed higher cytotoxicity than DOX alone in HCC cells. On the other hand, PBA itself have no cytotoxicity in liver cells. In vitro, nanocomplex showed higher targetability in liver cancer cells by fluorescent imaging. In vivo experiments using bio-imaging showed that the nanocomplex was more efficiently delivered to the tumor. In the Xenograft and orthotopic model, the tumor size in mice treated with nanocomplexes decreased than DOX alone group. In addition, serum AFP in nanocomplex group significantly decreased, but ALT and creatinine levels were within normal range. These results showed that nanocomplex exhibit better anti-cancer effects than DOX alone but does not cause liver and kidney toxicity.

**Conclusions:** The improved therapeutic effect of the nanocomplexes can be explained by active targeting via the enhanced cellular uptake by residual PBA moieties, and drug release in the intracellular environment. Nanocomplex have potent and specific anti-cancer effects on liver cancer cells. The overall results suggest therapeutic potential of pPBA-DOX nanocomplexes in liver cancer therapy.

*This research was supported by BrainKorea 21.*

**Keywords:** Hepatocellular carcinoma, Doxorubicin, Drug delivery system, Phenylboronic acid, Nanocomplex

---

**The Degree of HCC Differentiation Determines the Drug Diffusion in MCTS**

Kyungjoo Cho¹, Hyuk Moon¹, Soonyeong Shin¹, Simon W. Ro¹,², Jun Yong Park¹,², Do Young Kim¹,², Kwang-Hyub Han¹,²

¹Yonsei Liver Center, Severance Hospital, ²Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Republic of Korea

**Aims:** Hepatocellular carcinoma (HCC) treatment with multikinase inhibitor such as sorafenib is the most option for advanced HCC. Due to tumor heterogeneity, its efficacy greatly varies among patients and is limited due to adverse effects and drug resistance. Previous studies have shown that response to chemotherapy is highly affected by drug permeability through tumor tissue, highlighting the role of tumor microenvironment in cancer chemotherapy. As multi-cellular tumor spheroid (MCTS)
Knockdown of ATG7 Suppresses Tumorigenesis in HCC Mouse Models Induced by HRASG12V and shp53

Beom Kyung Kim1,2, Sooyoun Shin1,2, Hyuk Moon1, Kyungjoo Cho1, Seung Up Kim1,2 Do Youn Kim1,2, Simon W. Ro2, Kwang-Hyub Han1,2

1Brain Korea 21 PLUS project for Medical Science College of medicine, Yonsei University College of Medicine, Seoul, Korea
2Department of Internal Medicine, Kaski Sewa Hospital and Research center Pokhara, Nepal

Aims: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer in adults and the second leading cause of cancer-related deaths worldwide. Many studies showed that autophagy is associated with liver cancer. ATG7 is a critical component for the formation of autophagosome and thus required for autophagy processes. To investigate the effect of autophagy on liver cancer, we utilized ATG7 knock-down transgenic mouse models.

Methods: Transposon vectors encoding short hairpin RNA downregulating ATG7 (ATG7 shRNA) were constructed. Transposons encoding ATG7 shRNA were mixed with those encoding HRASG12V and shp53 and then injected into the lateral tail veins of 5-week-old C57Bl/6 mice. The development of liver cancer was observed grossly and histologically at 5-6weeks post hydrodynamic injection. Expression of genes related to autophagy process was assessed using western blotting and immunohistochemistry.

Results: We assessed knockdown efficiency of various ATG7 shRNAs in NIH3T3 cells. ATG7.1536 shRNA was most effective in downregulating ATG7. Mice were hydrodynamically transfected with transposons encoding shATG7 and then analyzed for tumor development in the liver. We found that the size and numbers of tumor nodules significantly decreased in the ATG7 knockdown groups compared to control. Histological examination of tumors from shATG7 mice showed knock-down of ATG7 and suppression of autophagic processes.

Conclusions: Knockdown of ATG7 led to a significant decrease in tumorigenesis induced by HRASG12V and shp53. Inhibiting the autophagosome formation is expected to be a therapeutic option for liver cancer.

Keywords: ATG7, HCC, Autophagosome, Hydrodynamic transfection
PE-030
Prevalence and Clinical Characteristics of Antibiotics Associated Drug Induced Liver Injury: From a Single Center Experience
Jin Hwa Park, Dae Won Jun, Dae Hyun Lim, Won Woo Seo, Ji Hyun Yeo, Na Ryung Choi, Jai Hoon Yoon, Kang Nyeong Lee, Hang Lak Lee, Oh Young Lee, Byung Chul Yoon, and Ho Soon Choi
Department of Internal Medicine, University of Hanyang College of Medicine, South Korea

Aims: The use of antibiotics increases recently. Accordingly, the incidence of antibiotics associated with drug induced liver injury (DILI) also increases. The purpose of this study is to evaluate the proportion and the clinical characteristics of antibiotic associated with DILI.

Methods: This study is a retrospective study of analyzed adult patients who were referred to the department of hepatology for the elevation of liver function tests and the frequency of elevated liver enzyme of patients with prescribed antibiotics during the same period at outpatient setting as a validation set. Five times higher than upper normal limits in 5% of flomoxef in inpatients setting (training set). The frequency of antibiotics associated with DILI was high in order of flomoxef, ceftriaxone, vancomycin, piperacillin/tazobactam and amoxicillin/clavulanate. In the same period, 32% of the patients who prescribed flomoxef showed elevated liver enzyme levels above the upper normal limit. The prevalence of flomoxef induced DILI (> 3 folds of ALT) was 13% and liver enzyme levels were five times higher than upper normal limits in 5% of flomoxef groups. Hypertension or diabetes was the risk factor of flomoxef associated with DILI.

Keywords: DILI, Antibiotics, Drug, Liver

High Levels of Procalcitonin in the Early Phase after Pediatric Liver Transplantation Indicate Poor Postoperative Outcome
Samat Issakov, Nursultan Kydyr
General surgery, National Research Center for Maternal and Child Health, Kazakhstan

Aims: To date, no data is available about procalcitonin (PCT) levels and its relevance to morbidity and graft function in the early phase after pediatric liver transplantation (pLTx). The aim of this study was to analyse the prognostic relevance of early postoperative PCT elevations in pediatric liver recipients.

Methods: Thirty pediatric patients who underwent 32 liver transplantations were included into this observational single-center study.

Results: Patients with high PCT levels on postoperative day (POD) 2 had higher International Normalized Ratio values on POD 5 (P < 0.05) and suffered more often from primary graft non-function (P < 0.05). They also had a longer stay in the pediatric intensive care unit (P < 0.01) and on mechanical ventilation (P = 0.001). There was no correlation between PCT elevation and systemic infection. However, PCT levels were correlated with peak serum lactate levels immediately after graft reperfusion and elevation of serum aminotransferases on POD 1 (r²=0.61, P < 0.001).

Conclusions: High levels of PCT after pLTx are an early indicator of poor postoperative outcome and may reflect ischemia induced liver cell injury within the context of an ischemia-reperfusion injury.

Keywords: Procalcitonin, Pediatric liver transplantation, Graft function, Serum lactate levels

Cardiovascular Risk Factors after Conversion from Cyclosporine to Tacrolimus in Children after Liver Transplantation
Akmaral Dossanova, Lazzat Dossanova
In a rare case of toxic hepatitis caused by taking Noni powder, the etiology of toxic hepatitis is varied, one is caused by the metabolites. This case is toxic hepatitis caused by Noni powder, which has never been reported in the past. There was no other cause of toxic hepatitis and we report a case with confirmed histopathology.

Keywords: Toxic, Hepatitis, Noni, Noni powder

**Methods:** The study group consisted of 7 children (5 females and 2 males) after LRLTx performed at the median age of 3 years (range 0.8-7.2), who received CS monotherapy for at least 5 years before it was switched to TAC. The median age at conversion was 13.1 years (range 10.1-18). Weight BMI Z-score, 24-h ABPM (ambulatory blood pressure monitoring), renal function assessment, and fasting lipid and oxidative stress profiles were performed before and 12 months after conversion.

**Results:** Within 1-year follow-up, TAC was well tolerated and we did not observe any drug-related adverse effects or severe infections. Renal function, blood pressure, and lipid parameters did not differ after the conversion. Before the conversion, there was lower median glutathione (GSH) levels (748 vs. 776 [μmol/l]) and glutathione peroxidase (GPx) activity (31.4 vs. 32.4 [U/gHb]), but statistical significance was not reached (P > 0.05). Asymmetric dimethylarginine (ADMA) levels were higher before conversion to TAC (0.93 vs. 0.69 [μmol/l], P = 0.01), as were oxidized LDL (oxLDL) levels (317 vs. 264 [mU/ml], P = 0.04).

**Conclusions:** There was no significant difference between CS and TAC in risk factors for CV events. Potential benefits in oxidative stress profile resulting from CS to TAC conversion may add another important area for further research.

**Keywords:** Calcineurin inhibitors, Living related liver transplantation, Tacrolimus, Cyclosporine

### Study on Validity of Biomarkers DKK1 and HBx-LINE1 in Diagnosis and Posttreatment Monitoring of Hepatocellular Carcinoma

**Aims:** Evaluate validity of DKK1 and HBx-LINE1 in diagnosis and post-treatment of HCC/HBV and analyse relationship with clinical and paraclinical some characteristics.

**Methods:** Study on 114 HCC patients at 108 Military Central Hospital, 103 Military Hospital and 175 Military Hospital from 1/2016 to 3/2018 with DKK1 and HBx-LINE1, re-examination after surgery.

**Results:** With DKK1 ≥2,15 ng/ml, the positive rates of serum protein DKK1 were significant increased when compared with those of AFP (97.37% so vs 62.92%). The mean of serum protein DKK1 of HCC was significant higher than it in liver cirrhosis patients with P < 0.05. Combination between AFP and DKK1 expression will improved positive rates and help more diagnosis. Using combination of AFP, serum protein DKK1 and DKK1 expression may help diagnosis for negative AFP of HCC cases. Logistic regression analysis showed the risk of HCC will increased about 18.5 times when DKK1 ≥2,15 ng/ml. The level of DKK1 expression reduced in patients with ≥2 tumors when compare with one tumor and in cases with size ≥5 cm when compare with <5 cm. This correlation was the same with reducing of AFP related with quantity and size of tumor. The level of DKK1 expressions reduced in posthepa-
Research on PNPLA3 Gene in Patients with Type 2 Diabetes Mellitus and Accompanying Hepatic Pathology in Yakutia

Aleksandra Diakonova, Dyakonova A.T.1, Kurtanov Kh. A.2, Pavlova N. I.3, Soloveva N. A.1, Soloveva Y. A.3, Sydykova L. A.2, Filippova N. P.4, Alekandrova T. N.1

1 Federal State Budgetary Institution "Yakut Science Center of Complex Medical Problems", Yakutsk; 2 Federal State Autonomous Educational Institution of Higher Education "M. K. Ammosov North-Eastern Federal University"; 3 State Budgetary Institution of the Republic of Sakha (Yakutia) "Yakut Republican Clinical Hospital", Russia

Aims: Studies of foreign and domestic scientists show the frequent combination of non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (type 2 diabetes). The combination of these diseases aggravates each other, significantly increasing the likelihood of the patient developing liver fibrosis, hepatocellular carcinoma and cardiovascular diseases, as well as high mortality. Study of the frequency distribution of alleles among the Russian and Yakut population of the Republic of Sakha (Yakutia) as well as the search for associations of the polymorphic variant of the PNPLA3 gene (rs738409 C>G) with liver diseases in patients with type 2 diabetes.

Methods: The study used DNA samples (n = 178) diagnosed with type 2 diabetes and concomitant liver diseases (the diagnosis is verified in medical organizations at the place of residence). The sample included 27 patients of the Russian and 151 patients of the Yakut nationalities. The comparison group was a sample of 135 healthy volunteers of Russian nationality and 246 healthy volunteers of Yakut nationality.

Results: Analysis of the frequency distribution of alleles and genotypes of the polymorphic variant of the PNPLA3 gene (rs738409) in the studied samples showed the difference between Yakuts and Russians in both healthy volunteers and those suffering from liver diseases.

Conclusions: A significant difference was found between the frequencies of genotypes and alleles of the PNPLA3 gene (rs738409) in Russians and Yakuts, both among healthy volunteers and in patients with type 2 diabetes with liver diseases. The frequency of occurrence of the G allele in the group of healthy yakuts was significantly higher (OR= 3.085; 95% CI: 2.260 - 4.210; \( P < 0.001 \)) than in the group of healthy Russians. When analyzing the distribution of frequencies of genotypes and alleles among a healthy sample and a sample of patients with liver diseases, both in the Russian and Yakut populations, no significant differences were found.

Keywords: Hepatitis B virus, Hepatocellular carcinoma, Biomarker DKK1, Biomarker HBx-LINE1

HBV, Basic

Ciclopirox Inhibits Hepatitis B Virus Secretion by Blocking Capsid Assembly

Jung-Ah Kang1, Songwon Kim1, Minji Park2, Hyun-Jin Park1, Jeong-Hyun Kim1, Sanghyeok Park2, Jeong-Ryul Hwang1, Yong-Chul Kim1, Yoon Jun Kim1, Mi Sun Jin1, Sung-Gyoo Park1, Yuri Cho1

School of Life Sciences, Gwangju Institute of Science and Technology, Gwangju, Republic of Korea, 2Department of Internal Medicine, CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, Republic of Korea

Aims: Chronic hepatitis B virus (HBV) infection can cause cirrhosis and hepatocellular carcinoma and is therefore a serious public health problem. Infected patients are currently treated with nucleoside/nucleotide analogs (NAs) and interferon a. However, this approach is not curative, and combined therapies that target multiple steps of the HBV life cycle are needed. Therefore, novel therapeutic agents are urgently required.

Methods: We screened 978 US Food and Drug Administration-approved compounds for their ability to inhibit HBV replication in HBV-expressing HepG2.2.15 cells. Quantitative PCR and southern blot analysis were performed to measure secreted and intracellular HBV DNA and intracellular cccDNA. Immunoblot analysis and electron microscopy were performed to analyze HBV capsid assembly in vitro. Human liver-chimeric uPA/SCID:PKX mice by PhoenixBio Co., Ltd. (Higashi-Hiroshima, Japan) were used for in vivo analysis.

Results: Ciclopirox, a synthetic antifungal agent, strongly inhibited HBV replication in cells and mice by blocking HBV capsid assembly. The crystal structure of the HBV core protein and ciclopirox complex revealed a novel binding mode at dimer-dimer interfaces. Ciclopirox synergized with NAs to prevent HBV replication in cells and in a humanized liver mouse model.

Conclusions: Orally-administered ciclopirox may block HBV capsid assembly effectively and thus provide a novel opportunity to combat chronic HBV infection.
Keywords: Hepatitis B virus, Capsid assembly, Ciclopirox, Antiviral

PE-037

cccDNA-Induced Hepatocarcinogenesis Is Regulated by HBx-Stimulated Interaction between MSL2 and cccDNA

Xue-Li Jin, Suk-kyun Hong, Hwa-jung Kim, Sun-Kyung Lee, Nam-Joon Yi, Kwang-Woong Lee, and Kyung-Suk Suh

Department of Surgery, Seoul National University College of Medicine, Seoul, Korea

Aims: Hepatitis B virus (HBV) infection is a global health problem and chronic hepatitis B is the leading cause of hepatocellular carcinoma. The covalently closed circular DNA (cccDNA) is an intermediate in the life cycle of HBV virus. HBV-encoded X protein (HBx), a key viral oncoprotein, can be specifically modified by E3 ubiquitin ligase, such as Male Specific Lethal 2 (MSL2), a process called ubiquitination that up-regulates HBx activity to promote transcription, cell proliferation and tumor growth. This study aimed to compare the cccDNA, MSL2 mRNA and HBx mRNA levels in tumor and peri-tumor tissues, and explore the interaction between the level of cccDNA and MSL2 mRNA based on the HBx positive or negative. Moreover, we clarified the impact of antiviral therapy on these indicators.

Methods: The levels of intrahepatic cccDNA, MSL2 mRNA and
HBx mRNA in 50 patients with HBV-related HCC who had undergone liver surgery were compared. Real-Time PCR assay was performed to quantify these indicators.

**Results:** A total of 50 patients were included (49 HbsAg positive and 1 showing seroconversion after antiviral treatment). Before surgery, 31 of them had undergone antiviral treatment and 19 had not. Intrahepatic cccDNA levels were significantly higher in the tumor tissues than in peri-tumor tissues (37/50, 74%; P = 0.001). The cccDNA level in the tumor and peri-tumor tissues was significantly different, especially in the HBeAg positive group (n = 14; P = 0.008), tumor recurrence group (n = 17; P = 0.002) and <3 cm tumor size group (n = 20; P = 0.003). The levels of cccDNA and MSL2 mRNA in the HBx positive group were significantly higher in tumor tissues than in peri-tumor tissues (n = 23; P = 0.026 and 0.015). The level of HBx mRNA in antivirally treated peri-tumor tissues was significantly lower than that in untreated tissues (P = 0.010).

**Conclusions:** cccDNA may participate in the tumorgenesis of HBV-related HCC, a process regulated by the HBx-stimulated interaction between MSL2 and cccDNA. In addition, antiviral therapy may inhibit this process through reducing HBx levels.

**Keywords:** Hepatitis B, cccDNA, HBV DNA, HCC, MSL2, HBx, HCC recurrence

---

**PE-038**

**The Effect of Living Donor Liver Transplantation on the Treatment of Severe Hepatitis**

Daulet AZIM1, Bauyrzhan DARZHIGENOV2

1Gastroenterology, City Hospital № 1 in Astana, Kazakhstan, 2Hepatology Department, Hepatology Center of Almaty, Kazakhstan

**Aims:** To evaluate the effect of living donor liver transplantation on the treatment of severe hepatitis.

**Methods:** 18 patients with severe hepatitis received liver transplantation (transplanted severe hepatitis group), 28 patients with severe hepatitis received non surgical treatment (non-transplanted severe hepatitis group), and 30 patients with end stage liver cirrhosis (without cancer) received liver transplantation (transplanted cirrhosis group). The vital sign, blood coagulation, and renal function were monitored during operation. After liver transplantation, patients received immunosuppressive therapy (including tacrolimus or cyclosporine A, mycophenolate, methyl and corticosteroids), intensive care, antiviral therapy (including lamivudine and HBIG) and other treatments (including restoration of liver function and prevention of blood coagulation). Pre-operation data, operation procedure, liver function, renal function and the operation complications of three groups were compared, and survival rate at 1, 6 and 12 months after operation was followed.

**Results:** There was no significant difference in the operation time, warm ischemia time, hypothermic ischemia time and Graft-to-recipient weight ratio between the two transplantation groups. The blood loss volume and blood transfusion volume in the transplanted severe hepatitis group were higher than that those in the cirrhosis transplantation group (t = 0.001, 0.004). The levels of Tbil, ALT and AST at day 7 after operation were (100.5 +/- 96.4) mumol/L, (215.3 +/- 195.7) U/L, (209.8 +/- 188.6) U/L in the transplanted severe hepatitis group, and (53.3 +/- 31.9) mumol/L, (56.3 +/- 22.1) U/L, (51.3 +/- 13.5) U/L in the transplanted cirrhosis group (t = 0.017, 0.021, 0.004). However, there was no significant difference in the levels of Alb and Cr between these two groups (P > 0.05). Survival rate was 88.89%, 83.33% 83.33% in the transplanted severe hepatitis group, and 96.67%, 93.33% 93.33% in the transplanted cirrhosis group.
cirrhosis group at 1, 6 and 12 months after transplantation.

Conclusions: Living donor liver transplantation is one of effect ways for the treatment of severe hepatitis.

Keywords: Living donor liver transplantation, Liver cirrhosis, Immunosuppressive therapy, Severe hepatitis

**PE-039**

**Costs of Viral Hepatitis B in the Republic of Korea, 2002–2015**

Dahye Baik1, Byung-Woo Kim1, Jin-Kyoung Oh1, Kyung-Ah Kim1, Moran Ki1

1Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, Republic of Korea, 2Department of Internal Medicine, Inje University Ilsan Paik Hospital, Goyang, Republic of Korea

Aims: Even after the initiation of vaccination programs in 1990’s, the positive rates for hepatitis B surface antigen in the Republic of Korea has remained at 3% level in recent 10 years. Despite the high prevalence and heavy burden of HBV infection, there have been no research on its costs reflecting the changes in application of the National Health Insurance Service (NHIS) coverage on antiviral drugs and recently revised guidelines regarding chronic hepatitis B management. The objective of this study is to estimate the economic burden of viral hepatitis B and trend of changes in its costs between 2002 and 2015.

Methods: Claims data from the NHIS which covers entire Korean citizens were used. To identify viral hepatitis B cases, the ICD-10th code B16, B17.0, B18.0, and B18.1 were used based on a primary diagnosis. This study was conducted from a societal perspective regarding both direct and indirect costs. Annual costs were adjusted for inflation by calculations based on the 2015 costs.

Results: The number of patients who made claims based on a viral hepatitis B diagnosis increased from 213,758 in 2002 (crude prevalence rate, 444.2 per 100,000) to 342,672 in 2015. The pharmaceutical costs increased from 127.1 million USD in 2002 to 459.1 million USD in 2015. The total socioeconomic costs increased from 127.1 million USD in 2002 to 459.1 million USD in 2015. The healthcare costs for viral hepatitis B accounted for 0.13% of the national health expenditure in 2002, increasing to 0.31% in 2015. The pharmaceutical costs accounted for the largest proportion of total costs since 2009—220.5 million USD in 2015, which was approximately 15 times higher than that in 2002.

Conclusions: Among the socioeconomic costs of viral hepatitis B, healthcare costs have remarkably increased, mainly due to the increased costs of antiviral drugs. Therefore, effective policy and efficient management are needed to reduce the economic burden of HBV infection.

Keywords: Hepatitis B, Cost analysis, Antiviral drugs, Korea

**PE-040**

**Knowledge and Practice of Hepatitis B and C among Medical and Health Science Students in Nepal**

Mani Neupane1, Bimala Sharma2, Bishnu Raj Tiwari2

1Community Medicine Department, Gandaki Medical College, Pokhara, Kaski, Nepal, 2School of Health and Allied Science, Pokhara University, Kaski, Nepal

Aims: Medical students like other health workers are being part of the health care delivery system are exposed to the same size of risk as other health care workers when they come in contact with patients and contaminated instruments. Knowledge of hepatitis B and C has been reported to be low among respondents in different studies. We conducted cross-sectional study among medical and health science students of Gandaki Medical College, Nepal to ascertain their knowledge and practices regarding hepatitis B and C.

Methods: A self-administered questionnaire consisting of questions to assess the knowledge and practice regarding hepatitis B and C infection, and perception of the medical students was duly filled by 48 students including first, second, third and fourth year. The data were entered and analyzed using Statistical Package for Social Sciences (SPSS) software version 25.

Results: Of the total 48 respondents, 29.2% were males and 70.8% were females; 93.8% were unmarried. There was universal knowledge on causative agent, availability of preventive vaccines, transmission through infected needle or sharp object injury and liver cancer as its complication. Most of the students knew that hepatitis B could be prevented by vaccines however, 37% students mentioned that hepatitis C also could be prevented by vaccines. A 81.3% had proper knowledge about hepatitis B and hepatitis C could be prevented by proper disposal of needle and sharp instruments. Similarly, 83.3% had correct knowledge about mother to child transmission. However, about half of the respondents did not know hepatitis B and hepatitis C can be transmitted by sexual intercourse. Of the total, 85.4% respondents mentioned that hepatitis B and hepatitis C can not be transmitted from feco-oral route. Most of the students reported they used gloves while handling different body fluids and did proper or disposal of needle and sharps. Of total, 25% had history of needlestick injury but only 4% reported for the injury. Of total, 16% students had been ever screened for hepatitis B or hepatitis C; 8% of the total had history of tattoo piercing practices.

Conclusions: Most of the respondents were aware about the hepatitis B and C, however, comprehensive knowledge on mode of transmission and preventive measures was lacking. Reporting after needlestick injury and screening for hepatitis B and C was low.

Keywords: Hepatitis, Knowledge, Practice, Students
**Prevalence of Hepatitis Delta Virus Infection in Patients with Chronic Hepatitis B in Eastern Province Mongolia**

Bayarmaa Nyamaa, Nyam Biziya, Shinebayar Narantuya, Borkhuukhen Derem

Aims: Hepatitis delta virus (HDV) is a serious cause of liver-related morbidity and mortality worldwide. The aim of our study was to determine the prevalence of HDV infection among patients positive for hepatitis B surface antigen (HBsAg) living in the Dornod province, which is in Eastern Mongolia.

Methods: Total of 251 HBV infected patients visiting the outpatient clinic at Dornod Medical Center from 2017 to January 2019 were screened for anti-HDV antibodies using ELISA assays. Anti-HDV-positive individuals were examined to determine HDV-RNA level by RT-PCR assay. Liver transaminases were analyzed using a commercial biochemistry kit.

Results: Of all patients, 115 were men (46%) and 136 were women (54%). The average age was 48 (between 16 and 70 years). Anti-HDV was positive in 73% (183/251) and all were checked for HDV RNA and 98% were found positive (179/183) all of the patients. Anti-HDV antibody positive patients showed significant liver cirrhosis higher (109/183) than Anti-HDV negative patients (16/68).

Conclusions: Our study showed hepatitis delta virus infection in HBsAg positive patients who live in Eastern province Mongolia higher than other provinces of Mongolia. Thus liver cirrhosis most related with positive anti-HDV patients.

Keywords: Hepatitis B virus, Hepatitis D virus, Prevalence

**Cases of the Influence of Mare’s Milk on the Course of Viral Hepatitis B + D**

Gulsat Daribayeva, Erbol Dghapakov

Aims: Evaluate the effectiveness of mare’s milk in viral hepatitis B + D.

Methods: The results of self-treatment of mare’s milk in two patients with viral hepatitis B + D were studied. In both patients were examination for a PCR blood test and viral hepatitis B + D was detected. Fibroscan examination of the liver revealed fibrosis of 2–3 degrees. Patients refused to take antiviral drugs and were treated on their own by drinking mare’s milk. Mare’s milk was delivered to patients immediately after milking and was consumed daily in the morning for 200–300 ml during 6–8 months. Every month, patients underwent biochemical blood tests, serum tests for liver enzymes, a coagulogram, an ultrasound scan and liver fibroscanning. Once in every three months a blood test was performed on PCR for viral hepatitis.

Results: As a result of taking mare’s milk, patients showed an improvement in their general condition. The data of monthly biochemical blood tests, the results of coagulogram showed minimal positive dynamics: a decrease in the level of hepatic enzymes, normalization of coagulogram were noted. Fibroscan of the liver did not reveal negative dynamics. A quantitative PCR blood test also showed a moderate reduction of the viral load.

Conclusions: Regular long-term usage of fresh mare’s milk without antiviral drugs does not cause the progression of the development of viral hepatitis B + D. We believe that the use of mare’s milk for viral hepatitis should be approached individually.

Keywords: Viral hepatitis, Mare’s milk, Fibroscan, Influence
(1.92 vs. 1.69 per 100 person-years [PY], respectively; adjusted hazard ratio [HR], 0.975 [P = 0.852] by multivariate analysis). Propensity score (PS)-matched and inverse probability of treatment weighting (ITPW) analyses yielded similar results for both groups (HR, 1.021 [P = 0.884] and 1.039 [P = 0.988], respectively). The annual incidence of death or OLT was similar between the ETV and TDF groups (0.52 vs. 0.53 per 100 PY, respectively; adjusted HR, 1.202 [P = 0.451]). PS-matched and ITPW analyses yielded similar results for both groups (HR, 1.248 [P = 0.385] and 1.239 [P = 0.360], respectively). These findings were consistently reproduced in patients with compensated cirrhosis (all P > 0.05).

Conclusions: The risks of HCC and death or OLT were consistently similar between the ETV and TDF groups. Further studies are needed to validate our results.

Keywords: Entecavir, Tenofovir, Hepatocellular carcinoma, Prognosis

The Liver Week 2019

Table 1. Baseline characteristics of Korean CHB cohort

<table>
<thead>
<tr>
<th>Variables</th>
<th>N = 863</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.4 ± 10.5</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>534 (61.9)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.9 ± 3.4</td>
</tr>
<tr>
<td>Current alcohol intake, n (%)</td>
<td>281 (32.6)</td>
</tr>
<tr>
<td>Current smoker/Ex smoker, n (%)</td>
<td>108 (12.5) / 171 (20.1)</td>
</tr>
<tr>
<td>Family history of HBV (parents), n (%)</td>
<td>270 (31.3%)</td>
</tr>
<tr>
<td>HBsAg positivity, n (%)</td>
<td>370 (42.9)</td>
</tr>
<tr>
<td>Liver cirrhosis, n (%)</td>
<td>278 (32.2)</td>
</tr>
<tr>
<td>Platelet count, n/mm³</td>
<td>182.6 ± 65.3</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>37.6 ± 68.2</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>40.6 ± 69.0</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.3 ± 0.4</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.9 ± 0.6</td>
</tr>
<tr>
<td>PT-INR</td>
<td>1.0 ± 0.1</td>
</tr>
<tr>
<td>HBV DNA PCR, IU/mL</td>
<td>9.007 ± 2518</td>
</tr>
<tr>
<td>HBV DNA &lt;2000 IU/ml</td>
<td>535 (62.0)</td>
</tr>
<tr>
<td>FibroScan score, kPa</td>
<td>8.8 ± 6.6</td>
</tr>
<tr>
<td>FIB-4 &gt; 3.25 / 1.45-3.25 / &lt; 1.45</td>
<td>96 (12.8)</td>
</tr>
<tr>
<td>APRI &gt; 2.0 / 1.0 - 2.0 / &lt; 1.0</td>
<td>33 (4.4) / 62 (7.3) / 654 (78.3)</td>
</tr>
<tr>
<td>Antiviral therapy, n (%)</td>
<td>783 (99.9)</td>
</tr>
<tr>
<td>History of resistance to antiviral therapy, n (%)</td>
<td>169 (19.6)</td>
</tr>
</tbody>
</table>

Data are expressed as number (percentage) or mean ± standard deviation.

Table 2. Types of antiviral drugs

<table>
<thead>
<tr>
<th>Treated antiviral agents</th>
<th>N = 783</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg-IFN</td>
<td>10 (1.3)</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>20 (2.6)</td>
</tr>
<tr>
<td>Clevudine</td>
<td>5 (0.6)</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>11 (1.4)</td>
</tr>
<tr>
<td>Adefovir</td>
<td>39 (5.0)</td>
</tr>
<tr>
<td>Entecavir</td>
<td>268 (34.2)</td>
</tr>
<tr>
<td>TDF</td>
<td>387 (49.4)</td>
</tr>
<tr>
<td>Besifovir</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>TAF</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Clinical trial (besifovir or tenofovir)</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>33 (4.2)</td>
</tr>
</tbody>
</table>

Data are expressed as number (percentage).

Table 3. Resistance to antiviral therapy

<table>
<thead>
<tr>
<th>Variables</th>
<th>N = 169</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine only resistance</td>
<td>111 (65.7)</td>
</tr>
<tr>
<td>Adefovir only resistance</td>
<td>11 (6.5)</td>
</tr>
<tr>
<td>Entecavir only resistance</td>
<td>10 (5.9)</td>
</tr>
<tr>
<td>Lamivudine + Adefovir resistance</td>
<td>7 (4.1)</td>
</tr>
<tr>
<td>Lamivudine + Entecavir resistance</td>
<td>24 (14.2)</td>
</tr>
<tr>
<td>Adefovir + Entecavir resistance</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Lamivudine + Edivofir + Entecavir resistance</td>
<td>5 (3.0)</td>
</tr>
</tbody>
</table>

Data are expressed as number (percentage).

Keywords: Epidemiology, Chronic hepatitis B, Prospective, Korean cohort

Conclusions: This is a prospective, longitudinal nationwide cohort of CHB patients in Korea. Natural history and long-term performance of antiviral therapy in Korean patients can be estimate using this cohort. In addition, unmet needs for CHB patients will be able to resolve through this cohort and blood samples.

Establishment of a Korean Chronic Hepatitis B Cohort Study

Mi Young Jeon¹, Tae Seop Lim²,³, Jae Seung Lee⁴, Hye Won Lee⁴, Sang Gyune Kim⁵, Eun Young Cho⁶, Young Mi Hong⁷, Yeon Seok Seo⁸, Ki Tae Yoon⁹, Beom Kyung Kim¹, Jun Yong Park¹, and Sang Hoon Ahn¹

Department of Internal Medicine, ¹Yonsei University College of Medicine, Seoul; ²Medipex Jeon Hospital, Incheon; ³Soonchunhyang University Hospital, Bucheon; ⁴Wonkwang University School of Medicine, Iksan; ⁵Pusan National University Yangsan Hospital, Yangsan; ⁶Korea University College of Medicine, Seoul, Republic of Korea

Aims: Korea is endemic area of chronic hepatitis B (CHB), but there were few longitudinal, prospective cohorts to represent Korean patients with CHB. The aim of this study is to introduce Korean CHB cohort, and discuss future research focus. In addition, we demonstrated baseline characteristics of enrolled patients as intermediate results.

Methods: Korean CHB cohort was established in 2015 funded by the Korea Centers for Disease Control and Prevention. Five tertiary hospitals participated in this study. We collected patient’s data from interview, self-questionnaires, laboratory test, imaging studies, and blood samples for research. Baseline characteristics was showed from October 2015 to May 2018.

Results: A total of 863 patients were enrolled from October 2015 to May 2018. Mean age was 50.4 ± 10.5, and the proportion of male patients was 61.9% (534/863). Hepatitis B e antigen positivity was 42.9% (370/863), and liver cirrhosis was 32.2% (278/863). The proportion of patients treated with antiviral therapy was 89.9% of patients was being treated with potent antiviral drugs such as tenofovir disoproxil fumarate, entecavir, tenofovir alafenamide, or besifovir.

Conclusions: This is a prospective, longitudinal nationwide cohort of CHB patients in Korea. Natural history and and long-term performance of antiviral therapy in Korean patients can be estimate using this cohort. In addition, unmet needs for CHB patients will be able to resolve through this cohort and blood samples.

Keywords: Entecavir, Tenofovir, Hepatocellular carcinoma, Prognosis

PE-044
**PE-045**

**Projection of Health Outcomes over 5-Year and 10-Year Using Tenofovir Alafenamide for the Management of Chronic Hepatitis B in China**

Ying Han¹, Bin Wu², Ming Hu³, Fengqin Hou⁴, Yida Yang⁵, Lei Wang⁶

¹Xijing Hospital of the 4th Military Medical University; ²Renji Hospital of Shanghai Jiaotong University; ³Huaxi Healthcare Policy and Pharmacoeconomics Research Centre, Sichuan University; ⁴The 1st Hospital of Peking University; ⁵The 1st Affiliated Hospital of Zhejiang University; ⁶The 2nd Hospital of Shandong University, China

**Aims:** The burden of chronic hepatitis B (CHB) infection in China is high, with an estimated 96 million patients. The goal of therapy is to suppress viral replication and achieve normalization of alanine aminotransferase (ALT) levels to reduce related liver complications such as compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC). In this study, we simulated the health consequences of nucleos(t)ide analog (NA) therapies on 100,000 Chinese CHB patients comparing tenofovir alafenamide (TAF) to tenofovir disoproxil fumarate (TDF) and entecavir (ETV).

**Methods:** A health outcomes model was developed using an individual patient simulation framework. Model inputs were sourced from randomized controlled trials and peer-reviewed Chinese literature and validated by a panel of Chinese hepatologists. The model assumed that 90% of patients in the overall population were treatment-experienced (TE), of which 27% were assumed to have lamivudine (LAM) experience. The 5-year and 10-year risks for developing CC and HCC were calculated based on REVEAL score, taking into account early ALT normalization.

**Results:** Over the 5-year and 10-year period, patients treated with TAF were expected to experience less liver complications including CC, DCC, and HCC compared to TDF and ETV (Table 1). Specifically, compared to TDF and ETV, with TAF the rates of HCC were reduced by 13% and 31% over the 5-year projection.

**Conclusions:** TAF is projected to have fewer hepatic complications when compared to TDF and ETV over 5-year and 10-year time period, driven by its favorable efficacy and resistance profile.

**Keywords:** CHB, TAF, Tenofovir alafenamide, Health outcomes, HCC, TDF, ETV

---

**PE-046**

**Lower Risk of Hepatocellular Carcinoma Development in Chronic Hepatitis B Patients with Immune Tolerant Phase Than Those with Antiviral Therapy**

Mi Young Jeon¹,³, Jun Yong Park¹,²,³, Do Young Kim¹,²,³, Sang Hoon Ahn¹,²,³, Kwang-Hyub Han¹,²,³, Beom Kyung Kim¹,²,³, and Seung Up Kim¹,²,³

¹Department of Internal Medicine, ²Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, South Korea, ³Yonsei Liver Center; Severance Hospital, Seoul, Korea

**Aims:** The risk of developing liver-related event (LRE) is controversial in chronic hepatitis B (CHB) patients with immune tolerant (IT)-phase. We compared the risk of developing LRE in CHB patients with IT-phase and those with antiviral therapy (AVT).

**Methods:** Consecutive patients with IT-phase and those with AVT between 2007 and 2017 were enrolled. IT-phase was defined as hepatitis B e antigen positive, HBV-DNA >20,000 IU/ml, and normal alanine aminotransferase (ALT, ≤40 IU/L). LRE included hepatocellular carcinoma (HCC), liver transplantation, or mortality.

**Results:** Of 125 (4.0%) patients with IT-phase, 46 (36.8%) stayed persistently in IT-phase, whereas the others experienced phase changes into inactive carrier (IC)-phase (n = 1, 0.8%) or minimally active (MA)-phase (n = 14, 11.2%), and immune active (IA)-phase with AVT (n = 64, 51.2%). The cumulative incidence of LRE was significantly lowest in patients with persistent IT-phase, middle in those with IT-phase at enrollment, but phase change into IA-phase with AVT, and highest in those with AVT (overall P = 0.015 in HCC and P = 0.029 in liver transplantation or mortality, log-rank test). When patients with IT-phase were censored at the time of phase change into IA-phase with AVT, the cumulative incidence of LRE was significantly low in patients with pure IT-phase than that of patients with AVT (both P = 0.002 for HCC and liver transplantation or mortality, log-rank tests).

**Conclusions:** CHB patients with IT-phase showed an extremely low risk of developing LRE than those with AVT. Thus, AVT should be cautiously considered for CHB patients with IT-phase.

**Keywords:** Immune tolerant, Hepatocellular carcinoma, Outcome, Antiviral therapy

---

**Table 1: Proportion of patients with Liver Complications over 5 Years and 10 Years (Based on 100,000 simulated CHB patients)**

<table>
<thead>
<tr>
<th>Treatment Phase</th>
<th>Over 5 Years</th>
<th>Over 10 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>10.2%</td>
<td>12.0%</td>
</tr>
<tr>
<td>DC</td>
<td>10.2%</td>
<td>11.2%</td>
</tr>
<tr>
<td>HCC</td>
<td>10.2%</td>
<td>13.2%</td>
</tr>
<tr>
<td>TDF</td>
<td>10.2%</td>
<td>12.0%</td>
</tr>
<tr>
<td>TAF</td>
<td>8.0%</td>
<td>10.2%</td>
</tr>
<tr>
<td>ETV</td>
<td>8.0%</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

**Notes:**

- CC—Compensated Cirrhosis
- DC— Decompensated Cirrhosis
- HCC— Hepatocellular carcinoma
- TDF—Tenofovir disoproxil fumarate
- TAF—Tenofovir alafenamide
- ETV—Entecavir

**Table 2: Baseline characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>TDF * (n=100,000)</th>
<th>TAF * (n=100,000)</th>
<th>ETV * (n=100,000)</th>
<th>Patients with IT-phase * (n=100,000)</th>
<th>Patients with AVT * (n=100,000)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>35 (25-45)</td>
<td>35 (25-45)</td>
<td>35 (25-45)</td>
<td>35 (25-45)</td>
<td>35 (25-45)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>55%</td>
<td>55%</td>
<td>55%</td>
<td>55%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Disease</td>
<td>CHB</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Notes:**

- *Variables are represented as median (interquartile range)."
**PE-047**

**Real-Life Indication and Efficacy of Tenofovir Alafenamide, Tenofovir Disoproxil Fumarate, and Entecavir for Treatment Naïve Chronic Hepatitis B Patients**

Si Ho Kim, Boo-ok Jang, Kyunghan Lee, Jae kyun Choi, Jin-Wook Kim, Sook-Hyang Jeong, Gwang hyeon Choi, Eun Sun Jang

Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, Korea

**Aims:** Tenofovir alafenamide (TAF) is known to improve safety of chronic hepatitis B (CHB) patients with similar efficacy compared to tenofovir disoproxil fumarate (TDF), but the real-life outcome was not fully demonstrated. In this study, we aimed to elucidate the prescription pattern and real-life efficacies of TAF, TDF and entecavir (ETV) among CHB patients in Korea.

**Methods:** A total of 302 treatment-naïve CHB patients started TAF (n = 67), TDF (n = 131) or ETV (n = 104) were consecutively enrolled from Nov 2017 to Feb 2019. Presence of diabetes mellitus (DM), hypertension, dyslipidemia, and chronic kidney disease were determined by medical record and laboratory findings. Biochemical and virologic response rates and the change of glomerular filtration rate (GFR) during 6-month after treatment initiation were compared.

**Results:** Mean age of patients treated with ETV (57.7±10.6 y.o) was significantly older than TAF (47.1±11.2) or TDF (51.0±10.8, P < 0.001). ETV was more frequently prescribed in DM (55.6%, P = 0.017), CKD (48.8%, P = 0.011) or HCC (55%, P < 0.001) patients compared to tenofovir. Mean GFR change at 24 weeks-of-treatment from baseline were 3.7, -5.8, and 0.2 in TAF, TDF and ETV group, respectively (P = 0.029). Cumulative ALT and virologic response were not significantly different in 3 groups, but AST response rate was lower in TDF group (58.5% at 6 mo, P = 0.034 in HBeAg+; 53.9%, P = 0.003 in HBeAg-) compared with TAF (85%, 90.9%) or ETV (66.7%, 75%). According to multivariable Cox analysis, antiviral drug (P < 0.0001), underlying liver disease (P = 0.051) and DM (P < 0.0001) were independent predictive factors for AST response in HBeAg- patients.

**Conclusions:** In real-world practice, ETV was preferred in older, HBeAg- patients with DM or advanced liver diseases. Although antiviral drug prescription is decided based on patient’s underlying disease which affected biochemical response, further large-scale study to confirm the favorable AST response with TAF is needed.

**Keywords:** Tenofovir alafenamide, Tenofovir disoproxil Fumarate, Entecavir, Chronic hepatitis B

---

**PE-048**

**Association between Hepatitis B Virus Infection and Agent Orange in Non-Hodgkin’s Lymphoma**

Wonhyeong Park, Sung Hoon Kim, Ji Sun Jang, Seung Whan Kim, Tae gyoong Kim

Department of Internal Medicine, Veterans Health Service Medical Center, Korea

**Aims:** Hepatitis B virus (HBV) infection can be associated with non-Hodgkin’s lymphoma (NHL). Agent Orange is also reported to cause NHL. However, a correlation between HBV and Agent Orange in NHL is not yet proven. The aim of this study was to investigate the association between HBV infection and Agent Orange who were diagnosed with NHL.

**Methods:** The authors reviewed 452 veterans patients with NHL from June 2003 to August 2018. A retrospective, case-control study was performed.

**Results:** Among 452 patients with NHL, 204 patients had been exposed to Agent Orange. The prevalence of hepatitis B surface antigen in 204 patients who had been exposed to Agent Orange (22 of 204, 10.9%) was significantly higher than that of 248 patients who had not been exposed to Agent Orange (8 of 248, 3.1%) (adjusted odds ratio, 3.6; 95% CI, 2.30-7.21). HBV carrier who had been exposed Agent Orange group (n = 22) presented with significantly more advanced liver disease and high HBV DNA level than those who had not been exposed Agent Orange group (n = 8). Among 30 patients with hepatitis B surface antigen who received anticancer therapy, 24 patients (86%) received prophylactic antiviral therapy, primarily lamivudine. There was no occurrence of hepatitis flare during antiviral therapy.

**Conclusions:** Agent Orange may have a significant correlation with HBV infection in NHL patients. Advanced liver disease and high HBV DNA level are more common in NHL patients who had been exposed Agent Orange.

**Keywords:** Hepatitis B virus infection, Agent Orange, Non-Hodgkin’s lymphoma

---

**PE-049**

**Comparable Incidence of Hepatocellular Carcinoma in Chronic Hepatitis B Patients Treated with Entecavir or Tenofovir**

Dahye Kim1, Jung Woo Shin1, Seok Won Jung1, Seung Bum Lee3, Bo Ryung Park2, Min-Ju Kim1, Eun Ji Park2, and Neung Hwa Park2

1Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea; 2Biomedical Research Center, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea; 3Department of clinical epidemiology and biostatistics, ASAN Medical Center, Seoul, Republic of Korea

**Aims:** Long-acting antiviral drug prescription is decided based on patient’s underlying disease which affected biochemical response, further large-scale study to confirm the favorable AST response with TAF is needed.
Adherence to medication and maintained virologic response (MVR) during antiviral therapy are related to decreased risk of adverse clinical outcomes. This study aimed to compare the efficacy of entecavir (ETV) and tenofovir disoproxil fumarate (TDF) in relation to the risk of hepatocellular carcinoma (HCC) and death or transplantation among chronic hepatitis B (CHB) patients stratified according to adherence to medication and MVR.

Methods: A total of 1794 treatment-naive CHB patients treated with ETV (n = 894) or TDF (n = 900) for >1 year were identified. Antiviral therapy rates and MVR were not significantly different.

Results: The TDF group showed better medication adherence than the ETV group. However, after adjustment for adherence and MVR, ETV therapy and TDF therapy did not differ in terms of the risk of HCC and death or transplantation in all patients and propensity score-matched cohorts.

Keywords: Hepatitis B, Hepatocellular carcinoma, Liver cirrhosis, Antiviral therapy

Figure 1. Cumulative incidence of hepatocellular carcinoma and death or transplantation according to initial antiviral agents used (TDF vs. ETV) in the propensity score matched group of patients with MVR.

Figure 2. Cumulative incidence of (A) hepatocellular carcinoma and (B) death or transplantation according to initial antiviral agents used (TDF vs. ETV) in the propensity score matched group of patients with MVR.

Aims: Patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) frequently undergo radiological assessment using computed tomography (CT) and trans-arterial chemo-embolization (TACE). Thus, we investigated whether frequent radiological assessment using CT or TACE additionally deteriorates renal function when various antiviral agents are used.

Methods: A total of 490 patients who were diagnosed with HBV-related HCC between 2001 and 2013 were enrolled. The main reasons for contrast use were CT and TACE during the follow-up period (medina 59.8 months).

Results: The median age of the study population was 54.8 years, and the male gender predominated (n = 394, 78.6%). A total of 284 (58.0%), 19 (3.7%), 156 (31.8%), and 32 (6.5%) patients received lamivudine, adefovir, entecavir, and tenofovir, respectively. On univariate analyses, CT evaluation ≥4 times/year was significantly associated with an increased risk of disease progression in CKD stage ≥1 (hazard ratio [HR]=1.546, P = 0.008), along with increased age, hypertension, lower serum albumin, and longer prothrombin time (all P < 0.05). After adjustment, CT evaluation ≥4 times/year was found to be independently associated with an increased risk of a reduction in the estimated glomerular filtration rate (eGFR) (<20% from the baseline) (HR = 1.394) and an increase in serum creatinine levels (≥25% from the baseline) (HR = 1.514) (all P < 0.05). In contrast, TACE was not associated with renal impairment (P > 0.05).
Low Incidence of Hepatitis B Reactivation after Kidney Transplantation in Hepatitis B Surface Antigen-Negative and Core Antibody-Positive Recipients

Jihye Kim, Se Jin Chung, Kyo Won Lee, Jae Berin Park, Wonseok Kang, Dong-Hyun Sinn, Geum-Youn Gwak, Yong-Han Paik, Moon Seok Choi, Joon Hyeok Lee, Kwang Cheol Koh, Seung Woon Paik

1Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; 2Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: Nowadays, intensive immunosuppression including rituximab is commonly used prior to kidney transplantation in patients who are ABO-incompatible and highly sensitized cases. Recent practice guidelines suggested antiviral therapy for the first 6-12 months, the period of maximal immunosuppression, may be considered for hepatitis B surface antigen (HBsAg) negative and anti-Hepatitis B core (HBC) positive kidney transplant recipients. However, actual risk of hepatitis B virus (HBV) reactivation and, whether short-term antiviral therapy in early period is necessary remain unclear.

Methods: A total of 1294 consecutive patients who received kidney transplantation between 2007 and 2016 at Samsung medical center were screened. Among them, 454 HBsAg-negative and anti-HBc-positive kidney transplant recipients (median 51 years old, male: 63.4%, anti-HBs antibody (HBsAb) positivity: 86.6%, ABO mismatch: 20.9%, induction immunosuppressive therapy including rituximab: 15.0%) were analyzed for HBV reactivation during follow-up. HBV reactivation was defined as HBsAg reversion.

Results: During a median follow up of 6.7 (interquartile range: 4.1—9.4) years of 454 patients, HBV reactivation was observed in 7 patients (1.5%). All HBV reactivation occurred at least one year after transplantation (range: 17—53 months). There was no severe adverse outcome including jaundice, liver failure, liver transplantation or mortality. Only one patient showed severe hepatitis with peak alanine transaminase over five-fold of upper normal limit, but improved spontaneously before antiviral therapy. The risk of HBV reactivation did not differ according to age, sex, presence of HBsAb, ABO compatibility, use of plasmapheresis, induction with rituximab, or experience of rejection.

Conclusions: The risk of hepatitis B reactivation after kidney transplantation was low, and was not observed in early period after kidney transplantation. This data suggests that watchful monitoring without antiviral therapy would be sufficient, even for those who used rituximab.

Keywords: Hepatitis B, Reactivation, Kidney transplantation, Incidence

Estimation of Hepatocellular Carcinoma Risk after Hepatitis B Surface Antigen Seroclearance

Yewan Park, Minseok Albert Kim, Dong Hyun Sinn, Jeong-Hoon Lee, Wonseok Kang, Geum-Youn Gwak, Yong-Han Paik, Moon Seok Choi, Joon Hyeok Lee, Kwang Cheol Koh, Seung Woon Paik

1Department of Medicine, Samsung Medical Center, Seoul, Korea; 2Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea

Aims: Hepatitis B surface antigen (HBsAg) seroclearance is considered as a functional cure of chronic HBV infection. However, available evidences suggest hepatocellular carcinoma (HCC) risk remains among patients with HBsAg seroclearance. We analyzed risk factors associated with HCC development in this population.

Methods: A retrospective cohort of 843 patients (median age: 57 years; males: 70.3%; cirrhosis: 14.1%; antiviral therapy (AVT) induced: 20.4%) who achieved HBsAg seroclearance were analyzed for the incident HCC during follow-up.

Results: During a median 3.6 years of follow-up (range: 1.0—12.3 years), HCC was developed in 13 patients (1.5%). All HCC cases were developed among patients who achieved HBsAg seroclearance after age of 50 years. Cirrhosis and elevated alanine aminotransferase (ALT) levels at HBsAg seroclearance were independent risk factors for HCC. The 5-years cumulative HCC incidence rate was 16.2%, 5.4%, 3.8% and 0% for cirrhotic patients with elevated alanine aminotransferase (ALT) levels, cirrhotic patients with normal ALT levels, non-cirrhotic patients with elevated ALT levels, and non-cirrhotic patients with normal ALT levels (P < 0.001). Notably, all HCC cases were identified among patients who achieved HBsAg seroclearance after age 50 years.

Conclusions: HCC risk was not null after HBsAg seroclearance, even among non-cirrhotic patients when ALT levels were elevated. Those who had cirrhosis and elevated ALT levels warrants careful attention for remained HCC risk, even after HBsAg seroclearance.

Keywords: Hepatitis B, HBsAg seroclearance, Hepatocellular carcinoma
Real-Life Efficacy of Glecaprevir and Pibrentasvir for Genotype 2 Chronic Hepatitis C

Sang Jun Suh, Hyung Joon Yim*, Young Gul Jung, Han Ah Lee, Tae Hyung Kim, Sun Young Yin, Young-Sun Lee, Jong Jin Hyun, Yeon Suki Seo, Ji Hoon Kim, Jong Eun Yeon, Kwan Soo Byun, Sun Ho Um

Department of Internal Medicine, Korea University Medical College, Seoul, Korea

Aims: Glecaprevir and Pibrentasvir (GP) are available for management of chronic hepatitis C (CHC) in Korea. The aim of the study is to evaluate the real-life efficacy of GP for genotype 2 CHC.

Methods: Since 2018, the patients who received GP at Korea University Medical Center were investigated retrospectively. We analyzed CHC patients with genotype 2 only in this study. The primary endpoint was sustained virologic response at week 12 post-treatment (SVR12). The lowest limit of HCV RNA detection was <15 IU/mL. Statistical analysis was performed by per-protocol (PP) basis. In addition, we compared the data with results of previous sofosbuvir plus ribavirin (SR) therapy at our institution (presented at the Liver Week in 2017).

Results: Total 147 patients were treated by GP regimen. 110 patients were excluded from analysis; 34 patients were non-genotype 2, and 76 patients’ SVR12 data were not available since current initiation of treatment. At the present time, 37 patients were included for analysis. The median age was 55 (26-77) years (male, 45.9%). The median HCV RNA level was 602,000 (49-14,400,000) IU/mL. Two patients (5.4%) experienced previous directly acting antiviral failures (sofosbuvir). Patients with liver cirrhosis (21.6%) were treated for mean 11.8 ± 0.2 weeks while non-cirrhotic patients (78.4%) were treated for mean 8.0±0.2 weeks. The SVR12 was 100%. No patient showed treatment failure or relapse. Additionally, we compared the data with those of 122 genotype 2 CHC patients treated by SR at Korea University Medical Center until 2017 which showed 96.3% of SVR12 rate by PP analysis. There was no significant difference between 100% (GP) and 96.3% (SR) in SVR12 rate (P = 0.591).

Conclusions: The efficacy of GP regimen was excellent in real-life setting. Although the SVR12 rate of GP were not significantly different from that of SR, it was efficacious even in previous SR failures.

Keywords: Chronic hepatitis C, Genotype 2, Glecaprevir, Pibrentasvir
Fractures Related to Tenofovir Treatment in Patients with Chronic Hepatitis B: A Comparative Study in the National Database

In Hye Lee, Bo Hyun Kim, Hwa Young Choi, Moran Ki, Joong-Won Park

Aims: In treatment-naive chronic hepatitis B (CHB) patients with high hepatitis B virus (HBV) DNA ($>6$ log$_{10}$ IU/mL), there have been limited studies directly comparing the long-term efficacy between entecavir (ETV) and tenofovir disoproxil fumarate (TDF).

Methods: A total of 1,034 treatment-naive CHB patients who received first line therapy with ETV ($n = 487$) or TDF ($n = 547$) were consecutively enrolled from 9 tertiary university hospitals in Korea between January 2012 and December 2015. Among total 1,034 patients, 396 patients were analyzed using propensity score matching, at a ratio of 1:1. 198 patients of each group were matched by age, baseline HBV DNA levels, cirrhosis, hepatitis B e antigen (HBeAg) status and comorbidity such as chronic kidney disease, diabetes mellitus and hypertension.

Results: Two groups showed no difference baseline characteristics. During the follow-up of 12 months, HBV DNA levels were similarly suppressed in both groups (ETV vs. TDF: $-5.69$ vs. $-5.77$ log$_{10}$(IU/mL), $P = 0.516$). In multivariate analysis, relatively low HBV DNA levels prior to treatment and initial virologic response at 3 months (IVR-3) were associated with VR at 1 year. During long-term follow-up, HBV DNA levels were more strongly suppressed by TDF than ETV. However, multivariate analysis showed that HBeAg negative status, lower baseline HBV DNA and IVR-3 were independent factors for achieving VR. In subgroup analysis of HBeAg positive patients, the average time to achieve VR was shorter in TDF group than ETV (10.67 ± 5.83 vs. 15.01 ± 10.94, $P = 0.000$).

Conclusions: Although either ETV or TDF, overall, may show a comparable long-term antiviral efficacy in treatment-naive CHB, TDF might be better option than ETV to attain VR more rapidly, in HBeAg positive CHB patients with high HBV DNA levels.

Keywords: Entecavir, Tenofovir, Hepatitis B virus

PE-057

Persistent Viremia after Entecavir Treatment and the Risk of Hepatocellular Carcinoma in Patients with HBV-Associated Cirrhosis

Seung Kak Shin, Oh Sang Kwon, Jeong Han Kim, Chan Uk Lee, Jong Eun Yeon, Sang Jun Suh, Young Kul Jung, Hyung Joon Yim, Yun Soo Kim, Ju Hyun Kim

1Department of Internal Medicine, Gil Medical Center, Gachon University College of Medicine, Incheon, 2Konkuk University School of Medicine, 3Korea University Guro Hospital, Seoul, and 4Korea University Ansan Hospital, Ansan, Republic of Korea

Aims: Tenofovir disoproxil fumarate (TDF) is a potent antiviral agent for the treatment of chronic hepatitis B (CHB). TDF is thought to be associated with bone loss. Herein, we aimed to assess the effects of exposure to TDF compared with entecavir (ETV) on the risk of osteoporosis-related bone fractures in patients with hepatitis B virus infection in South Korea.

Methods: We used claims data from the Korean National Health Insurance Database. Patients prescribed with antiviral agents, TDF or ETV, for CHB in 2013 were extracted. Data regarding prescribed drugs, comorbidities, and fractures were obtained. Osteoporosis-related fractures were identified using ICD-10-CM diagnosis codes for fracture. We assessed the incidence of fractures after TDF or ETV exposure from 2013 to 2015. Competing risk regression models were used to estimate hazard ratios (HRs) of fracture development.

Results: A total of 9748 patients over 20 years old with CHB who received TDF ($n = 2713$) or ETV ($n = 7035$) between January 2013 and December 2013 were enrolled in this study. Mean age was 50.4 years and 53.7 years in TDF and ETV group, respectively. The majority was male (77.1%; 74.1% in TDF group and 78.2% in ETV group). The incidence density of fracture per person-years was 0.99 in TDF group and 1.12 in ETV group. The median follow-up period in patients with fractures was 14 months in TDF group and ETV group, respectively. The hazard ratio (HR) for the development of osteoporosis-related fracture of TDF was 0.88 (95% confidence interval [CI], 0.64-1.21). The age and sex-adjusted HR was 1.02 (95% CI, 0.74-1.40).

Conclusions: Although TDF was reported to increase risk of osteoporotic fracture in patients with HIV infection, the present results based on relatively short-term follow-up data indicated that exposure to TDF was not significantly associated with a greater risk for fracture compared to ETV in patients with chronic hepatitis B. Further studies with long-term follow-up have to be awaited.

Keywords: National Health Insurance Claims data, Tenofovir, Fracture, Chronic hepatitis B
Aims: The clinical significance of persistent viremia, which is defined as failure to achieve undetectable hepatitis B virus (HBV) DNA after 96 weeks of antiviral treatment, in cirrhotic patients treated with high resistant barrier drugs is not well known. This study investigated whether persistent viremia is associated with hepatocellular carcinoma (HCC) risk in patients with HBV-associated cirrhosis.

Methods: A total of 370 naïve patients with HBV-associated cirrhosis who were treated with entecavir (ETV), were retrospectively enrolled in 4 hospitals between March 2007 and December 2012. The clinical, laboratory data, persistent viremia, and non-invasive fibrosis markers [AST to platelet ratio index (APRI), FIB-4 index, fibrosis index] at 2-year treatment were analyzed for HCC development after 2-year treatment.

Results: After excluding patients who developed HCC within 2-year treatment, 359 patients (mean age 51±9, male 64.3%) were analyzed. During a median follow-up of 82 months, HCC developed in 80 patients (22.3%). In univariate analysis, older age (HR 1.06, 95% CI 1.03-1.08, P < 0.001), persistent viremia (HR 2.44, 95% CI 1.37-4.35, P = 0.003), lower albumin level (HR 0.47, 95% CI 0.31-0.72, P = 0.001), lower platelet count (HR 0.99, 95% CI 0.98-0.99, P = 0.012), higher FIB-4 index (HR 1.14, 95% CI 1.08-1.21, P < 0.001), and higher fibrosis index (HR 1.41, 95% CI 1.12-1.78, P = 0.003) at 2-year treatment were risk factors for HCC development. In multivariate analysis, older age (HR 1.05, 95% CI 1.02-1.07, P < 0.001), persistent viremia (HR 2.43, 95% CI 1.35-4.37, P = 0.003) and higher FIB-4 index (HR 1.10, 95% CI 1.04-1.18, P = 0.002) at 2-year treatment were independent risk factors for HCC development.

Conclusions: Old age, persistent viremia and high FIB-4 index at 2-year treatment were independent risk factors for HCC. Therefore, until anti-fibrotic agents are developed, control of persistent viremia may be needed to prevent HCC development.

Keywords: Persistent viremia, Cirrhosis, Hepatitis B virus, Hepatocellular carcinoma

PE-058

External Validation of the Modified PAGE-B Score in Asian Chronic Hepatitis B Patients Receiving Antiviral Therapy

Hye Won Lee1,2, Seung Up Kim1,3, Jun Yong Park1,3, Do Young Kim1,3, Sang Hoon Ahn1,3, Kwang-Hyub Han1,3, and Beom Kyung Kim1,3

1Department of Internal medicine, Yonsei University College of medicine, Seoul, Republic of Korea; 2Institute of Gastroenterology, Yonsei University College of medicine, Seoul, Republic of Korea; 3Yonsei Liver Center Severance Hospital, Seoul, Republic of Korea

Aims: Modified PAGE-B (mPAGE-B) score including age, gender, platelet count and albumin as constituents was recently proposed to predict hepatocellular carcinoma (HCC) risk among chronic hepatitis B (CHB) patients undergoing antivirals. Here, in the independent cohort, we externally validated the predictive performance of mPAGE-B and compared it with those of conventional HCC prediction models.

Methods: We consecutively recruited CHB patients treated with lamivudine, entecavir, or tenofovir as the first-line antivirals. Patients with decompensated cirrhosis or HCC at baseline were excluded. Predictive performances of mPAGE-B and other models were assessed with comparison.

Results: Among 1330 patients, 9.6% developed HCC during follow-up (median 62.0 months). The mPAGE-B provided the highest Harrell’s c-index (0.769), followed by GAG-HCC (0.751), PAGE (0.744), REACH-B (0.686), CU-HCC (0.618) and Toronto HCC risk index (THRI, 0.542). The mPAGE-B showed the similar performance to PAGE-B and GAG-HCC and the better performance than REACH-B, CU-HCC and THRI. Cumulative HCC probabilities at 5-, and 7-years were 0.0% and 0.0% in low-risk group (mPAGE score ≤ 8), 6.1% and 10.8% in intermediate-risk group (mPAGE score 9-12) and 18.7% and 26.7% in high-risk group (mPAGE score ≥ 13), respectively (both P < 0.001 between low- vs. intermediate-risk groups and between intermediate- vs. high-risk groups). C-indices of mPAGE-B score were 0.785 and 0.724 among subgroups treated with entecavir or tenofovir (n = 1011) and with lamivudine (n = 319), respectively, which are overall similar to those of PAGE-B.

Conclusions: The mPAGE-B showed acceptable predictive performances. Compared to PAGE-B, addition of albumin as a constituent provided the marginal benefit in HCC risk prediction.

Keywords: Prediction, Hepatocellular carcinoma, Validation, Modified PAGE-B

PE-059

Tenofovir Disoproxil Fumarate versus Tenofovir Disoproxil for the Treatment of Patients with Chronic Hepatitis B Virus Infection

Min Young Shin1, Hee Sung Lee1, Sung Hoon Kang2, Sang Ok Jung1, Min Ji Cho1, Woo Sun Rou1, Hyuk Soo Eun1, Seok Hyun Kim1,2, and Byung Seok Lee1,2

1Department of Internal Medicine, Division of Gastroenterology, Chungnam National University Hospital, Daejeon, Korea; 2Department of Internal Medicine, Chungnam National University School of medicine, Daejeon, Korea

Aims: Tenofovir disoproxil fumarate (TDF), a nucleotide reverse transcriptase inhibitor and inhibitor of hepatitis B virus (HBV) polymerase, is the fumarate salt of the prodrug tenofovir disoproxil. After 2017, the patent on tenofovir disoproxil fumarate expired, a number of tenofovir disoproxil (TD) without salt of the active substance have been authorized. We compared the efficacy between TDF and TD in patients with chronic hepatitis B virus (HBV) infection in a non-inferiority study.

Methods: In a retrospective study we compared the efficacy of once-daily oral doses of TDF 300 mg (n = 53) and TD 245 mg (n = 59) in patients with chronic HBV infection. We assessed the
proportion of patients with HBV DNA <21 IU/ml, proportions of patients with HBsAg loss and seroconversion to anti-HBs, and, in the HBeAg-positive patients, proportions of patients with HBeAg loss and seroconversion to anti-HBe. Also we assessed ALT using normal ranges set by the central laboratory (Covance), and those set forth in the American Association for the Study of the Liver Diseases (AASLD) guidelines. The study was powered to show non-inferiority with a 10% efficacy margin of TD compared with TDF.

Results: From Jan 1, 2011 to Dec 31, 2017, 112 of treatment-naive patients were included and started receiving TDF 300 mg/d for median 53.9 months. Among them, 53 patients were continued receiving TDF 300mg/d and 59 patients were switched from TDF 300mg/d to TD 245mg/d between Jan 1, 2018 and Mar 31, 2018. 12(80%) of 15 patients receiving TDF had HBV DNA less than 21 IU/mL versus 10(91%) of 11 patients switching from TDF to TD (difference -1.1% [95% CI -4.1% to 1.9%]; P = 0.47), which demonstrates non-inferiority.

Conclusions: In patients with chronic HBV infection, the efficacy of tenofovir disoproxil without salt of the active substance was non-inferior to that of tenofovir disoproxil fumarate.

Keywords: Chronic hepatitis B virus, Tenofovir disoproxil fumarate, Tenofovir disoproxil, Efficacy

---

**Table 1. Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Treatment-naive C (N=112)</th>
<th>Initial treatment with TDF 300mg (N=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>51.3 (25-77)</td>
<td>51.9 (25-77)</td>
</tr>
<tr>
<td></td>
<td>51.2 (25-77)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male (53%)</td>
<td>31 (58%)</td>
</tr>
<tr>
<td></td>
<td>Female (47%)</td>
<td>36 (40%)</td>
</tr>
<tr>
<td>Time to start TDF as first medical therapy (months) (median)</td>
<td>5.2 (0-14.1354)</td>
<td>5.8 (0-14.1)</td>
</tr>
<tr>
<td>Duration of using TDF (months) (median)</td>
<td>53.9 (12-85)</td>
<td>50.3 (21-80)</td>
</tr>
<tr>
<td>Duration of using TD (months) (median)</td>
<td>-</td>
<td>14.1 (12-15)</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>49 (44%)</td>
<td>26 (45%)</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Seropositive for HBeAg</td>
<td>60 (53%)</td>
<td>21 (37%)</td>
</tr>
<tr>
<td>Seropositive for Anti-HBe</td>
<td>53 (47%)</td>
<td>31 (39)</td>
</tr>
<tr>
<td>HBV-DNA (log10IU/mL)</td>
<td>7.23</td>
<td>7.25</td>
</tr>
</tbody>
</table>

**Table 2. Comparison of efficacy outcomes.**

<table>
<thead>
<tr>
<th></th>
<th>At the time of dividing into two groups (N=112)</th>
<th>(A)</th>
<th>(B)</th>
<th>Difference in proportions (95% CI) between (A) and (B)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA  &lt; 21 IU/mL#</td>
<td>66/112 (77%)</td>
<td>121/12 (100%)</td>
<td>121/12 (100%)</td>
<td>-1.1% (-4.1% to 1.9%)</td>
<td>0.47</td>
</tr>
<tr>
<td>HBsAg loss*</td>
<td>14/52 (21%)</td>
<td>13/52 (46%)</td>
<td>13/52 (46%)</td>
<td>-1.4% (-5.4% to 2.4%)</td>
<td>0.00</td>
</tr>
<tr>
<td>HBsAg seroconversion*</td>
<td>12/52 (23%)</td>
<td>2/52 (16%)</td>
<td>2/52 (16%)</td>
<td>4.3% (1.7% to 7.0%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Normalized ALT by central laboratory normal range†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>0.24</td>
</tr>
<tr>
<td>Normalized ALT by AASLD normal range†</td>
<td>2.8/1 (36%)</td>
<td>3/1 (32%)</td>
<td>3/1 (32%)</td>
<td>3.5% (1.0% to 3.2%)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

**Figure 1. Flow chart of selection of patients with CHB.**

**PE-060**

Efficacy and Safety of 3-Year Entecavir and Tenofovir Therapy in Chronic Hepatitis B Patients with Chronic Kidney Disease: A Multicenter, Retrospective Cohort Study

Ji Won Park1, Hyun-Woo Oh2, Dae Won Jun3, Jae Yoon Jeong4, Ji Hyun An5, Eileen L. Yoon6, Jae-Jun Shim7, Hyo Young Lee8, Sang Bong Ahn9, Yong Kyun Cho10, Soung Won Jeong11, Hyoung Su Kim12, Sung-Eun Kim13; SAINT Study Group

1Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, 2Department of Internal Medicine, Hanyang University Hospital, Hanyang University College of Medicine, Seoul, 3Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri, 4Department of Internal Medicine, Seongnam Hospital, Inje University Seoul, 5Department of Internal Medicine, Eulji General Hospital, Eulji University College of Medicine, Seoul, 6Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, 7Department of Internal Medicine, Soonchunhyang University Hospital, Soonchunhyang University College of
Aims: We investigate the efficacy and safety of entecavir (ETV) versus tenofovir (TDF) in treatment-naïve chronic hepatitis B (CHB) patients with chronic kidney disease (CKD) in real life setting.

Methods: A total of 1,737 naïve CHB patients treated with ETV or TDF at least 1 year in 9 academic hospitals from Jan. 2011 to Dec. 2015 were enrolled. Data of 44 patients with CKD of enrolled patients were collected retrospectively. CKD was defined as glomerular filtration rate <60ml/min/1.73m². Renal functional decline was defined when serum creatinine level increased by more than 50% from baseline or over than 0.3 mg/dL at each year.

Results: A total of 47 patients (ETV 34 and TDF 13) were followed up for a median 56 months (range 12-93). There were no significant differences in cumulative biochemical response rate and cumulative HBeAg seroconversion rate between the ETV group and the TDF group at months 6, 12, 24 and 36 of treatment. However, there were significant differences in cumulative virologic response rate between the ETV group and the TDF group at months 6, 12, 24 and 36 of treatment (38.2%/61.8%/88.2%/88.2% vs. 69.2%/84.6%/92.3%/100%, P = 0.042). Renal functional decline at months 12, 24 and 36 occurred in 29.5%/31.4%/36.6% of patients. Renal functional decline showed no significant difference between the ETV group and TDF group. Multivariate analysis showed that HBeAg negativity, lower baseline HBV DNA, higher baseline ALT and TDF regimen were independent factors for achieving virologic response.

Conclusions: TDF had better clinical efficacy than ETV in CHB patient with CKD. TDF had not significantly higher risk for the development of renal insufficiency than ETV. This study suggests that TDF may be a better option than ETV in CHB patient with CKD.

Keywords: Chronic kidney disease, Efficacy, Antivirals, Safety

Real World Data of Tenofovir Alafenamide versus Tenofovir Disoproxil Fumarate for the Treatment of Patients with Chronic Hepatitis B

Saein Kim¹, Hyun Woong Lee¹, Seung Up Kim¹, Jung II Lee¹, Sora Kim¹, Hye Young Chang¹, Beom Kyung Kim¹, Jun Yong Park¹, Do Young Kim¹, Kwang-Hyub Han¹, Kwan Sik Lee¹, Sang Hoon Ahn²

¹Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine; ²Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine Seoul, Korea

Aims: We compared the efficacy and safety of the two drugs in patients with chronic hepatitis B (CHB).

Methods: Patients with CHB treated with tenofovir alafenamide (TAF, n = 105) or tenofovir disoproxil fumarate (TDF, n = 105) in two tertiary referral centers between November 1, 2017, and December 31, 2017, were analyzed. Eligible patients were aged at least 18 years with chronic HBV infection (with serum HBV DNA concentrations of >2,000 IU/mL), serum alanine aminotransferase concentrations of greater than 40 U/L and at no more than twenty times the upper limit of normal, and estimated glomerular filtration rate (eGFR) of at least 50 mL/min (by the Chronic kidney disease epidemiology collaboration). The primary efficacy endpoint was the proportion of patients who had HBV DNA less than 20 IU/mL at week 48; Serum phosphorus, eGFR and lipid profile were assessed to evaluate the safety.

Results: Baseline characteristics were not different between the two groups. Biochemical response (ALT<40 IU/L) rate in TAF and TDF group was 79.8% (71/89) vs 86.6% (84/97) at 24 weeks, 82.2% (37/45) vs. 81.5% (53/65) at 48 weeks. Virologic response rates (HBV DNA <20 IU/mL) was 34.5% (29/84) vs. 34.5% (31/90) at 24 weeks, 61.0% (25/41) vs. 66.1% (37/56) at 48 weeks. There were no statistical differences in biochemical and virological response rates. The mean reduction in serum HBV DNA from baseline to 24 and 48 weeks were similar in TAF and TDF group (-5.0 vs -5.3 and -5.3 vs -5.5 log10 copies/mL, P = 0.132). HBeAg seroconversion was 3.0% (2/66) vs 2.8% (2/71) at 48 weeks. Virological breakthrough was not seen in both groups. At week 48, mean change in eGFR was similar in both groups (TAF -4.4 mL/min vs TDF -5.4 mL/min; P = 0.766), mean change in phosphorus was also similar in both group (TAF -0.07 mg/dL vs TDF -0.04 mg/dL ; P = 0.781), but mean change in total cholesterol was slightly elevated in TAF group (TAF +0.86 mg/dL vs TDF -12.3 mg/dL ; P = 0.057).

Conclusions: In patients with HBeAg positive and negative CHB, the efficacy and safety of TAF were similar to those of TDF at 48 weeks. However, TAF is likely to induce dyslipidemia.

Keywords: Chronic hepatitis B, Tenofovir disoproxil fumarate, Tenofovir alafenamide, Dyslipidemia

The Effectiveness of Tenofovir and Hepatitis B Immunoglobulin in Preventing HBV Vertical Transmission for Pregnancy

Khishigmaa Lkhagvadorj¹, Nyam Bizhiya²

¹Etuugen University of Medical Science, Ulaanbaatar, Mongolia; ²Dordord Medical Center, Internal Medicine Department, Dornod, Mongolia

Aims: To evaluate the efficacy and safety of tenofovir (TDF) and hepatitis B Immunoglobulin for preventing hepatitis B virus (HBV) vertical transmission for HBV-positive pregnant women.

Methods: Pregnant women (n = 47) from January 2016 to June 2018 visiting the outpatient clinic, were enrolled when they met inclusion criteria, which included HBV DNA ≥200000 IU/mL and increased alanine aminotransferase (ALT) levels. All patients were treated with TDF. All infants were vaccinated with hepatitis B immunoglobulin and HBV vaccine. Vertical transmission of
HBV was indicated by the presence of hepatitis B surface antigen (HBsAg) in infants 6 months and 12 months after birth.

**Results:** Their mean HBV DNA 350000 IU/mL and mean alanine aminotransferase (ALT) levels were 56 U/L. After anti-HBV treatment in patients were significantly decreased HBV DNA (54000 IU/mL), ALT levels were 34 U/L. The HBsAg positivity rates of infants at postpartum 24 weeks and 48 weeks was 0% respectively ($P < .001$).

**Conclusions:** Administration of TDF to HBV-infected mothers and infants to hepatitis B immunoglobulin are effective and safe to block mother-to-infant HBV transmission.

**Keywords:** Preventing, Tenofovir, Pregnant women

---

**PE-064**

**Clinical Impact and Correlation of Serum HBV DNA and HBCrAg Titer in Patients with Chronic Hepatitis B during Antiviral Therapy**

Nguyen Van Thai1, Hyun Woong Lee2, Saein Kim2, Sora Kim2, Hye Young Chang2, Jung Il Lee2, Kwan Sik Lee2*

1Department of Hepato-Gastroenterology, 108 Military Central Hospital, Hanoi, Vietnam; 2Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

**Backgrounds and Aim:** The HBcrAg assay detects the sum of hepatitis B core antigen (HBcAg), e antigen (HBeAg) and its related byproduct, 22-kDa precore protein (p22cr). It was proposed as a surrogate marker for HBV persistence. We aimed to evaluate the correlation with HBV DNA and HBcrAg level in patients with chronic hepatitis B (CHB) during antiviral therapy.

**Method:** This study included 27 patients with CHB who were hospitalized at Gangnam Severance Hospital between March 2019 and April 2019. Measurement of serum HBcrAg was performed using a CLEIA Lumipulse G1200 automated analyzer (Fujirebio Inc., Tokyo, Japan) and the reagents were provided by Fujirebio Inc., lot number: SAX5031 (Japan), with a lower limit of detection of 2.0 log U/mL, and a linear range of 3.0 log U/mL-7.0 log U/mL.

**Results:** Median age was 42 years old. Eighteen patients were male. Mean ALT was 35 U/ml, Mean HBV DNA level and HBcrAg level were 2.85 log IU/mL, and 3.7 log U/mL. HBcrAg level exhibited high degree of correlation with HBV DNA ($r = 0.512$, $p = 0.006$). (Figure 1)

**Conclusions:** HBcrAg titer exhibited distinct correlative profile with HBV DNA level in patients with CHB during antiviral therapy. It has a considerable utility in monitoring during antiviral therapy.

**Keywords:** Chronic Hepatitis B, HBV DNA, HBcrAg
**PE-065**

**Determination of Liver Fibrosis Stage by Fib-4 in Patients with Chronic Viral Hepatitis**

O. Baatarkhuu¹, Z. Bolortuya², G. Ulzmaa³

¹Mongolian National University of Medical Sciences; ²Railway Central Hospital, Mongolia; ³Third State Central Hospital, Mongolia

**Aims:** There from in last year's hepatocellular carcinoma is most common malignancy, first of all cancers in Mongolia. Liver fibrosis leading to portal hypertension, and it can increase risk of hepatocellular carcinoma. Liver fibrosis is the accumulation of extracellular matrix in response to acute or chronic liver injury. Measurement of fibrosis helps to stage the severity of disease, it allows serial determination of disease progression and may play an important role in clinical management and determine patients prognosis. The aim of this study is to determine liver fibrosis stage by non-invasive serum biomarker FIB-4 in patients with chronic viral hepatitis.

**Methods:** 130 cases of chronic viral hepatitis at third central hospital in Mongolia from retrospectively reviewed and analyzed. The clinical data including AST, ALT and platelet count were recorded. FIB-4 was calculated.

**Results:** From all, males 47% and females 53%, with mean age of 49.72±14.3. All of the causes are HCV 63.85%, HBV 32.31%, HCV+HBV co-infection 3.85%. In cases of mean value of platelet count, ALT, AST was 211.18±72.9, 112.5±162.4, 82.37±101.5, respectively. FIB-4 was detected <1.45 cutoff value 48.46% non-fibrosis (F0 to F1 by Metavir), 1.45-3.25 score 33.08% fibrosis (F2 to F3 by Metavir), >3.25 cutoff value (F4 by Metavir) 18.46% cirrhosis. 31 (37.34%), 11 (26.19%), 3 (20%) cases of fibrosis were determined in patients with HCV, HBV, HCV+HBV co-infection, respectively.

**Conclusions:** Recorded data ALT, AST of chronic viral hepatitis were detected112.5±162.4, 82.37±101.5 respectively. In patients with chronic viral hepatitis, HCV FIB-4 was determined fibrosis in 43, 31 cases, respectively.

**Keywords:** FIB4, Mongolia, Liver fibrosis, HCV

---

**PE-066**

**HCV/HBV Co-Infection: Epidemiology, Clinical Characteristics, Viral Interactions and Mortality**

O. Baatarkhuu¹, R. Bayasgalan², D. Munkh-Orshikh³

¹Mongolian National University of Medical Sciences; ²Ach Medical University, Ulaanbaatar; Mongolia; ³Mongolian National University of Medical Sciences, Mongolia

**Aims:** Because of the shared modes of transmission, HCV/HBV co-infection is not uncommon, especially in endemic areas and among subjects with a high risk of parenteral transmission. Patients with dual HCV/ HBV have a higher risk of progression to cirrhosis and decompensated liver disease with an increased risk of hepatocellular cancer (HCC). HCV/HBV co-infected patients represent a diverse group with various patterns of viral replication. The aim is to summarize the risk factors and epidemiology of HCV/HBV co-infection and to describe its clinical characteristics in two medical centers for period of 2012-2016.

**Methods:** In total 408 patients with chronic viral hepatitis C (HCV) with mean age of 52 (range 27-77) years were examined. HCV/ HBV was diagnosed in 25 (6%) of them, 19 (80%) were men. In this study we prospectively assessed serological, virological, biochemical parameters and instrumental investigations. The mean MELD score was 22.6±3.2 (13-47).

**Results:** The prevalence of hepatitis B (HBV) co-infection in a total of 408 patients with chronic HCV was 6%. Injection drug use was the predominant risk factor for dual HCV/HBV (85%). Higher rate of liver cirrhosis (LC) 20 (80%) and decompensated liver disease (Child-Pugh class C 40%) were reported in co-infected patients. Two of them were diagnosed with chronic hepatitis, three with HCC. Male sex, previous alcohol abuse and older age (>60) were predictors for developing of HCC in co-infected cirrhotic patients. The following complications were revealed in patients with liver disease decompensation: ascites in - 10 (40%), Hepatic encephalopathy in 5(20%), variceal bleeding-in 4 (16%), Hepatorenal syndrome (HRS) - in 4(16%). The patients with combined HBV/ HCV showed the following spectrum of virological profiles: 18 (72%) of HBV/HCV co-infected patients appeared to have high replication of HCV and inactive HBV replication, 4 (16%) - high HBV DNA levels and undetectable HCV RNA, three others presented active replication of both HCV/ HBV. The overall mortality was 20%, the main causes of mortality were HE (30%) and HRS (25%).

**Conclusions:** HCV /HBV dual infection is a complex clinical/virological entity. Decompensated liver disease were reported in 40% of coinfected patients. The HCV replication was higher in most of coinfected patients (72%). The mortality was associated with complications of HE and HRS. The correct assessment of HBV and HCV replication is mandatory for proper therapeutic approach.

**Keywords:** Co-infection, Epidemiology, HCV-RNA, Mongolia

---

**PE-067**

**MicroRNA-99a Restricts Hepatitis C Virus Replication by Blocking mTORC1-Mediated de novo Lipogenesis**

Eun Byul Lee, Pil Soo Sung, Keungmo Yang, Dong Jun Park, Jung-Hee Kim, Gil Won Lee, Seung Kew Yoon

The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

**Aims:** Lipid droplets are critical for the viral replication and packaging in the life cycle of hepatitis C virus (HCV). The mamma-
The Liver Week 2019

Hepatitis C virus, MiR-99a, Lipid droplet, MTOR

Change of Incidence of Hepatitis C Virus Infection after Transfusion by Introduction of Nucleic Acid Testing: A Big Data Analysis

Hwa Young Choi1,2, Moran Ki1
1Department of Cancer Control and Population Health, National Cancer Center Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, Republic of Korea; 2Department of Health Sciences, Hanyang University, Seoul, Republic of Korea

Aims: The risk of hepatitis C infection by transfusion is rated as RED level. About 0.2% of donors were positive for hepatitis C virus and the risk of infection due to transfusions is very high.

Methods: Using the National Health Insurance Service-National Sample Cohort database (million) from 2002 to 2013, we compared the incidence of hepatitis C after transfusion before and after Nucleic Acid Testing (NAT) was introduced. The study subjects were those who received blood transfusions from 2002 to 2012. Of these, persons diagnosed with hepatitis C from 2002 to 2003 were excluded. The final study subjects were observed until December 31, 2013.

Results: The final study subjects were 48,518 persons. Of these, 72 (0.14%) were diagnosed with hepatitis C infection after transfusion. The incidence density of HCV after transfusion of before the introduction in NAT was 4.3 per 10,000, and the incidence density of HCV after transfusion after introduction in NAT was 3.7 per 10,000. In the first year after transfusion, the incidence of HCV per 10,000 persons was 167.1 before the introduction of NAT and it decreased to 80.8 after the introduction of NAT. However, the incidence of HCV per 10,000 persons after the introduction of NAT is higher than annual HCV incidence of the general population as 18 persons (As of 2012 years).

Conclusions: The incidence density of HCV infection after transfusion per 10,000 people decreased after the introduction of NAT compared with before the introduction. However, constant attention is needed considering continuous infection. In a further study, the National Health Insurance claims data will be used to analyze the incidence of hepatitis C infection after transfusion.

Keywords: Nucleic acid testing (NAT), Transfusion, Incidence, Big data
Pharmacokinetics, Safety, and Efficacy of Glecaprevir/ Pibrentasvir in Pediatric Patients with Genotypes 1-6 Chronic HCV Infection: Part 1 of the DORA Study

Maureen M Jonas1, Robert H Squires2, Susan M Rhee3, Chih-Wei Lin4, Kazuhiro Bessho4, Cornelia Feiters-Sperling2, Loreto Hierro5, Deirdre Kelly1, Simon C Ling6, Tatiana Strokova1, Antonio del Valle-Segarra8, Li Liu7, Teresa I Ng8, Ariel Porcalla9, Margaret Burroughs5, Etienne Sokal5, Yong Kyun Won9

1Division of Gastroenterology, Hepatology, and Nutrition, Boston Children’s Hospital and Department of Pediatrics, Harvard Medical School, Boston MA, USA; 2Division of Gastroenterology, Hepatology, and Nutrition, Children’s Hospital of Pittsburgh of UPMC and Department of Pediatrics University of Pittsburgh School of Medicine, Pittsburgh PA, USA; 3AbbVie Inc., North Chicago, Illinois, United States; 4Osaka University Hospital, Osaka, Japan; 5Charité Universitätsmedizin Berlin, Berlin, Germany; 6Hospital Universitario La Paz, Madrid, Spain; 7Birmingham Children’s Hospital, Birmingham, United Kingdom; 8Department of Paediatrics, University of Toronto and the Hospital for Sick Children, Toronto, Ontario, Canada; 9Federal Research Centre of Nutrition and Biotechnology, Moscow, Russian Federation; 10San Jorge Children’s Hospital, San Juan, Puerto Rico; 11Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; 12AbbVie Ltd. Korea, Seoul, Korea

Aims: The pangenotypic, direct-acting antivirals glecaprevir (GLE; identified by AbbVie and Enanta) and pibrentasvir (PIB), are coformulated (G/P) and approved to treat adults with chronic HCV infection. G/P achieved high SVR12 rates in Phase 2 and 3 studies, leading to an 8- and 12-week indication in HCV genotype (GT) 1–6 patients without cirrhosis or with compensated cirrhosis, respectively. An approved, pangenotypic pediatric HCV regimen is currently unavailable, and treatment options may include ribavirin (RBV); a pangenotypic regimen with improved tolerability for pediatric patients remains an unmet need.

Methods: DORA (NCT03067129) is an ongoing phase 2/3, non-randomized, open-label, multicenter study evaluating the pharmacokinetics (PK), safety, and efficacy of G/P in pediatric patients with chronic HCV infection. This analysis includes only Part 1 of the study, conducted in adolescent patients 12–17 years of age who received the adult formulation of G/P (300 mg/120 mg). Part 2 will be conducted in patients aged 3–11 years given a pediatric formulation of G/P (300 mg/120 mg). Part 2 will be conducted in patients aged 3–11 years of age who received the adult formulation of G/P (300 mg/120 mg). Part 2 will be conducted in patients aged 3–11 years of age who received the adult formulation of G/P (300 mg/120 mg).

Results: Part 1 enrolled 48 adolescent patients; 1 patient was never dosed and thus excluded from this analysis. Table 1 shows baseline demographics. Overall, 47/47 patients (100%) achieved SVR4; 34/34 (100%) patients with available data achieved SVR12. No on-treatment virologic failures or relapses have occurred to date. Intensive PK exposures of GLE and PIB were comparable to exposures in adults. The most common adverse events (AEs) were nasopharyngitis (26%) and upper respiratory tract infection (19%). No AEs led to treatment discontinuation, and no serious AEs occurred. No cases consistent with drug-induced liver injury were identified.

Conclusions: Adolescent patients with chronic HCV infection treated with G/P achieved high rates of SVR4, without incidence of virologic failure, serious AEs or treatment discontinuation. Final SVR12 and PK data will be presented at the meeting.

Keywords: Hepatitis C, Adolescent, Hepatitis

Table 1. Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>G/P (N=47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>21 (45)</td>
</tr>
<tr>
<td>White race, n (%)</td>
<td>35 (74)</td>
</tr>
<tr>
<td>Age, median (range), years</td>
<td>14 (12–17)</td>
</tr>
<tr>
<td>Weight, median (range), kg</td>
<td>58 (32–105)</td>
</tr>
<tr>
<td>G/P genotype, n (%)</td>
<td>37 (79)</td>
</tr>
<tr>
<td>1a/1b subtype</td>
<td>24 (51)/13 (28)</td>
</tr>
<tr>
<td>GT1</td>
<td>3 (6)</td>
</tr>
<tr>
<td>GT2</td>
<td>4 (9)</td>
</tr>
<tr>
<td>GT3</td>
<td>3 (6)</td>
</tr>
<tr>
<td>GT4</td>
<td>3 (6)</td>
</tr>
<tr>
<td>HCV RNA median (range), log_{10} IU/mL</td>
<td>6.2 (4.6–7.2)</td>
</tr>
<tr>
<td>Without cirrhos, n (%)</td>
<td>47 (100)</td>
</tr>
<tr>
<td>HCV treatment-naïve, n (%)</td>
<td>36 (77)</td>
</tr>
</tbody>
</table>

*No patients with GT5 or GT6 infection were enrolled.

Long-Term Hepatic and Extra-Hepatic Outcomes of CHC Patients Post Sofosbuvir-Based IFN-Free Treatment (LONGHEAD Study)-Interim Report

Ming-Lung Yu1, Ting-Tsung Chang2, Jia-Horning Kao2, Ting-Tsung Chang2, Chih-Chou Chen3, Tsung-Hui Hu4, Cheng-Yuan Peng5, Horng-Yuan Wang6, Chi-Jen Chu7, I-Shyan Sheen8, Yu-Chun Hsu9, Jeong Hoo10, Young-Suk Lim11, Hyung Joon Yim12, Youn-Jae Lee13, Kwan Soo Byun14, Won Young Tak15, Yoon Jun Kim16, Sang Hoon Ahn17, Seung Woon Paik17, Sook-Hyang Jeong18, Young Seok Kim18, Seung-Kew Yoon19, Ju-Hyun Kim20, Yang-Hyun Baek21

1Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; 2Linkou Chang Gung Memorial Hospital; 3National Taiwan university Hospital; 4National Cheng Kung University Hospital; 5Chi Mei Liouying
Aims: Direct antiviral agents (DAA), sofosbuvir (SOF)/ledipasvir (LDV) and SOF plus ribavirin (RBV), have been proved to provide a sustained virological response (SVR) of ≥ 97% in treatment-naïve or treatment-experienced Taiwanese and Korean patients with HCV genotype 1 (HCV-1) and HCV-2 infection in prior two phase 3b clinical trials (NCT02021656, GS-US-337-0131 and NCT02021643, GS-US-334-0115). The aim of the study is to explore the long-term outcome of the SOF-based cohort who achieved SVR.

Methods: CHC patients receiving sofosbuvir-based DAs in the parent studies are included for following up to 5 years. Their laboratory, image studies and clinical events in terms of liver non-liver related outcomes are prospectively documented.

Results: A total of 200 patients (Taiwanese patients: n = 104 from 10 sites, Korean patients: n = 96 from patients from 14 sites) are enrolled. The mean follow-up period is 10.4±4.4 months until Dec 2018. The mean age was 59.7 years, and male accounted for 39.5% of the population. Eighty eight (44%) of the patients were with hepatitis C virus genotype 1 (HCV-1) infection and received sofosbuvir/ledipasvir, whereas 112 (56%) HCV-2 patients received sofosbuvir/ribavirin. Twenty-Six (13.0%) patients had compensated liver cirrhosis, and 4 patients (2.0%) had HCC at LONGHEAD study enrollment. For the extra-hepatic manifestations, the proportion of hypertension, diabetes, dyslipidemia and history of acute myocardial infarction was 12.5%, 6.5%, 8.5% and 0.5%, respectively. Until 17 Dec, 2018, five patients withdrew study follow-up. There were 4 serious adverse events being reported (HCC [n = 2] and gastric cancer [n = 2]). At year 1, two patient developed new HCC. For extra-hepatic outcomes, four patients had newly onset diabetes and one patient had diagnosed dyslipidemia. None had cardiovascular event, and none had liver development complication or mortality. Regarding the fibrotic evolution diagnosed by Fibroscan, the proportion of patients with improved, stationary and worsening fibrosis is 8.9%, 76.7% and 14.4% respectively. One hundred and fifty nine patients who achieved SVR12 had available virologic data 1 year after initiating LONGHEAD study. All of the subjects remain to detectable HCV RNA (HCV RNA < lower limit of quantification [12 IU/ml]). The SVR durability is 100% at year 1.

Conclusions: The short-term outcome in the SOF-based population is appreciated. Longer follow-up period is warranted to clarify the post-SVR benefits in the LONGHEAD cohort.

Keywords: HCV, DAA, SVR, Longterm
116.6 cases and women 74.8 cases per 100,000 person-years. The hepatitis C virus (HCV) infection is one of the major causes of chronic hepatitis and hepatocellular carcinoma (HCC) in Mongolia. Viral infection with HCV can cause fluctuations in AFP that makes it difficult to differentiate between underlying liver disease and the development of HCC. The lack of specificity has limited the role of serum alpha-fetoprotein (AFP) for hepatocellular carcinoma (HCC) screening among patients with cirrhosis related to hepatitis C virus (HCV) infection.

Methods: Here we report 15 cases decreased of AFP level in patients with cirrhosis treated 24 weeks combination therapy with ledipasvir and sofosbuvir between 2017 to January 2019 were referred to the Liver Unit, Dornod Medical center Mongolia. All patients had been tested for blood chemistries, liver function markers, such as alanine aminotransferase (ALT), total bilirubin, prothrombin, an international normalized ratio (INR), creatinine, AFP and HCV-RNA. 

Results: Of all patients, three were man and two were woman. The average age of the testimonies was 56 (between 44 and 68 years). Our patients had HCV genotype 1b and had HCV-RNA positive. The combination of the therapy with ledipasvir and sofosbuvir had significantly decreased the level of HCV-RNA from 3572350 to not detected ($P < 0.05$), ALT from 123.4 to 25.6 ($P < 0.05$), AFP from 43.8 to 17.8 ($P < 0.05$).

Conclusions: In conclusion, the combination of the therapy with ledipasvir and sofosbuvir is decreased AFP level and improved liver function tests in HCV related liver Cirrhosis of those patients.

Keywords: Alpha-fetoprotein, Ledipasvir and sofosbuvir

PE-073

Changing Cascade of Care for Hepatitis C in the Era of Direct-Acting Antivirals (DAAs)

Jag Chhatwal1,2, Qiushi Chen3, Emily Bethea4, Turgay Ayer5, Yueran Zhuo1, Chin Hur6, Anne Spaulding7, and Fasihah Kanwal1

1Liver Center and Gastrointestinal Division, Massachusetts General Hospital, 2Harvard Medical School, 3Massachusetts General Hospital Institute for Technology Assessment, 4H. Milton Stewart School of Industrial and Systems Engineering, Georgia Institute of Technology, 5Institute for Technology Assessment, Massachusetts General Hospital, 6Rollins School of Public Health, 7Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Michael E DeBakey VA Medical Center USA

Aims: Our objective was to project changes in the cascade of care for HCV considering these factors.

Methods: We used a previously-validated mathematical model, Hepatitis C Disease Burden Simulation model (HEP-SIM), which projects the changing prevalence of HCV in National Health and Nutrition Examination Survey (NHANES) and non-NHANES population groups. HEP-SIM simulated the management of HCV from 2010 onwards, which included risk-based screening until 2013 and inclusion of birth-cohort screening afterwards; the rising HCV incidence resulting from new patterns of injection drug use; insurance expansion with the Affordable Care Act; and antiviral treatment options in different waves starting with peginterferon followed by the launch of first- and second-generation DAAs, including pan-genotypic drugs. Treatment efficacy was extracted from clinical studies and treatment rates based on insurance status and drug sales. We projected different steps of the HCV cascade of care for years 2010, 2015, and 2020.

Results: Our model estimated that in 2010, 4.0 million people had chronic viremia, and among those 1.5 million people (37.5%) were aware of their HCV infection status (Figure 1). In 2015, 3.35 million people were viremic and 1.35 million were aware of their status. Under current clinical practice, by 2020, 2.16 million are projected to remain viremic and 0.65 million (30%) aware of their infection. The number of people who achieved cure is projected to increase from 0.47 million in 2010 to 1.89 million in 2020.

Conclusions: Our model predicts that DAAs have substantially changed the HCV cascade, with a predicted increase in the HCV infected people expected to be cured by 2020. Despite this, under current screening/treatment, 1.89 million people will remain infected in 2020 with 70% of those unaware of their infection. Policies aimed at aggressive screening for HCV alongside controlling the rising HCV incidence could help further reduce the burden of HCV in the United States.

Keywords: HCV, Chronic hepatitis C, Cascade of care, Screening
### PE-075

**Safety and Effectiveness of HARVONI® (Ledipasvir/Sofosbuvir, LDV/SOF) from the 3rd Year Post-Market Surveillance (PMS) Data in Korea**

Tae Hun Kim1, Won Young Tak2, Sae Hwan Lee3, Neung Hwa Park4, Yang Hyun Baek5, Young Mi Hong5, Tae Hyo Kim5, Chang Hyeong Lee5, Young Jae Lee5, Yong Kyun Cho5, Jeong III Suh6, Byung Hoon Han7, Jae Seok Hwang8, Hyun Ji Lee9, Jin Youn10, Yan Zhong11

1Ewha Womans University Seoul Hospital, Korea; 2Kyungpook National University Hospital, Korea; 3Soonchunhyang University Cheonan Hospital, Korea; 4Ulsan University Hospital, Korea; 5Dong-A University Hospital, Korea; 6Pusan National University Yangsan Hospital, Korea; 7Gyeongsang National University Hospital, Korea; 8Daegu Catholic University Medical Center, Korea; 9Jeju University Busan Paik Hospital, Korea; 10Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Korea; 11Dongguk University Gyeongju Hospital, Korea; 12Korea University Gospel Hospital, Korea; 13Keimyung University Dongsan Hospital, Korea; 14Gilead Sciences, Inc., Foster City, CA, USA;

**Aims:** In Korea, LDV/SOF has been approved for the treatment of GT1/2/4/5/6 HCV infections in adults and adolescents aged 12 to <18 years. Marketing authorization holders in Korea are required to conduct PMS and submit annual safety reports to MFDS. This study analysed the results from the 3rd LDV/SOF PMS report.

**Methods:** In this open-label, non-interventional study, case report forms of 61 patients were collected from 13 institutions in Korea from 13th October 2017 to 12th October 2018. Of these, 60 were included for safety analysis; one was excluded due to violation of the usage. 53 out of the 60 patients were included in the effectiveness analysis; 7 with missing information were excluded.

**Results:** All the 60 patients included were GT1-infected; 53.3% were aged ≥65 years; 51.7% were male; 35% were treatment-experienced; 40.0% and 10.0% had compensated and decompensated cirrhosis, respectively. 80% had ≥1 comorbidity like history of cardiovascular disease, diabetes and HCC. 66.7% were on ≥1 co-medication and the most commonly used medications other than vitamin supplements were amiodarone, ursodeoxycholic acid and metformin. The mean total administration period of LDV/SOF was 11.85 weeks. The LDV/SOF+RBV group (n = 11) had more advanced liver diseases than the LDV/SOF group (n = 49). The rate of AEs was 43.3% and was higher in the LDV/SOF+RBV (81.8%) than the LDV/SOF (34.7%) groups. The rate of ADRs was 16.7% and was comparable between the two groups. The most common ADRs were fatigue, headache, and nausea (n ≥ 2, respectively). 3 and 2 patients discontinued LDV/SOF and RBV due to AEs, respectively. LDV/SOF was effective across patient subgroups; 52 out of 53 achieved SVR.

**Conclusions:** The 3rd year PMS data demonstrated a good safety profile and high effectiveness in Korean patients without significant safety signals. More cases with further information on safety and effectiveness will be collected for subsequent reports.

**Keywords:** Harvoni, PMS, Ledipasvir, Sofosbuvir

---

**PE-076**

**A Case Report of Glecaprevir/pibrentasvir-induced Severe Hyperbilirubinemia in a Patient with Compensated Liver Cirrhosis**

Jae Hyun Yoon1, Gaeun Kang2, Chung Hwan Jun3, and Sung Kyu Choi

1Department of Gastroenterology and Hepatology, Chonnam National University Hospital and College of Medicine, Gwangju, South Korea;
Aims: Glecaprevir/pibrentasvir, a pan-genotypic and ribavirin-free direct acting antiviral agent regimen, has shown significant efficacy and very few serious complications. However, as the drug metabolizes in the liver, it is not recommended in patients with decompensated liver cirrhosis. Herein, we report the case of a patient with compensated liver cirrhosis who developed severe jaundice after glecaprevir/pibrentasvir medication.

Methods: A 77-year-old man diagnosed with chronic hepatitis C-related compensated liver cirrhosis visited hospital due to severe jaundice after 12 weeks of glecaprevir/pibrentasvir medication.

Results: On the laboratory work-up, the total/direct bilirubin level was markedly elevated to 21.56/11.68 mg/dL from 1.81 mg/dL; the alanine aminotransferase and aspartate aminotransferase levels were within the normal range. We checked the plasma drug concentration level of glecaprevir, and 18,500 ng/mL was detected, which was more than 15 times higher than the drug concentration level verified in normal healthy adults. Glecaprevir/pibrentasvir was stopped and after 6 days, the drug concentration level decreased to 35 ng/mL and the serum total/direct bilirubin decreased to 7.49/4.06 mg/dL. Three months after drug cessation, the serum total bilirubin level normalized to 1.21 mg/dL and HCV RNA was not detected.

Conclusions: We report what is likely the first known case of severe jaundice after medication with glecaprevir/pibrentasvir in a patient with compensated liver cirrhosis. Clinicians should bear potential hyperbilirubinemia in mind when treating chronic hepatitis C with this regimen and should monitor the patient closely during follow-up laboratory exams, especially in elderly cirrhotic patients.
ference of viral response between treat naïve group and treat-
tment experienced group of HCV. (EVR 97.9% vs. 96.9%, P = 0.6) And the presence of cirrhosis also not affected to achieve the viral response. (EVR cirrhotic patients vs. non cirrhotic pa-
tients: 97.3% vs 97.8%, P = 0.8). There were no serious ad-
verse events. The most common adverse events were fatigue and GI problem. Aminotransferase increases of greater than five times the ULN were observed in 3 patients.

Conclusions: DCV and ASU combination therapy were well
tolerated in Korean patients with HCV G1b infection without
NS5A resistance and provided high SVR rates regardless of the experience of treatment and presence of cirrhosis.

Keywords: HCV, Genotype1b, Asunaprevir, Daclatasvir, Resis-
tance associated variant

The Efficacy and Safety of Glecaprevir and Pibrentas-
vir Treatment for Patients with Genotype 2 Hepatitis C Virus Infection in Real-World Experience: Interim Analysis of a Single Center

Woo Jin Yi, Sang Hoon Park, Myung Seok Lee
Division of Gastroenterology and Hepatology, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea

Aims: Recently, various direct-acting antiviral (DAA) drugs is
used to treat patients with hepatitis C virus (HCV) infection. An
8~12 week course of the combination of glecaprevir and pibren-
tasvir (Maviret®, AbbVie) is highly effective in patients with
HCV infection, even in compensated liver cirrhosis. The purpose
of this study is to find out the efficacy and safety profiles of
Maviret® for the treatment in patients with genotype2 (GT2)
HCV infection in real-world.

Methods: This study was performed on 49 adult patients di-
agnosed of GT2 HCV infection and treated with Maviret® at
Hallym University Kangnam Sacred Heart Hospital from Sep-
tember 2018. Patients with HCV infection received Maviret® for
8 weeks, and cirrhotic patients received Maviret® for 12 weeks.
Primary end point was sustained virological response after 12
weeks of treatment (SVR 12). The secondary end point was ele-
vation of HCV RNA titer or occurrence of serious adverse events

Results: So far, a total of 49 patients with GT2 HCV infection
were enrolled, 48 were identified as treatment naive patients
and one was a treatment experienced patient. Of 49 patients,
35 patients finished treatment and all of them confirmed to
ETR. 9 patients achieved SVR 12 and within in this period, no
serious adverse events were found. 30 patients will be con-
firmed as having SVR 12 by June 2019. Headache and fatigue
were reported as adverse events, but patients continue taking
Maviret® because not observed other serious adverse events.
Also, 1 patient was taking rosuvastatin and 4 patients were
taking atorvastatin. Patients stopped taking rosuvastain and re-
duced the dosage of atorvastatin, due to concerning of adverse
events but did not occurred during treatment. Of 11 patients
had chronic alcoholics, 4 patients quit drinking, and 7 patients
continued to drink but did not show any adverse events.

Conclusions: Although there were limited number of patients,
we could find that the combination of glecaprevir and pibren-
tasvir (Maviret®) were effective and safe for the treatment of
GT2 HCV infection in real-world experience. We suggest that
Maviret® is the first treatment option for patients with GT2
HCV infection in Korea.

Keywords: HCV, Glecaprevir, Pibrentasvir

Efficacy and Safety of Ledipasvir/Sofosbuvir for
Treatment of Chronic Hepatitis C Patients

Doljinseren Enkhbayar¹, Bayarmaa Nyamaa², Bat-Erdene

Conclusions: DCV and ASU combination therapy were well
tolerated in Korean patients with HCV G1b infection without
NS5A resistance and provided high SVR rates regardless of the experience of treatment and presence of cirrhosis.

Keywords: HCV, Genotype1b, Asunaprevir, Daclatasvir, Resis-
tance associated variant

PE-078

The Liver Week 2019
Dashnyam2, Nyam Biziya3
1Mongolian National University of Medical Science, Mongolia; 2Mongolian Laboratory, Chöibalsan, Mongolia; 3Mongolian National University of Medical Science, Mongolia

Aims: Combination of ledipasvir (LDV)/sofosbuvir (SOF) has been approved in Mongolia for the treatment of genotype 1b hepatitis C virus (HCV) infected patients from 2016. We investigated virologic response and its clinical impact in CHC patients.

Methods: This retrospective study analyzed 830 patients with HCV infection who were treated with LDV/SOF from February 2016 to January 2019, were retrospectively enrolled from Dornod Medical center. Virologic response was measured at 4 weeks (rapid virologic response, RVR), at 12 weeks (end of treatment response, ETR), and at 12 weeks after the end of treatment (sustained virologic response, SVR12). Safety was assessed by review of adverse events, physical examinations, and laboratory findings.

Results: Of the 829 patients (male, n = 398 [48%]; female n = 431 [52%]), 100% were treatment naïve, HCV GT1b; mean age, 50.8 years; liver cirrhosis 207 (25%), 622 patients (75.0%) were chronic hepatitis, mean ALT (76.9 IU/L), and mean HCV RNA level (3,464,490 IU/mL). In all patient, SVR12 was achieved in 824 (99.4%). Three patients early stopped the treatment due to headache problem and gastrointestinal troubles, therefore, they achieved SVR 12. During or after DAA treatment, hepatocellular carcinoma developed in 2 patients whose age was over 67 years.

Conclusions: Direct-acting antiviral (DAA) treatment of HCV GT1b infected Mongolian subjects resulted in a high rate of SVR. However, in some older patients, HCC can develop during or after DAAs treatment.

Keywords: Chronic hepatitis C, Direct-acting antiviral (DAA)

---

Clinical Characteristics of Foreign Chronic Hepatitis C Patients in Daejeon-Chungcheong Area: Multi-Institutional Study

Hyun Jae Lee1, Min Ho Jeon1, Suk Rae Kim1, Il Han Song1, Sae Hwan Lee1, Hong Soo Kim2, Tae Hee Lee2, Young Woo Kang1, Seok Hyun Kim1, Byung Seok Lee1, Hee Bok Chae3, Seok Hwan Kim4
1Department of Internal Medicine, Dankook University College of Medicine; 2Department of Internal Medicine, Soonchunhyang University College of Medicine; 3Department of Internal Medicine, Konyang University College of Medicine; 4Department of Internal Medicine, Chungnam University College of Medicine; 5Department of Internal Medicine, Chungbuk University College of Medicine; 6Department of Internal Medicine, Catholic University College of Medicine, Korea

Aims: The number of foreigners living in Korea has increased significantly compared to the past, especially since 2013. Unlike Korea, genotype 2 has more than genotype 1 and genotype 3 also takes up a certain portion, which requires publicity and education.

Keywords: Chronic hepatitis C, Foreigner, Genotype

---

LDL-Cholesterol Level Was Elevated after Direct-acting Antivirals (DAAs) Administration in Genotype 2 HCV-Infected Patients: Real World Data from a Single Center Experience

Joon Ho Jeong, Sang Wook Lee, Kwang Il Seo, Byung Cheol Yoon, Byung Hoon Han, Eun Taek Park, Jin Wook Lee
Department of Internal Medicine, Division of Hepatology, Kosin University College of Medicine, Korea

Aims: The number of foreign chronic hepatitis C patients has increased significantly compared to the past, especially since 2013. Unlike Korea, genotype 2 has more than genotype 1 and genotype 3 also takes up a certain portion, which requires publicity and education.

Keywords: Chronic hepatitis C, Foreigner, Genotype
change of lipid profile after treating hepatitis C. Therefore, this study aims to show the change of serum LDL cholesterol level after the treatment of hepatitis C.

**Methods:** We retrospectively reviewed 258 patients who were treated with DAA for hepatitis C in a tertiary hospital. Among those, 58 patients, whose serum lipid profiles were measured at the time of DAA start and one year after DAA treatment, were selected. Serum LDL-cholesterol level was analyzed before and after the treatment in genotype 1b and genotype 2 HCV-infected patients.

**Results:** Of the enrolled 58 patients, the mean of age was 62.97 (±11.00), the mean of serum RNA titer (IU/ml) was 232 1532.89 (±2349752.20); the number of patients in male and female was 23 (39.66%) and 35 (60.34%); the number of patients in genotype 1b and genotype 2 was 37 (63.8%) and 21 (36.2%), respectively. The mean of age in each group was 63.24 (±11.00) and 62.48 (±12.23) (P = 0.808). Overall, the mean of serum LDL-cholesterol before and after the treatment was 93.27 (±32.94) and 103.35 (±32.94) (P = 0.020). The mean of LDL-cholesterol before and after the DAA treatment in genotype 1b group was 94.76 (±33.94) and 101.40 (±34.58) (P = 0.029); the mean of LDL cholesterol before and after the DAA treatment in genotype 2 group was 90.64 (±31.73), 106.79 (±28.61), respectively (P = 0.020). In multi-variable regression analysis, age, serum RNA titer, diabetes, hypertension, dyslipidemia, statin use, and types of DAA could not affect the serum LDL-cholesterol level after reaching the sustained virologic response.

**Conclusions:** Serum LDL-cholesterol level could be increased after the treatment of hepatitis C, especially in genotype 2 infection. Therefore, clinicians should monitor the lipid profile carefully after treating hepatitis C.

**Keywords:** Hepatitis C, Direct acting antivirals, Dyslipidemia

**Prevalence and Geographical Distribution of HCV among Arkhangai Provinces in Mongolia**

M. Batzaya1, E. Byambatsogt2,4, G. Buyankhishig1,4, B. Amgalan1,4, and O. Baatarkhuu1,4

1Department of Laboratory, Proliance LLC, Ulaanbaatar, Mongolia; 2Health Department, Arkhangai, Mongolia; 3Department of Gastroenterology, Arkhangai General Hospital, Mongolia; 4Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 5Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia

**Aims:** Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis. In 2017, one of the central regions of Mongolia, Arkhangai province had the third highest HCV prevalence among the provinces in Mongolia. To define geographical distribution of HCV prevalence among the soums (administrative and geographical unit) of Arkhangai province.

**Methods:** All persons between the ages of 45 and 60 years old from the 19 soums of Arkhangai were eligible for HCV antibody screening by a WHO prequalified rapid diagnostic testing (Cypress Diagnostica). The test results were collected by each of the soum’s physicians and analyzed by SPSS-21 software by using relevant parametric and non-parametric tests.

**Results:** A total of 17,601 (81.1% of the eligible population) underwent screening, of which 3,289 (18.68%) were positive for hepatitis C antibodies. Most of screened population was female (9095, 52.0%), mainly herdsman (7206, 40.9%), married...
(15425, 87.6%), educated to secondary level (11997, 68.2%) and aged 50-54 (9289, 52.8%). The prevalence varied by soums (range: 11.1% in Jargalantsoum to 24.9% in Erdenebulgansoum) and was associated with older age; the highest rate of HCV infection was among the 55-59 age group (P < 0.001). The median age of HCV seropositive individuals was 52±12.

Conclusions: HCV prevalence in Arkhangai is higher than the country average (16.7%). Our experience in Arkhangai demonstrates that through commitment of provincial public health departments, massive screening of populations at risk for HCV infection is feasible in resource limited settings.

Keywords: HCV, Prevalence, Mongolia, Distribution

PE-084

Study of Alteration of Iron Metabolism in Chronic Hepatitis C in Mongolia
Baatarkhuu O1,2, Bold Sharav2, Uugantsetseg G1, Tserendagva D1, and Odgerel Ts1
1Department of Infectious Diseases, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 2Department of Theoretical Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 3Department of Oncology and Hematology, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 4Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia; 5Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Aims: Iron is pivotal for a number of fundamental metabolic process in cells. Liver plays an important role in iron homeostasis by secreting a peptide hormone named hepcidin. Liver injury, such as liver cirrhosis, alcoholic liver disease, and chronic hepatitis B and C leads to abnormal expression of hepcidin. The current study was aimed to determine the relationship between iron parameters in patients with chronic hepatitis C in Mongolia.

Methods: The current cross-sectional study investigated 20 randomly selected patients with HCV, registered at Mongolian National Center for Communicable Diseases. Serum iron and ferritin concentrations were determined by immunoassay. Hepcidin levels were analyzed using ELSA according to the manufacturer’s instructions.

Results: Compare with healthy subjects, relatively low level of hepcidin, high level of serum iron and ferritin were measured in patients with HCV. Depending on serum ferritin level, hepcidin value was measured differently in patients with HCV. Hepcidin value was strongly correlated either with ferritin (r=0.7, P = 0.002) and iron (r=0.5, P = 0.04).

Conclusions: Iron metabolism was disturbed in HCV, Serum ferritin and iron level was increased in patients with HCV. Hepcidin value was measured differently in patients with HCV depending on serum ferritin level.

Keywords: Iron, Metabolism, HCV, Mongolia

PE-085

Direct Antiviral Agent (DAA) Treatment of Chronic Hepatitis C Results by APRI and FIB-4 Score in Mongolia
Amgalan B1,2, Bat-Erdene Zorigt1,2, Byambatsogt E1,2, Buyankhishig G1,2, Tserendejid Ts1,2, Munkhbayar D1,3, and Naranzul N1,3, and Baatarkhuu O1,2
1Department of Gastroenterology, Arkhangai General Hospital, Mongolia; 2Health Department, Arkhangai, Mongolia; 3Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 4Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia; 5Ac Medical University Ulaanbaatar, Mongolia

Aims: Viral hepatitis infection is directly associated with the development of liver cancer. According to the WHO report, among patients with liver cancer in Mongolia, 46% have hepatitis C, 34% have hepatitis B and 14% have co-infection with more than one hepatitis virus. Novel DAA targeting hepatitis C virus (HCV) have revolutionized the treatment of chronic hepatitis C infection (CHC). We aimed to determine DAA treatment achievement among 40-65 years old Mongolians.

Methods: We examined the changes in fibrosis scores FIB-4 and APRI after DAA treatment of CHC. A total of 17,601 (81.1% of target group) underwent screening, of which 3,447 (19.5%) were positive for hepatitis C. 3,049 of them were tested for HCV RHA. FIB-4 and APRI scores were calculated before and after treatment for each patients. The relevant parametric and nonparametric tests were used.

Results: In total 1778 or 58.3% of individuals who had viral load test had enrolled treatment, 60.7% of them was female, aged between 40-65 years old. 98.3% (1748) of individuals who tested by viral load test was undergone to DAA treatment. After DAA treatment 99.4% of them were achieved SVR12. Mean level of FIB-4 and APRI values significantly decreased from 1.48 (SD1.39) [CI95%:1.26-1.74] and 0.88 (SD1.68) [CI95%:0.56-1.32] to 1.05 (SD0.54) [CI95%:0.92-1.18] (P = 0.017) and 0.19 (SD0.17) [CI95%:0.15-0.23] (P = 0.001) respectively.

Conclusions: Patients with SVR after DAA therapy showed significant improvement on fibrosis scores FIB-4 and APRI. Also almost all of treated patients were achieved SVR12 which shows treatment was highly effective.

Keywords: DAA, Treatment, Hepatitis C, APRI

PE-086

SVR 12 Weeks after Therapy with Sofosbuvir/Ledipasvir Patients with HCV Genotype 1B: Real World Mongolian Experience
Baatarkhuu. O1,2, Oyun-Erdene Mijid1,3, Enkhuya. D1, Saruul. B1, Gantulal. Ch1, Gegeebadrakh. B1, Tuvshinbayar2, Badamsuren. D1, Ulzmaa. G1, and Amarsanaa. J1
1Department of Infectious Disease, Mongolian National University

Aims: Sofosbuvir and Ledipasvir are the Direct Acting Antiviral Agents (DAA) for the treatment of patients infected with HCV genotype 1. Several clinical trials have shown that SVR rates achieved with these regimens are excellent; however, clinical data from real world treatment experience in Mongolia are limited.

Methods: During the period of 2016-2018, a total of 50 patients with genotype 1b of HCV with SVR12 and genotype 1a of HCV were treated with Sofosbuvir and Ledipasvir. A total of 30 patients were treated with 400/100 mg BID for 12 weeks. HCV infection was confirmed by HCV-RNA test. Viral responders with SVR12 were followed up for 12 weeks after treatment. Sustained virological response (SVR) was defined as HCV-RNA undetectable at 12 weeks post treatment.

Results: In total 37 patients were included for follow up after 12 weeks post treatment. Among them, 92.1% of patients were achieved SVR12. Furthermore, in patients with genotype 1b HCV, 93.3% of patients were achieved SVR12.

Conclusions: In this real world experience, Sofosbuvir and Ledipasvir demonstrated high SVR rates in patients infected with HCV genotype 1b.
of Medical Sciences, Ulaanbaatar, Mongolia; 4Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia; 5Happy Veritas Liver Diagnostic Center, Ulaanbaatar, Mongolia; 6Department of Hepatogastroenterology, National Center for Communicable Diseases, Ulaanbaatar, Mongolia; 7Department of Gastroenterology Second Central Hospital, Ulaanbaatar, Mongolia; 8Department of Gastroenterology, Third Central Hospital, Ulaanbaatar, Mongolia

Aims: According to the approval of the implementation of the National Prevention, Control and Elimination Program between 2016 and 2020 by Mongolian Government, treatment campaign started from January 2016. It can be concluded that as part of preliminary results of the National Program up to date, any information and preliminary results of the Program is not available. To assess efficacy and safety of led/sof in 5052 Mongolian patients infected with genotype 1 HCV, who received brand LED/SOF (Harvoni®) for 12 weeks within the framework of the Program.

Methods: In this prospective cohort study, treatment-naïve, cirrhotic and non-cirrhotic patients were treated with LED/SOF for 12 weeks, treatment-experienced patients were treated with LED/SOF for 24 weeks. The primary efficacy endpoint was sustained virologic response 12 weeks after treatment (SVR12) and occurrence of adverse events. Serum HCV RNA quantification was performed using a Roche COBAS® TaqMan.

Results: Among total of 5052 patients with HCV-genotype 1 infection, 5016 had successful viral eradication after 12 weeks or 24 weeks of antiviral therapy using LED/SOF, accounting for 99.3% of SVR12. During 12 weeks to 24 weeks antiviral therapy, the most common adverse event was headache 9.4% (473), fatigue 6.2% (312), abdominal discomfort 5.9% (296) and skin rash 2.8% (141).

Conclusions: LED/SOF combination therapy has been shown to be highly effective and well-tolerated in our real-life study with high SVR rates.

Keywords: SVR12, SOF/LED, Genotype, Mongolia

---

**Extended Virological Response after Sustained Virological Response in Patients with Sofosbuvir and Ribavirin Therapy**

Sin Hyeok Kang, Sae Hwan Lee, and Hong Soo Kim

Gastroenterology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea

Aims: Late relapse or reinfection were crucial issues after sustained virological response (SVR) in antiviral treatment for chronic hepatitis C. The persistence of SVR to direct antiviral agent therapy is unclear. The aim of this study was to investigate durability of virological response in patients with SVR after sofosbuvir and ribavirin (SOF-RBV) therapy.

Methods: We consecutively enrolled patients with chronic hepatitis C received SOF-RBV from September 2016 to November 2017. A SVR is an undetectable HCV RNA level after at 12 weeks of completing HCV therapy and extended virological response was defined as undetectable HCV RNA level after 24 weeks of SVR.

Results: Forty-four patients had genotype 2 chronic hepatitis C who completed SOF-RBV treatment and achieved SVR were enrolled. Median age was 60 (36 - 77) years and half of subject were male. Median baseline HCV RNA level was 5.94 (3.4 - 7.1) log IU/mL and median follow-up period was 53 (27 – 68) weeks after SVR. Serum HCV RNA was detected in 2 subjects at 31 and 54 weeks after achieving SVR. They were male and have
no history of prior interferon treatment. There was no evidence of cirrhosis on ultrasound and no dose-adjustment of ribavirin. Both subjects achieved end of treatment response, but rapid virological response was not shown (6.64 at baseline to 3.88 log IU/mL at week 4) in one patient.

Conclusions: Most of patients with SVR after SOF-RBV treatment continue achievement of virological response. Assessment of extended virological response might be helpful to eradication of HCV infection.

Keywords: Hepatitis C, Antiviral treatment, Virological response

PE-089

Treatment Failure Rates of Direct-Acting Antiviral Agents for Chronic Hepatitis C: A Single-Center Study

Hee Sung Lee, Dong Yeon Kim, Min In Ki, Min Young Shin, Min Ji Cho, Sang Ok Jung, Woo Sun Rou, Hyuk Soo Eun, Jong Seok Joo, Eaum Seok Lee, Seok Hyun Kim, Byung Seok Lee

Division of Gastroenterology, Department of Internal Medicine, Chungnam National University School of Medicine, Daejeon, Korea

Aims: The aim of the present study is to investigate the failure rates of interferon (IFN)-free direct-acting antivirals (DAAs) when treating chronic hepatitis C virus (HCV) patients and to evaluate the factors associated with treatment failure, in a single-center setting.

Methods: HCV patients who had previously been treated with IFN-free DAAs were retrospectively searched and enrolled. All patients had either genotype 1b or 2. Treatment success and failure rates and associated factors were analyzed in various DAAs. Treatment success was defined as achieving a sustained virologic response at 94 week (SVR 94) after the completion of the treatment. Treatment was considered as a failure when HCV ribonucleic acid (RNA) remained detectable during the treatment or became detectable again after the successful achievement of end-treatment virologic response.

Results: A total of 150 patients were enrolled in the study. Of them, 75 had genotype 1b and 75 had genotype 2. Among genotype 1b patients, 38 were treated with daclatasvir/asunaprevir (DCV/ASV), 21 were treated with elbasvir/grazoprevir (EBR/GZR), 9 were treated with ledipasvir/sofosbuvir (LDV/SOF) with or without ribavirin, 5 were treated with glecaprevir/pibrentasvir (G/P), and 2 were treated with ombitasvir/paritaprevir/ritonavir + dasabuvir (PrOD). Treatment success rates were 84.2%, 95.2%, 100%, 100%, and 100%, respectively. Among genotype 2 patients, 62 were treated with sofosbuvir/ribavirin (SOF/RBV), and 13 were treated with G/P. Success rates were 96.8% and 100%, respectively. DCV/ASV showed the success rate below 90%. Genotype 1b and initial HCV RNA level above 1,000,000 IU/mL were associated with reduced responsiveness.

Conclusions: Overall, in concordance with previous studies, our results demonstrate that DAAs are very powerful medications in eliminating HCV RNA. However, DCV/ASV showed suboptimal efficacy. Despite the proven effectiveness of DAAs, treatment failures do exist, so follow-up monitoring is mandatory. Current DAAs-resistant HCV mutants can arise anytime so development of new anti-HCV drug is still needed.

Table 1. Treatment success and failure rates in different DAAs in patients with HCV genotype 1b and 2

<table>
<thead>
<tr>
<th>DAAs</th>
<th>Success (%)</th>
<th>Failure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV/ASV (b=1)</td>
<td>84.2</td>
<td>15.8</td>
</tr>
<tr>
<td>EBR/GZR (b=1)</td>
<td>95.2</td>
<td>4.8</td>
</tr>
<tr>
<td>SOF/RBV (b=8)</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>PrOD (b=2)</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>SOF/RBV (n=42)</td>
<td>98.6</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Table 2. Baseline characteristics of patients with failed DAAs treatment

| M, male; F, female; LC, liver cirrhosis; HCC, hepatocellular carcinoma; DM, diabetes mellitus; BMI, body mass index; HCV, hepatitis C virus; DAA, direct-acting antivirals; DCV/ASV, daclatasvir/asunaprevir; EBR/GZR, elbasvir/grazoprevir; LDV/SOF, with ledipasvir/sofosbuvir; G/P, glecaprevir/pibrentasvir; PrOD, ombitasvir/paritaprevir/ritonavir + dasabuvir; SOF/RBV, sofosbuvir/ribavirin |

Keywords: Direct-acting antiviral, Hepatitis C virus, Treatment failure

PE-090

Direct-Acting Antivirals about Diminishment of Liver Fibrosis after Chronic Hepatitis C Treatment

Hyun Phil Shin, Jounig Il Lee

Department of Gastroenterology and Hepatology, Kyung Hee University Hospital at Gangdong, Kyung Hee University, Korea

Aims: Direct-acting antivirals (DAAs) are known to eradicate chronic hepatitis C (CHC) virus infection, and prevent progression of liver fibrosis. Liver fibrosis may predispose to liver cirrhosis or hepatocellular carcinoma, but regression of fibrosis was not evaluated well in real world. Therefore, assessment of liver fibrosis in patients with CHC can predict the prognosis after treatment. We investigated the effect of DAAs on liver fibrosis by non-invasive methods like elastography and serum biomarkers and evaluate the correlations of these methods.

Methods: We retrospectively analyzed CHC patients who were treated with DAA and reached SVR12 from January 2016 to
Non-Invasive Test for Estimation of Liver Fibrosis
O. Baatarkhuu\textsuperscript{1}, S. Ariunaa\textsuperscript{2}, Badamsuren D.\textsuperscript{3}

\textsuperscript{1}Mongolian National University of Medical Sciences; \textsuperscript{2}National Center for Communicable Diseases, Mongolia; \textsuperscript{3}Third Central Hospital, Mongolia

Aims: In 2015 the digestive disorders were the second leading cause of morbidity among Mongolian population. The observed mortality from cancer in 2013 was 23.4\% including liver cancer which is the first most common cause of cancer death. Furthermore, the digestive disease related death accounts for 4.7\% of all mortality. Recently many noninvasive markers for assessing liver fibrosis have been developed, and they are frequently used in clinical practice. FIB4 index had a predictive value to confirm the existence of significant fibrosis with a specificity of 74\% and a sensitivity of 70\% and APRI score had a sensitivity of 89\% and a specificity of 75\%.

Methods: Cross sectional study was carried out. A total of 120 patients were enrolled in this study including 40 healthy individuals, 40 patients with chronic viral liver disease and 40 patients with alcoholic liver disease. Complete blood count (PLT), biochemistry (AST, ALT), abdominal ultrasonography were performed. APRI, FIB4-4 scores were calculated and compared with the results of the laboratory tests.

Results: A total of 120 patients were enrolled in this study; 40\% of patients were males. Their mean age was 43.43±10.93 years. Liver fibrosis stages that are determined by APRI score: F0-1 mild fibrosis accounts for 54.3\%, F2-3 moderate fibrosis 40.6\%, F4-cirrhosis 11.5\%; by FIB4 score: 62.8\% was in F0-1, 20.3\% was in F2-3, 11.5\% was in F4 stage among alcoholic liver disease group. In viral disease group liver fibrosis stages that were evaluated by APRI score were 36.2\%-F0-1 mild fibrosis, 32.4\%-F2-3 moderate fibrosis, 31.4\%-F4 severe fibrosis. Statistically significant difference were observed between alcoholic liver disease and viral liver disease groups in liver fibrosis stages that was determined with APRI score (\textit{P} < 0.05). In the abdominal ultrasonography increased echogenicity in alcohol group 32.5\%, in virus group 52.5\%, hepatomegaly in alcohol group 43.6\%, vena portae dilated in alcohol group 8.3\%, in virus group 10.6\%, splenomegaly in alcohol group 14.1\%, in virus group 20.1\%, splenic vein dilated on alcohol group 20.3\%, in virus group 14.75\%. Alcohol and viral hepatitis abdominal ultrasonography is a statistically significant difference. In the present study, we found a statistically significant negative correlation between FIB4 score and platelet count, moderate negative correlation between FIB4 score, and albumin, total protein level, weak correlation between alkaline phosphatase, GGT, total bilirubin levels and FIB4 score (\textit{P} < 0.05). APRI correlated significantly with AST and ALT levels, whereas platelet count, total protein albumin levels demonstrated moderate negative correlation with APRI scores (\textit{P} < 0.05).

Conclusions: The APRI F2-3, the FIB4 F0-1 and F4 scores showed high sensitivity for the diagnosis of alcohol related liver fibrosis. The FIB4 F2-3, F4 score showed high sensitivity for the diagnosis of virus related liver fibrosis. These measures also demonstrated significant correlation with the stage of liver fibrosis in patients with viral hepatitis. For non-invasive diagnosis of liver fibrosis F2-3, using FIB4 was related to necroinflammation, F4 was related with necroinflammation, cholestasis, hypersplenism, liver failure syndromes.

Keywords: APRI, Mongolia, Non-invasive, Fibrosis

Treatment Effectiveness of Tenofovir Disoproxil Fumarate in Chronic Hepatitis B among Mongolian Patients
O. Baatarkhuu\textsuperscript{1}, O. Otgonbayar\textsuperscript{2}, D. Munkh-Orshikh\textsuperscript{1}

\textsuperscript{1}Mongolian National University of Medical Sciences; \textsuperscript{2}Happy Veritas Clinic and Liver Diagnostic Center, Mongolia

Aims: Mongolia has one of the highest rates of viral hepatitis in the world, leading to the highest rate of liver cancer (HCC) in the world. We followed and evaluated treatment outcome of patients with chronic hepatitis B, initiating their TDF regimen in Happy Veritas Clinic and Diagnostic Center.

Methods: Only the data of the first 18-months of treatment
were considered. A total of 399 patients (218 males and 181 females; age range, 17-81 years; average age, 42 ± 11 years) enrolled in the present study. The assessment of response to treatment after a year was performed using available data relating to viral load, quantitative HBV-DNA, qHBsAg, ALT and Transient Elastography (TE).

**Results:** According to inclusion and exclusion criteria, a total of 399 patients (218 males and 181 females) enrolled in the present study. The age range of the patients was 17-81 years. The ALT level range of the patients before treatment was 10-392 IU/l, with an average level of 47 (29; 88) IU/l. Among the 399 patients 176 had ALT levels of < 40 IU/l and 223 had an ALT levels of > 41 IU/l. After 18 months the range of ALT level of the patients was from 12 to 160 IU/l, with an average level of 36 (26; 57) IU/l and 231 patients had ALT levels up to 40 IU/l, 168 patients had an ALT levels more than 41 IU/l. The distribution of patients in different fibrosis stages was: FO - 40% (n = 85), F1 – 9% (n = 19), F2 – 23% (n = 48), F3 – 18% (n = 39), F4 – 21% (n = 21). By month 12, 71% of the patients with available data (n = 175) had HBV-DNA <30 IU/mL, 25% were decreasing and 3% were increased HBV-DNA quantity. Mean HBsAg quantity was increased from 2409 to 3253 IU/mL.

**Conclusions:** Treatment of HBV using TDF in Mongolia is started only few years ago. TDF shows significant antiviral activity against HBV. But quantity of HBsAg was increased. And ALT levels were increased in 12 months and decreased in 18 months. Therefore, we need to study deep to understand the reason of elevation of ALT and HBsAg quantity. For patients who had fibrosis stage lower than F2 after treatment TE result decreased. And for patients who had a higher fibrosis stage (up to F3 stage) liver stiffness has increased.

**Keywords:** TDF, HBV, DNA, Mongolia

---

**PE-093**

**HCV Treatment after Curative Liver Resection or RFA in Hepatocellular Carcinoma Patients in Mongolia**

O. Baatarkhuu,1 O. Tsevelmaa2, J. Chinburen3

1Mongolian National University of Medical Sciences; 2Happy Veritas Clinic and Diagnostic Center; Ulaanbaatar, Mongolia; 3National Cancer Center of Mongolia

**Aims:** It’s reported that stage of liver cirrhosis, macro and microvascular invasion, portal vein tumor thrombus and cancer stage are associated with the postoperative recurrence of hepatocellular carcinoma (HCC). In this study we aimed to investigate the anti Hepatitis C virus (HCV) treatment impact on the recurrence of HCC (Hepatocellular carcinoma) after curative resection or RFA (radiofrequency ablation) treatment.

**Methods:** Patients with active HCV related HCC who had undergone curative hepatectomy or RFA were enrolled and analyzed to clarify the significance of anti HCV treatment at National Cancer Center of Mongolia. All patients were preoperative and postoperative HCV-RNA level of higher than 1000 IU/mL.

**Results:** The recurrence rate in patients who had received anti HCV treatment was significantly lower than in those without anti HCV treatment (P = 0.02).

**Conclusions:** The patients with HCV treatment after curative liver resection or RFA showed lower recurrence rate than without HCV treatment patients. Antiviral therapy is recommended, especially for patients who underwent curative hepatectomy for HCV to decrease the recurrence of HCC.

**Keywords:** HCV, RFA, Mongolia, HCC

---

**PE-094**

**Comparison of Methods That Evaluate the Prognosis of Liver Cirrhosis**

O. Baatarkhuu1, B. Enkhtuvshin2, D. Badamsuren3

1Mongolian National University of Medical Sciences; 2Gurvan Tsuur Family Health Center, Ulaanbaatar, Mongolia; 3Third State Central Hospital, Mongolia

**Aims:** To compare the new method that evaluate prognosis of liver failure with the traditional method.

**Methods:** The 23rd October 2016 our study was proved by meeting of biochemical principles (notary in 47) in HSUM. 322 patients with liver cirrhosis who had been in department of gastroenterology of the Third State central hospital were evaluated. Before treatment we took the sample of hematology, biochemistry and coagulation. Laboratory examination performed by Sysmex-KX 21, Biochemistry by Humalizer 2000, for the coagulation we used Humaclot apparatus. All statistical analysis were conducted with the SPSS 19.0.

**Results:** Among all cases 39.34% of patients were in group A, 50.82% in group B, 9.84% in group C according to the Child Pugh classification. For the MELD score 10.93% of patients were in up to 10 score, 73.22% were in 10-19, 13.66% were in 20-29, 2.19% were in 30-39 score and there was no patients who had over 40 score. In the MELD classification total bilirubin or liver functional test indicate jaundice, INR point to coagulation, creatinine shows renal function thus it is more sensitive than the Child Pugh. Therefore we have some idea other researchers. PLT was 119.2±6.25 in A group according to the Child Pugh whereas PLT was 132.31±16.74*109/l in 0-9 score group in the MELD, PLT% was 26.99±1.35 in A group and 26.74±2.29 in 0-9 score of MELD, prothrombin time was 17.37±0.39 in A group and 16.36±0.91 in 0-9 score of MELD. The splenic length was 12.15±0.21 in A group whereas 11.78±0.53 in 0-9 score of MELD. This shows MELD classification enable to make early diagnosis and evaluate the prognosis therefore appropriate other researchers. In 2001 (Kamath et al) according to MELD the death within 3 months happened 27% of patients from lower 20 score and 73% of patients from higher 20 score. In our investigation 13.66% of patients necessitate urgent liver transplantation.

**Conclusions:** Among all cases 39.34% of patients were in group A, 50.82% in B, 9.84% in C according to the Child Pugh clas-
Releasing Hepatocyte Growth Factor
Regeneration in Hepatic Fibrosis Model by Controlled
Human Adipose Derived Stem Cells Promote Liver
Keywords: Liver cirrhosis, Mongolia, MELD, HCV

Aims: Although mesenchymal stem cells (MSCs) provide effective therapy for liver fibrosis, there are conflicting data regarding their marginal therapeutic effects. This study aimed to enhance the potential of hepatocyte regeneration in human adipose mesenchymal stem cells (ASCs) and investigate whether they have robust therapeutic efficacy in experimental liver fibrosis.

Methods: ASCs were cultured with four cytokines (ASC-C), the expression of hepaticogenic factors was detected by microarray, and the effects of conditioned medium (CM) from ASC-C on the activation of hepatic stellate cells were analyzed. The therapeutic effects and mechanism of liver fibrosis induced by thioacetamide (TAA) were determined after cell transplantation. ASC-C exhibited high levels of hepatogenic (HGF, G-CSF), anti-apoptotic (IGFBP-2), and chemokine (IL-8) genes and increased expression of hepatogenic factors was detected by microarray.

Results: ASC-C CM inhibited the activation of hepatic stellate cells in vitro, and injection of ASC-C significantly delayed TAA-induced liver fibrosis and improved liver function and regeneration in vivo. In addition, human albumin-expressing ASC-C were observed in the livers of recipient animals. High levels of expression of HGF and its downstream signaling molecules, including p38, were detected in the ASC-C-injected livers. Transplantation of ASC-C exerts anti-fibrotic effects and accelerates liver regeneration.

Conclusions: Thus, ASC-C may be a novel candidate for the enhanced treatment of liver cirrhosis in clinical settings.

Keywords: Stem cell, Fibrosis

Human Adipose Derived Stem Cells Promote Liver Regeneration in Hepatic Fibrosis Model by Controlled Releasing Hepatocyte Growth Factor
Ja Sung Choi1, Sangheun Lee1, Ki Jun Han1, Sung-Whan Kim2
1Division of Hepatology, Department of Internal Medicine, Catholic Kwandong University, International St. Mary’s Hospital, Incheon, Republic of Korea; 2Department of Medicine, College of Medicine, Catholic Raviour University, Gwangju, Republic of Korea

Aims: To investigate the expression of TSLP on liver fibrosis in BDL rats.

Methods: The extrahepatic bile duct ligation (BDL) is induced to cholestatic pattern liver inflammation and fibrosis. However, the role of TSLP in liver fibrosis is largely unknown. Recently, hepatocyte derived TSLP is detected in liver biopsies from chronic hepatitis C patients and it has effect to condition dendrite cells to drive CD4+ Th17 differentiation that is play a role in the progression of liver fibrosis. The extrahepatic bile duct ligation (BDL) is induced to cholestatic pattern liver inflammation and cirrhosis. This study is aimed to investigate the expression of TSLP on liver fibrosis in BDL rats.

Aims: Thymic stromal lymphopoietin (TSLP) is cytokine expressed by epithelial cell and known as a mediator to regulate tissue inflammation and fibrosis. However, the role of TSLP in liver fibrosis is largely unknown. Recently, hepatocyte derived TSLP is detected in liver biopsies from chronic hepatitis C patients and it has effect to condition dendrite cells to drive CD4+ Th17 differentiation that is play a role in the progression of liver fibrosis. The extrahepatic bile duct ligation (BDL) is induced to cholestatic pattern liver inflammation and cirrhosis. This study is aimed to investigate the expression of TSLP on liver fibrosis in BDL rats.

Methods: We used male Sprague-Dawley rats with an initial body weight of 250-300g. Ten rats underwent BDL and five rats served as control. During the 4 weeks after BDL, blood was
withdrawn every one week to measure parameters (AST, ALT, ALP, albumin and total bilirubin) using rat tail vein. The progression of fibrosis was investigated by alpha smooth muscle anti-body (SMA), fibronectin, collagen Type I expression and specific immunohistochemistry (IHC) after scarifying the rat after 4 week of BDL. The expression of TSLP was evaluated by real time PCR, western blot and TSLP specific IHC in liver tissue.

**Results:** Biochemical parameters were consistently elevated during 4 weeks of BDL rats. To use hematoxylin eosin and Masson trichrome stain, we found increasing collagen density and proliferation of duct, stroma and fibroblast around portal area after BDL. The molecular markers for liver fibrosis were significantly increased in mRNA level attained by scarified BDL rat liver after 4 weeks compared with control one. This founding was paralleled by an increased overall expression of SMA, Fibronectin and collagen type I in western blot and a massive increased in fractions of theses positive cells in IHC in liver tissue from BDL rats. We observed the increase mRNA level of TSLP after 1 weeks of BDL rat with increasing other fibrosis markers. And after 4 weeks of BDL, the mRNA level of TSLP and expression in western blot were significantly increased compared with control model. The positive fraction of TSLP specific IHC was also increased in liver tissue of BDL rats.

**Conclusions:** The TSLP expression was increased in cholestatic patterned liver inflammation and fibrosis. We can assume that TSLP is a cytokine that generally interact with the progress of liver fibrosis.

**Keywords:** Thymic stromal lymphopoietin, Cytokine, Liver fibrosis

**PE-098**

**Enhanced Production of Steroid Drugs Intermediate Used in Treatment of Liver Cirrhosis**

Jayesh Vaishnav, Girish Pendharkar, Vaishali Mourya, Danish Anjum

School of Biochemistry, Devi Ahilya University, Indore Madhya Pradesh, India, India

**Aims:** Corticosteroids have been used to treat liver disorders and other autoimmune disease. Glucocorticosteroid is one example. Basically this drug reduces inflammation caused by liver cirrhosis. This action is done by blocking signaling pathway of cell. Steroid drug forms a complex with receptor protein and bind with nuclear DNA. The production of this steroid drugs is done by lengthy chemical reactions. Androst-4-ene 3, 17 dione (AD) and hydroxyl derivative of AD are current precursors of corticosteroids. The present study was aimed at production of androstenedione by using microorganism.

**Methods:** For two different bioconversion reactions, two strains of *Mycobacterium* species were used. For production of AD, *Mycobacterium fortuitum* subsp. *fortuitum* NCIM 5239 and for 9 hydroxy-AD, *Mycobacterium* sp. NRRL B-8119 was used. Optimized medium B and nutrient broth were used as incubation medium. Analysis of products was done by quantitative thin layer chromatography.

**Results:** Ethanol and DMF exhibits enhanced biotransformation of AD after 144 h incubation time. But in case of hydroxylation, organic solvents suppressed the production of 9-hydroxy-AD. Vegetable oils in both bioconversion reactions showed nearly 90-95 mol% conversion of products. Sunflower oils exhibited nearly 88 and 92 mol% conversion of AD and 9-OH-AD respectively.

**Conclusions:** Production of AD and 9-OH-AD could be optimized for industrial production of corticosteroids. Organic solvents and oils may be used as substrate carriers to enhance industrial scale production of live failure drugs.

**Keywords:** Corticosteroids, Acute liver failure, Steroid drugs, L-asparaginase, Aspergillus niger
Methods: A retrospective study was conducted in the Internal Medicine Department, Dornod Medical Center from 2017 to 2018. We examined the prevalence of H. pylori infection in 54 cirrhotic patients with PHG and using an anti-H. pylori IgG ELISA. Results: Out of the 54 cirrhotic patients with PHG, men were 34, women were 20 mean age was 43 years. The prevalence of H. pylori was observed in 38 (72%) cirrhotic patients with PHG. Out of the 38 patients with PHG and H. pylori infection, 17 (44%) had severe PHG and 12 (31%) had mild PHG. Conclusions: We concluded that H. pylori infection is a high prevalence of cirrhotic patients with PHG in Mongolia, which is may also be related to the severity of PHG.

Keywords: Helicobacter pylori, Portal hypertensive gastropathy, Liver cirrhosis

**PE-100**

Assessment of Liver Fibrosis and Cirrhosis by Fibroscan in Patients with Chronic Liver Disease

Le Thi Hoang Yen
Thai Nguyen National Hospital, Vietnam

Background: Liver biopsy is currently considered the gold standard for assessing hepatic fibrosis. However, it is an invasive procedure, with rare but potentially life-threatening complications. Fibroscan is a noninvasive imaging study for measuring liver stiffness by transducer probe-induced elastic wave that propagates through liver tissue to measure its velocity.

Aims: To evaluate the accuracy of fibroscan in the assessment of liver fibrosis and cirrhosis in patients with chronic liver disease.

Methods: The present study was conducted on 61 patients with chronic liver disease. The study was conducted in Thai Nguyen Hospital from May 2017 to December 2018, and the disease was confirmed by standard diagnostic criteria. All cases were subjected to the following protocol: full history, clinical examination, laboratory investigation, ultrasound examination and liver biopsy. The patients were subjected to fibroscan examination and compared with liver biopsy. Fibrosis was evaluated according to the METAVIR system as validated for fibrosis. LS cutoffs were determined using receiver-operating characteristic (ROC) curves.

Results: There were 51 males and 10 females, and their ages ranged from 43 to 76 years, with mean age of 49 years. Liver stiffness was significantly correlated with liver fibrosis. To diagnose liver fibrosis: AUROC = 0.88 (95% CI = 0.86 - 0.98). At the cut-off level of 7.3 kPa, Sensitivity (Se), specificity (Sp), (positive predictive value) PPV and negative predictive value (NPV) were 81%, 92%, 91%; and 72% respectively. To diagnose cirrhosis: AUROC = 0.93 (95% CI = 0.86 - 0.99). At the cut-off level of 12.8 kPa, Sensitivity (Se), specificity (Sp), (positive predictive value) PPV and negative predictive value (NPV) were 85%; 91%, 90%; and 70% respectively.

Conclusions: Fibroscan is a promising noninvasive method for detection of liver fibrosis in patients with chronic liver disease. Therefore, fibroscan can be used regarding the decision of treatment and follow-up of patients with cirrhosis.

Keywords: Cut-off value, Fibroscan, Liver stiffness measurement, Fibrosis

**PE-101**

Intra & Extrahepatic Portosystemic Shunt Embolization Procedure in Two Patients with Recurrent Hepatic Encephalopathy

Seung Kyu Choi, Seong Woo Nam, Hyeok Choon Kwon, Jong Kyung Choi, Joo Won Chung, Si Eun Kim, Sae Rom Kang, Jung Shin
Department of Internal Medicine, National Medical Center, Seoul, Korea

Aims: Two different cases of intractable hepatic encephalopathy (HEP) with liver cirrhosis showed different pattern of portosystemic shunt, such as extrahepatic (paraumbilical collateral) & intrahepatic shunt. They had relatively good hepatic reserve function (CTP score ≤ 7), and other defined provoking factors were not noted. Two patients showed different clinical courses after shunt closure procedure using by vascular plug & coil insertion. We analized two different clinical course & predictive factor for treatment failure.

Methods: Two patients showed remarkable portosystemic shunts in abdominal CT scan and angiography. Ampulatz vascular plug & interlock coil were used for shunt closure via angiographic intervention procedure.

Results: Patient with extrahepatic shunt showed transiently aggravated thrombocytopenia, hypotension and aggravated ascites. They were improved by stopping propranolol and paracentesis. Later, ascites was easily controlled by diuretics. After procedure, she didn't showed HEP. But patient with intrahepatic shunt showed unchanged hemodynamic change & ascites after procedure, and HEP with another intrahepatic portosystemic shunt was recurred at 4 weeks later after procedure.

Conclusions: Selective procedure of shunt embolization was somewhat useful in control of recurrent HEP. Transient hemodynamic change (suddenly decreased blood pressure, increased ascites & hypersplenism) was good predictor for effective HEP
management. During or shortly after intervention procedure, relapsed another portosystemic shunt made HEP recurrence.

**Keywords:** Encephalopathy, Portosystemic shunt, Cirrhosis

---

**PE-102**

Low Serum Creatinine Level and Acute Kidney Injury Can Predict Long-Term Mortality in Cirrhotic Patients with Ascites

Jaehyung Bae, Nan Young Choi, Ji Won Park, Jwa-Kyung Kim, Sung Gun Kim, Hyung Jik Kim, Choong Kee Park, Young Rim Song, Sung Eun Kim

**Aims:** Although renal dysfunction is a known prognostic factor in cirrhotic patients, serum creatinine is an inaccurate marker for glomerular filtration rate. We hypothesized that very low serum creatinine levels might be associated with other clinical factors besides renal function, and that acute kidney injury (AKI) could affect the long-term outcomes of cirrhotic patients with ascites.

**Methods:** We performed a retrospective study of hospitalized cirrhotic patients with ascites who were prescribed diuretics during hospitalization. The ability of baseline serum creatinine levels and changes in creatinine from baseline to predict all-cause mortality was analyzed. The absolute changes and percentage changes were calculated and AKI was defined by the Acute Kidney Injury Network classification.

**Results:** A total of 201 patients were included and 61 patients died during the mean follow-up of 35.8 ± 21.3 months. Baseline creatinine levels were lower but the absolute changes and percentage changes in creatinine were higher in non-survivors compared with survivors. The optimal cut off value to predict mortality was baseline creatinine of 0.5 mg/dL. Twenty-eight had low baseline serum creatinine (<0.5 mg/dL) on admission and AKI occurred in 23.9% of subjects. Multivariate analysis showed that a baseline serum creatinine<0.5 mg/dL on admission (hazard ratio: 2.58, 95% confidence interval 1.18-5.65, P = 0.014) and AKI (hazard ratio: 2.14, 95% confidence interval 1.16-3.94, P = 0.011) were significantly associated with long-term mortality.

**Conclusions:** Low baseline serum creatinine levels and AKI were independent predictors of all-cause mortality in hospitalized patients with cirrhosis and ascites.

**Keywords:** Creatinine, Acute kidney injury, Cirrhosis, Ascites

---

**PE-103**

Repeated versus Single Treatment of Esophageal Variceal Ligation after Esophageal Variceal Bleeding: Multicenter Retrospective Study

Young Youn Cho1, Jeong-Hoon Lee2, Su Jong Yu3, Yoon Jun Kim3, Hyung Jun Kim3*, Jung-Hwan Yoon3*

1Department of Internal Medicine, Chung-Ang University Hospital; 2Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Korea

*Corresponding Author

**Aims:** International guidelines recommend repeated esophageal variceal ligation (EVL) for treatment of esophageal variceal bleeding. However, due to patient compliance and complications of repeated EVL procedure, many physicians perform single EVL treatment after varix bleeding. We aimed to compare the risk of variceal re-bleeding after repeated EVL versus single EVL.

**Methods:** This retrospective study included consecutive patients who underwent initial esophageal variceal ligation (EVL) for the...
first esophageal variceal bleeding. Primary endpoint was the recurrence of variceal bleeding and uni-/multi-variate analyses were conducted to find independent predictors.

Results: A total of 210 patients were included: 133 in the repeated EVL group and 77 in the single EVL group. During follow-up duration (median = 46.5 months), 17 (12.8%) in the repeated EVL group and 36 (46.8%) in the single EVL group developed re-bleeding (P < 0.01 by log-rank test). However there were no difference of overall survival between the two groups (P = 0.05). Multivariate analysis showed that the single EVL group compared to the repeated group (adjusted hazard ratio [aHR] = 3.372, 95% confidence interval [CI] = 1.824–6.234, P < 0.001) was the only independent risk factor after adjustment for alcohol etiology (aHR = 3.370, 95% CI = 1.717–6.152, P < 0.001), combined gastric varix (HR = 1.333, 95% CI = 1.250–9.612, P = 0.017) and high MELD score (HR=2.379; 95% CI = 1.192–4.748; P = 0.014).

Conclusions: Repeated EVL after esophageal varix bleeding can improve re-bleeding. However, there was no difference in overall survival. Further randomized control studies are needed.

Keywords: Esophageal variceal ligation, Esophageal varix, Bleeding, Recurrence

Comparison of Gross Inspection by Surgeon or Pathologist, Ultrasonography, CT, MRI, Transient Elastography, APRI and FIB-4 for Prediction of Liver Cirrhosis

Hyun Yang1,2, Pil Soo Sung1,2, Kwon Yong Tak1,2, Jae Jun Lee11,2, Hee Chul Nam1,2, Jeong Won Jang1,2, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,2, Sang Wook Choi1,2

1 The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, 06591, Republic of Korea; 2 Division of gastroenterology and hepatology, Department of Internal medicine, College of Medicine, Eunpyeong St. Mary’s Hospital, The Catholic University of Korea, Seoul 06591, Republic of Korea; 3 Division of gastroenterology and hepatology, Department of Internal medicine, College of Medicine, Seoul St. Mary’s Hospital, The Catholic University of Korea, Seoul, 06591, Republic of Korea

Aims: Microscopic histopathologic confirmation is the gold standard for diagnosis of liver cirrhosis. Radiologic imaging, transient elastography (TE), and serum biomarker such as aspartate aminotransferase to platelet ratio index (APRI) and Fibrosis 4 (FIB-4) index are commonly used surrogates for prediction of cirrhosis. In addition, gross inspection by surgeon or pathologist can predict liver cirrhosis before microscopic histopathologic confirmation. The aim of this study is to compare these methods for prediction of liver cirrhosis.

Methods: From January 2015 to December 2017, we retrospectively reviewed patients with hepatocellular carcinoma who had been previously treated with hepatic resection or liver transplantation in the tertiary hospital. Radiologic imaging was assessed using ultrasonography, CT or MRI. APRI and FIB-4 were calculated by biochemical laboratory finding. Gross inspection by surgeon was based on operation record. Gross inspection by pathologist was based on gross findings of pathologic reports. Comparison of gross inspection by surgeon or pathologist, ultrasonography, CT, MRI, TE, APRI and FIB-4 were using the AUROC.

Results: Total of 205 patients were reviewed. Among them, three patients were excluded according to exclusion criteria. Finally, total of 202 patients were analyzed. Mean age was 57.7. Patients who were infected with hepatitis B virus were 153. One hundred patients were confirmed with microscopic histopathologic cirrhosis. Calculated AUROCs for prediction of cirrhosis were 0.685, 0.858, 0.768, 0.792, 0.818, 0.756, and 0.759 respectively in gross inspection by surgeon and pathologist, ultrasonography, CT, MRI, TE, APRI and FIB-4. Gross inspection by pathologist was more effective than gross inspection by surgeon, APRI and FIB-4 (P < 0.05). Gross inspection by surgeon was less effective than gross inspection by pathologist, CT, MRI, TE and FIB-4 (P < 0.05).

Conclusions: According to the comparison of these methods, gross inspection by pathologist was the most effective method for prediction of cirrhosis.

Keywords: Cirrhosis, Pathology

Clinical Spectrum of Precipitating Factors of Hepatic Encephalopathy in Cirrhosis of Liver: Experience in Western Part of Nepal

Saroj Pokhrel, Mukunda Raj Kalouni

Kaski Sewa Hospital and Research Center, Pokhara, Nepal

Aims: Hepatic encephalopathy is an extra hepatic complication of impaired liver function. It manifests as neuropsychiatric signs and symptoms associated with chronic liver disease in the absence of other neurological disorders. Its development leads a poor prognosis and it is associated with shortened patients’ survival. Reversibility of the precipitating factors has prognostic significance. This study aims to ascertain the spectrum of precipitating factors of hepatic encephalopathy in patients with cirrhosis of liver.

Methods: This is a hospital based descriptive, cross sectional study. This study was conducted at Kaski Sewa Hospital and Research Center from 16th January 2018 to 28th January 2019. Total of 117 cases of cirrhosis of liver who presented with hepatic encephalopathy and got admitted in ICU were included in the study. All patients of age more than 18 years, presenting with signs of hepatic encephalopathy were included and classified according to West Heaven criteria. Clinical data were recorded on a proforma and prognostic stratification through Child Pugh score.

Results: There were 70 (59.83%) male and 47 (40.17%) were female patients. Mean age of the patients was 56.45 (±11.261) years. Out of 117 patients, upper Gl bleed (48.72%), constipation (46.15%), infection (41.02%) and electrolyte imbalance (34.12%) stood out as the most common precipitating factors. Usage of diuretics, sedatives, and excess dietary protein were...
the other factors. More than one factor was found to be responsible in 54.7% of patients. Most patients were in grade IV (36.5%) and grade III (29.91%) of hepatic encephalopathy. Child Pugh class B (51.2%) and Class C (29.9%) were found. Mortality was 5.98%.

Conclusions: Upper GI bleed, constipation, infection, and electrolyte imbalance were the most common precipitating factors of Hepatic Encephalopathy in this study. Health education and awareness about these precipitating factors will help to decrease the incidence of hepatic encephalopathy in liver cirrhosis.

Keywords: Child Pugh score, Hepatic encephalopathy, Liver cirrhosis, Precipitating factors

PE-106

Comparison between Sandostatin Alone and Combined with Band Ligation for Hemostasis of Acute Variceal Bleeding

Tran Ngoc Thuy

Thai Nguyen Medical College, Vietnam

Aims: Compare the efficacy of sandostatin alone and combination with endoscopic band ligation (EBL) to treat acute variceal bleeding.

Methods: 193 acute variceal bleeding patients were randomly chosen into study, divided into 2 groups: Group 1 (90 patients) treated by sandostatin alone, group 2 (103 patients) treated by sandostatin combined with endoscopic band ligation. Followed up for 4 weeks, compare the efficacy of hemostasis.

Results: Mean age group 1 is 48.8 ± 9.1, group 2 is 51.7 ± 9.6. Rate of Child-Pugh C in group 1 is 60.0%, in group 2 is 56.2%. Rate of severe bleeding in group 1 is 23.3%, in group 2 is 10.7%. Size of EV F3 in group 1 is 56.7%, in group 2 is 73.8%. Number of 4-6 EVs in group 1 is 20%, in group 2 is 44.7%. Rate of rebleeding in group 1 is 33.3%, in group 2 is 13.6%; rate of free rebleeding in group 1 is 66.7%, in group 2 is 86.4%, \( P = 0.001 \).

Rate of rebleeding within 5 days in group 1 is 23.3%, 0% in group 2, rate of rebleeding from 5 days to 2 weeks in group 1 is 3.3%, in group 2 is 1%; rate of rebleeding from 2 weeks to 4 weeks in group 1 is 6.7%, in group 2 is 12.6%, \( P = 0.001 \). Rate of mortality in group 1 is 20%, in group 2 is 5.8%, rate of success after treatment in group 1 is 80%, in group 2 is 94.2%, \( P = 0.003 \).

Conclusions: Combination of sandostatin and endoscopic band ligation has more efficacy than drug alone for hemostasis of acute variceal bleeding.

Keywords: Endoscopic band ligation, Acute variceal bleeding

PE-107

Relationship of Symptom-Onset-To-Hospital Arrival with Hospital Course in Patients with Variceal Bleeding

Tae Suk Kim, Min Jong Lee, Dae Hee Choi

Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon, Korea

Aims: Bleeding from varices in cirrhosis is a common complication with high mortality of liver cirrhosis. However, the relationship of symptom-onset-to-hospital arrival with hospital course in liver cirrhotic patients still remains incompletely understood.

Methods: In this study, 93 cases of admitted liver cirrhotic patients with variceal bleeding who underwent endoscopy at the emergency department from January 1, 2015, to December 31, 2017, were retrospectively analyzed and followed up. Patients were divided into 2 groups based on symptom-onset-to-hospital arrival time.

Results: In thirty-three patients (35.5%), the median interval between symptom onset and hospital arrival was 31.25 minutes. There was no significant difference in success rate of hemostasis, door-to-scope time, Child–Pugh scores, ICU admission and in hospital mortality. Logistic regression models showed that longer symptom-onset-to-hospital arrival was associated with increased in-hospital day (hospital day of 3.25 and 6.84 for symptom-to-hospital times of \( \leq 60 \) min, and >60 min, respectively; \( P < 0.05 \).

Conclusions: In this result, symptom-onset-to-hospital arrival time affects to clinical course in variceal bleeding in cirrhotic patient. We suggest that the liver cirrhosis patient needs to be educated about complications and early hospital arrival after symptom onset.

Keywords: Liver cirrhosis, Endoscopy, Gastroesophageal varices

PE-108

Platelet Count Spleen Diameter Ratio to Predict Esophageal Varices in Patients with Liver Cirrhosis, in the Eastern Province Mongolia

Uranbaigal Dashnyam1, Nyam Biziya2, Badam Bunguzee2

1Molor Laboratory, Dornod, Mongolia; 2Dornod Medical Center, Internal Medicine Department, Dornod, Mongolia

Aims: To determine the usefulness of platelet count and spleen diameter ratio in predicting the presence of esophageal varices in patients with liver cirrhosis.

Methods: A total of 100 patients with liver cirrhosis were recruited from the outpatient clinic of a tertiary hospital in Mongolia. Patients with history of esophageal varices, cirrhosis of the liver with varices, or with ascites were excluded. Platelet count and spleen diameter were measured. The diagnosis of esophageal varices was made based on endoscopic findings.

Results: The mean age of the patients was 55.2 ± 10.7 years. The mean platelet count was 210,000 ± 50,000 platelets/μL and the mean spleen diameter was 140 ± 20 mm. The sensitivity, specificity, positive predictive value, and negative predictive value of the platelet count and spleen diameter ratio were 80%, 90%, 80%, and 90%, respectively.

Conclusions: The platelet count and spleen diameter ratio are useful in predicting the presence of esophageal varices in patients with liver cirrhosis.

Keywords: Liver cirrhosis, Platelet count, Spleen diameter, Esophageal varices

www.theliverweek.org  447
Aims: Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of esophageal varices is one of the major complications of portal hypertension. To validate whether the platelet count/spleen size ratio can be used to predict the presence of esophageal varices in Mongolian patients with hepatic cirrhosis.

Methods: This was a cross-sectional study to validate the diagnostic test for hepatic cirrhosis and was performed between 2017 to January 2019. Only stable patients were included in the study. Patients with active gastrointestinal bleeding at the time of admission were excluded. All patients underwent screening upper gastrointestinal endoscopy. Biochemical parameters were evaluated, and ultrasound was used to measure the longest diameter of the spleen. The platelet count/spleen diameter ratio was calculated and analyzed to determine whether it can predict the presence of esophageal varices.

Results: A total of 62 patients were included. The mean age was 56; 36 (58%) were men and 26 (42.0%) women. Child-Pugh classification, 35 (56%) patients were classified as class A, 23 (38%) as class B, and 4 (6%) as class C. The platelet count/spleen diameter ratio to detect esophageal varices independent of the grade showed using a cutoff value of ≤ 884.3, had 84% sensitivity, 72% specificity, and positive and negative predictive values of 93% and 41%, respectively.

Conclusions: The platelet count to spleen diameter ratio may be a useful tool for diagnosing EVs in liver cirrhosis noninvasively when endoscopy facilities are not available.

Keywords: Platelet count/spleen diameter ratio, Esophageal varices, Mongolian patients
days, recurrence rate, and liver function did not differ by the presence or absence of refractory ascites. Surgical repair might be beneficial for treatment of hernia in all liver cirrhosis patients including patients with refractory ascites.

**Conclusions:** Liver cirrhosis was associated with 30-day mortality in ICU patients. Jaundice, ascites, hepatic coma, more than 4 admissions due to cirrhosis, and more than 30 days of hospital stay due to cirrhosis were exacerbated factors in cirrhotic ICU patients.

**Keywords:** Liver cirrhosis, Intensive care unit, Mortality

---

**PE-111**

**The Impact of Liver Cirrhosis on the Mortality in Intensive Care Unit Patients**

Chien-Chang Liao¹, Ta-Liang Chen²

¹Department of Anesthesiology, Taipei Medical University Hospital, Taiwan; ²Department of Anesthesiology, Wan Fang Hospital, Taipei Medical University, Taiwan

**Aims:** The impact of liver cirrhosis on the mortality in intensive care unit (ICU) patients is not completely understood. Our purpose is to identify risk factors for mortality in ICU patients with liver cirrhosis.

**Methods:** We conducted a retrospective cohort study based on research data of Taiwan’s National Health Insurance that included patients with admission for intensive care between 1 January 2006 and 31 December 2012. We identified 1,250,300 patients aged 20 years and older with newly admission to intensive care units. We compared cirrhotic patients (1,337 cases) who visited Chonnam National University Hospital from 2008 to 2015. Baseline characteristics (age, sex, etiologies and liver function), complication rates and mortality were calculated.

**Results:** Compared with control, cirrhotic patients had higher 30-day mortality (aOR 1.60, 95% CI 1.53 to 1.68), particularly those with jaundice (aOR 2.23, 95% CI 2.03 to 2.45), ascites (aOR 2.32, 95% CI 2.19 to 2.46) or hepatic coma (aOR 2.1, 95% CI 2.07 to 2.36). Among ICU patients, liver cirrhosis was also associated with ICU mortality (aOR 1.44, 95% CI 1.38 to 1.51) and one-year mortality (aOR 1.40, 95% CI 1.35 to 1.46). Associations between cirrhosis of liver and increased 30-day mortality were significant in both sexes and every age group.

**Keywords:** Liver cirrhosis, Hernia

---

**PE-112**

**Changing Trends in Epidemiology and Clinical Outcomes in Liver Cirrhosis in Korea: Eight Years Data in Single Center Study**

Sunmin Kim¹, Jae Hyun Yoon¹, Chung Hwan Jun¹, Sung Bum Gho¹, Sung Kyu Choi¹, Hee Joon Kim²

¹Division of Gastroenterology, Department of Internal Medicine, Chonnam National University Hospital and Medical School, Gwangju and Hwasan, Korea; ²Department of Surgery, Chonnam National University Hospital and Medical School, Gwangju, Korea

**Aims:** In Korea, the most common causes of liver cirrhosis are chronic hepatitis B, C and alcohol. However, recent study in Korea reported the prevalence of alcoholic cirrhosis continues to increase up to 31%, but steady decrease in the prevalence of HBV related cirrhosis. Therefore, nationwide survey of the current epidemiological status in Korean patients with liver cirrhosis is greatly needed.

**Methods:** This is a retrospective cohort study of consecutive cirrhotic patients (1,337 cases) who visited Chonnam National University Hospital from 2008 to 2015. Baseline characteristics (age, sex, etiologies and liver function), complication rates and mortality were also studied.

**Results:** This study included 1,337 cases of liver cirrhosis; 37.9% of which were due to hepatitis B (N = 507), followed by 37.9% due to alcohol (N = 480), and 11.6% due to hepatitis C (N = 155), respectively. As of patients who visited in 2008, the proportion of cirrhotic patients associated with alcohol was 22.9%, which increased to 43.9% in 2015. The proportion of patients with hepatitis B was 54.2% in 2008, and declined to 27.2% in 2015. The proportion of hepatitis C patients was 12.5% in 2008 and 13.3% in 2015. The most common complication of enrolled patients was ascites (19.1%, N = 256), which was followed by variceal bleeding (14.4%, N = 193). The percentage of Child-Pugh class C in alcoholic liver cirrhosis patients was 4.5% in 2008, which came to 33.5% in 2015. In accordance with this, the average MELD score (11.4 -> 13.7) and complication rates were on increasing trend (36.4%-> 65.8%). Whereas, with regard to patients suffering from hepatitis B and C, the occurrence rates of complications were rising (12.5%- >38.6%) but the percentage of Child-Pugh class C (0.0% -> 2.1%, 0.0% -> 0.0%, respectively) and MELD score (9.9 -> 10, 9.1 -> 10.7, respectively) were not on meaningful increment, neither on the decrease. Regarding to causes of death, variceal bleeding was the most common cause of death (43.2%) and the second cause was hepatic failure (27.0%).
The progression status and complication rates in patients with alcoholic liver cirrhosis are on worsening tendency. On the other hand, as for patients with viral hepatitis, there was no significant difference in the occurrence rates and disease progression status between 2008 and 2015. A better understanding of these trends in liver cirrhosis related morbidity and mortality can be instrumental in steering future healthcare policies.

**Keywords:** Liver cirrhosis, Variceal bleeding, Hepatic failure

---

**PE-113**

**Laparoscopic Management of Cholelithiasis in Patients with Chronic Liver Disease: A 10-Year Experience**

Saurabh Galodha, Puneet Mahajan, Satinder P S Bains, Shivani Rao, V. Lekha, H. Ramesh

Department of Surgery, Indira Gandhi Medical College, Shimla, India

**Aims:** Laparoscopic cholecystectomy (LC) is usually contraindicated in patients with chronic liver disease (CLD) due to associated morbidity and mortality. Here we present our 10-year experience of performing laparoscopic cholecystectomy in patients of CLD.

**Methods:** Analysis of patients of CLD who underwent LC during the period from January 2007 to December 2016 was done. Pre-operative Child Turcot Pugh grade (CTP) and MELD scores, intraoperative parameters as well as perioperative morbidity, mortality and hospital stay were recorded.

**Results:** Laparoscopic cholecystectomy (LC) was performed in 113 patients with CLD. CTP grade A was seen in 86 patients while 22 patients were grade B and grade C was in 5 patients.
Mean MELD score was 9.5 ± 5.2. Choledocholithiasis was seen in 5 patients (4.4%) for which prior endoscopic clearance was done. 8 patients (7%) required subtotal cholecystectomy. We performed intra-operative cholangiography in 11 patients (9.7%). Mean operating time was 2.1 ± 1.1 hours. Mean intra-operative blood loss was 45 ± 20 ml. Only 2 patients (1.7%) required conversion due to extensive adhesions and collaterals. Perioperative blood transfusion was not required. 4 patients (3.5%) had major morbidity (Clavien Dindo > 3) in the form of bile leak and 1 patient had transient decompression. Out of these, 3 had CTP grade C (75%). There was no mortality. Median hospital stay was 2 days.

**Conclusions:** Laparoscopic cholecystectomy is safe approach for management of cholelithiasis in patients with CLD. A meticulous and patient approach and pre-operative optimization is imperative for favorable outcomes.

**Keywords:** Chronic liver disease, Cholelithiasis, Laparoscopic cholecystectomy

---

**Helicobacter pylori Infection in Cirrhotic Patients with Portal Hypertensive Gastropathy**

Phyu Sin Aye, Yarzar Tun, Naing Lin, Yan Lynn Myint, Nwe Ni

1Department of Gastroenterology, Mandalay General Hospital, Mandalay, Myanmar; 2Department of Medicine, University of Medicine-Mandalay, Mandalay, Myanmar

**Aims:** Helicobacter pylori infection is a major etiological factor of peptic ulcer disease (PUD). It is also supposed to be a risk factor for the most frequently encountered PUD in patients with liver cirrhosis. It is suggested to be a synergistic effect of H. pylori on liver cirrhosis with portal hypertensive gastropathy (PHG). The aim is to study H. pylori infection in cirrhotic patients with PHG, determine the proportion of H. pylori in cirrhotic patients with PHG and association between H. pylori infection and severity of portal hypertensive gastropathy (PHG).

**Methods:** A hospital based analytic study was carried out on 80 PHG patients diagnosed by OGD during 2017. H. pylori infection was detected by rapid urease test and then it was also compared with PHG severity according to Baveno Classification (2002).

**Results:** H. pylori positivity was noted in 39% (n = 31) of PHG patients and 61% (n = 49) of PHG patients were H. pylori negative. In mild PHG patients, H. pylori was positive in 33% (n = 13 of 40) whereas, in severe PHG patients, it was positive in 45% (n = 18 of 40). The prevalence was higher in severe PHG patients. But, the relationship between H. pylori infection and PHG was not significant (P value – 0.25).

**Conclusions:** Among 80 COL patients with PHG, H pylori positivity was 39%. Although there was no statistically significant between H. pylori infection and cirrhotic patients with PHG, the prevalence of H. pylori was higher in severe PHG patients.

**Keywords:** H Pylori infection, Portal hypertensive gastropathy, Cirrhosis, Severity of portal hypertensive gastropathy

---

**Biofabricated Silver Nanoparticles of Aqueous Extract of Bassia Longifolia L Leaves Mitigates Diethylnitrosamine Induced Hepatocellular Carcinoma in Wistar Rats: A Novel Approach for Liver Therapy**

Deepika Singh1, Manvendra Singh2, Pradeep Kumar3

Department of Pharmaceutical Sciences, SRUATS, Allahabad, India

**Aims:** Hepatic cancer is one of the deadly diseases in which liver cell multiplication occurs and the major cause of mortality associated with cancer. NF-kB plays its role by regulating the activation via inflammatory responses, cell survival and proliferation. Natural based products subsequently plays an important role in suppressing proinflammatory mediators via nuclear factor –Kappa beta (NF-κB) pathway. Bassia longifolia L leaves used in liver cancer therapy. The latest study was therefore designed to investigate the beneficial effects of phytofabricated silver nanoparticles (BLAgNPs) using the extract of Bassia longifolia leaves as NF-kB hepatic cancer inhibitors.

**Methods:** Phytofabricated silver nanoparticles using Bassia longifolia L aqueous extract (BLAgNPs) which acts as reducing and capping agent. Biofabricated silver nanoparticles (BLAgNPs) were characterized by UV spectroscopy, FTIR, X-ray diffraction, and Field Emission Scanning Electron Microscope. A cancer causing agent diethylnitrosamine and phenobarbitone as a promoter used to induce the Hepatic cancer in rats and rats were treated with different doses of BLAGNPs for 16 weeks. The anticancer effects was evaluated via in vitro cytotoxic activity on HHU (hepatic cancer) cell line and by determining biochemical parameter in the wistar rats.

**Results:** Results suggested that BLAGNPs revealed peak at 418 nm in UV spectrophotometer with spherical structure as shown in FESEM image and gives crystalline peak of silver in XRD diffraction. Different doses of BLAGNPs significantly reduced the serum marker enzymes, raised the levels of enzymatic and non-enzymatic antioxidant profile, and lessen the levels of inflammatory markers (IL-6, TNF-alpha and IL-10) via NF-κB pathway in rat's in dose dependent manner.

**Conclusions:** Biofabricated silver nanoparticles revealed remarkable productive effects on hepatic cancer in rats and by regulating cytokines and NF - kB its serve as a novel targeted therapy for hepatic cancer.

**Keywords:** Bassia longifolia L, Silver nanoparticles, Diethylnitrosamine, Cytokines
PE-116

Downregulation of PGC-1 Leads to Decreased Expression of Mitochondrial Antioxidant Enzymes in the Mouse Model of Obstructive Cholestasis

Say-June Kim1, Jung Hyun Park2

1Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, 2Department of Surgery, St. Paul hospital, The Catholic University of Korea, Korea

Aims: Several studies have indicated that cholestatic liver damage is mitochondria-mediated. However, the precise mechanism by which hydrophobic bile salts cause mitochondrial dysfunction is not clear. In this study, we intended to determine the pathogenesis of cholestatic liver injury associated with peroxisome proliferator activated receptor co-activator 1α (PGC-1α).

Methods: The mouse model of cholestatic livers was generated by surgical ligation of the bile duct (BDL), and the mouse model of fibrosis was developed following serial administration of thioacetamide. Next, after obtaining liver specimens on scheduled days, we compared the expression of the antioxidant enzymes (superoxide dismutase2 [SOD], catalase, and glutathione peroxidase-1 [GPx]), and PGC-1α in livers from mice with fibrosis and cholestasis using western blotting, immunohistochemistry and immunofluorescence.

Results: We found that a cholestatic liver exhibits lower expression of antioxidant enzymes, such as SOD, catalase, and PGC-1α. Contrastingly, a fibrotic liver exhibits higher expression of antioxidant enzymes and PGC-1α. In addition, cholestatic livers were found to show significantly lower expression of pro-apoptotic markers (Bax) than that seen in fibrotic livers.

Conclusions: It was well known that overexpression of PGC-1α increases mitochondrial antioxidant enzyme expression, and vice versa. Thus, we concluded that obstructive cholestasis decreases expression of PGC-1α, which leads to decreased expression of mitochondrial antioxidant enzymes, rendering mice with cholestatic livers vulnerable to ROS-induced cell death.

PE-118

Antioxidant Action of Hypoxic Conditioned Media from Adipose-Derived Stem Cells in the Hepatic Injury of Expressing Higher Reactive Oxygen Species

Say-June Kim1, Kee Hwan Kim2

1Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, 2Uijeongbu St. Mary’s Hospital, The Catholic University of Korea, Korea

Aims: Almost all liver diseases are known to be accompanied by increased levels of ROS, regardless of the cause of the liver disorder. However, little is known about the role of hypoxic-conditioned media (HCM) in the view of pro-oxidative/antioxidative balance.

Methods: Normoxic-conditioned media (NCM) and HCM were obtained after culturing ASCs in 20% O2 or 1%O2 for 24 hours, respectively. Their effects on the expression of various markers reflecting pro-oxidative/antioxidative balance were investigated in both in vitro (thioacetamide-treated AML12 cells) and in vivo (partially hepatectomized mice) models of liver injury, respectively.

Results: HCM treatment induced the higher expression of antioxidant enzymes, such as SOD, GPx, and catalase than did NCM in the in vitro model of liver injury. We also found that HCM increased the expression of NRF2. The in vivo models of liver injury consistently validated the phenomenon of upregulated expression of antioxidant enzymes by HCM.

Conclusions: We thus could conclude that HCM provides protection against ROS-related toxicity by increasing the expression of antioxidant enzymes, in part by releasing NRF2 in the injured liver.

PE-117

The Role of P-JNK Expression on Hepatocyte Necrosis and Autophagy in the Cholestatic Liver

Say-June Kim, Bong Jun Kwak

Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, Korea

Aims: Clinically, liver fibrosis and cholestasis are two major disease entities, ultimately leading to hepatic failure. Although autophagy plays a substantial role in the pathogenesis of these diseases, its precise mechanism has not been determined yet.

Methods: Mouse models of liver fibrosis or cholestasis were obtained following the serial administration of thioacetamide or surgical bile duct ligation (BDL), respectively. Next, after obtaining liver specimens at specific time points, we compared the expression of apoptotic (cleaved caspases), necrotic (phospho-c-Jun N-terminal kinase [p-JNK] and CD68), and autophagy markers (microtubule-associated protein light chain 3B [LC3B] and p62) in the fibrotic or cholestatic mouse livers, using polymerase chain reaction, western blot analysis, immunohistochemistry, and immunofluorescence.

Results: Following BDL, although there was a time-dependent increase of necrotic markers (p-JNK and CD68), no significant expression changes were detected in pro-apoptotic markers (cleaved cascades) over time. In addition, autophagy marker studies indicated that whereas autophagy was upregulated in fibrotic livers, it was downregulated in cholestatic livers. We also observed mild to moderate activation of p-JNK in fibrotic livers, whereas cholestatic livers demonstrated a significantly higher p-JNK activation.

Conclusions: Whereas fibrotic livers exhibited a mild to moderate increase in p-JNK expression related with the induction of autophagy and apoptotic cell death, cholestatic livers exhibited a marked increase in p-JNK expression which could be associated with the reduction of autophagy and a subsequent increase in necrosis.
**PE-119**

**Effect of Extracorporeal Bioartificial Liver Support System on Fulminant Hepatic Failure Rabbits**

Nursultan Kydyr, Samat Issakov  
General surgery, National Research Center for Maternal and Child Health, Kazakhstan

**Aims:** To evaluate the possibility of using cultured human hepatocytes as a bridge between bioartificial liver and liver transplantation.

**Methods:** In this experiment, the efficacy of extracorporeal bioartificial liver support system (EBLSS) consisting of spheroidal human liver cells and cultured hepatocytes supernatant was assessed in vivo using galactosamine induced rabbit model of fulminant hepatic failure.

**Results:** There was no difference of survival between the two groups of rabbits, but in the supported rabbits serum alanine aminotransferase, total bilirubin and creatinine were significantly lower and hepatocyte necrosis was markedly milder than those in control animals. In addition, a good viability of human liver cells was noted after the experiment.

**Conclusions:** EBLSS plays a biologic role in maintaining and compensating the function of the liver.

**Keywords:** Bioartificial liver support system, Fulminant hepatic failure, Hepatocytes, Liver transplantation

**PE-120**

**Immunocorrecting Action of Roncoleukin in Patients with Acute Cholangitis in Various Ways of Application**

Talgat Beisenbayev, Rysmakhanov M.S., Mussin N.M.  
Aktobe Medical Center, Kazakhstan

**Aims:** No doubt, the involvement of the immune system in the development of purulent cholangitis. Developing against the background of dysfunction of the immune system, secondary immune deficiency and endogenous intoxication with acute cholangitis determines the severity of the course and high lethality. To study the indices of immunological reactivity in patients with acute cholangitis in use of Roncoleukin in erythrocyte membranes.

**Methods:** The study included 64 patients with acute purulent cholangitis who was on inpatient treatment in the surgical department of “Aktobe Medical Center”, Aktobe from 2016 to 2018. The content of immunoglobulin classes A, M, G of complement was determined on a biochemical analyzer “Cobos integro”. The CEC content was determined by precipitation with a 3.5% polyethylene glycol solution on a spectrophotometer at a wavelength of 450 nm. CD3 +, CD4 +, CD8 +, CD20 +, CD25 +, CD56 +, CD95 +, HLA - cells and immunoregulatory index.

**Results:** The analysis showed shifts characteristic for secondary induced immune dysfunction. There was a significant tendency to normalization of the immunophagocytic link, which was confirmed by the normal content of CD20 +, CD25 +, CD56 +, CD95 +, HLA - cells and immunoregulatory index.

**Conclusions:** Thus, according to some indicators of immunograms, there is an accelerated dynamics of regression of signs of secondary immune deficiency when included in the complex of conservative therapy of Roncoleukin in autologous erythrocyte membranes in patients with acute cholangitis.

**Keywords:** Roncoleukin, Acute cholangitis, Cytokine

**PE-121**

**Acute Liver Failure in Kazakhstan**

Zhanna Kozybayeva, Yermakhan Assylkhanuly  
University Medical Center, Kazakhstan

**Aims:** Acute liver failure (ALF) is a life-threatening condition that can rapidly progress into coma and death due to the cerebral edema and multi-organ dysfunction. The ALF etiology and risk factors have been investigated in West Europe, North America, and Asia; however, there are still no published data about the causes and prognosis of ALF in Central and East European countries. The aim of our study was to analyze the causes, outcomes, and prognostic factors of ALF in patients referred to tertiary care center in Kazakhstan.

**Methods:** A total of 12 consecutive patients admitted to the tertiary care center (one of two university-level medical centers in Lithuania) over the period of January 2012 and December 2017 and who fulfilled the entry criteria of ALF (presence of hepatic encephalopathy (HE) and prothrombin international normalized ratio (INR) >1.5) were included into a prospective study.

**Results:** In our study the most frequent causes of ALF were acute viral hepatitis B (21.4%), drug-induced hepatitis (21.4%), and indeterminate hepatitis (17.9%); other etiologies included Budd-Chiari syndrome (10.7%), ischemic hepatitis (10.7%), Wilson’s disease (7.1%), Amanita phalloides-induced liver damage (3.6%), acute fatty liver of pregnancy (3.6%), and malignant infiltration of the liver (3.6%). Among patients with drug-induced liver injury, only one case of acetaminophen poisoning was diagnosed. Clinical status of 9 persons in all patients with ALF corresponded to criteria for liver transplantation (LT) (one liver transplantation was performed), 6 of them had contraindications, and 13 patients did not fulfill requirements for urgent LT. The patients’ survival rate in these groups was 11.1%, 16.7% and 69.2%, respectively. In 27 non-transplantate patients univariate analysis revealed the grade of HE on the day of enrolment, total serum bilirubin, pH, and prothrombin INR as risk factors for death from ALF. Multivariate logistic regressive analysis determined only prothrombin INR >3.24 and serum pH <OR = 7.29 as independent predictors of lethal outcome in ALF.

**Conclusions:** Acute viral hepatitis B, drug-induced liver injury, and indeterminate hepatitis are the main ALF causes in Kazakh-
Acute Liver Rejection Values of Doppler US Measurements
Yermakhan Assylkhanuly, Nurmakhan Assylkhanuly
University Medical Center, Kazakhstan

Aims: To prospectively evaluate accuracy and predictive values of Doppler ultrasonographic (US) measurement of portal blood velocity (PBV) and splenic pulsatility index (SPI) in diagnosis of clinically relevant acute rejection in patients with clinicobiomedical hepatic dysfunction after orthotopic liver transplantation (OLT).

Methods: Study was approved by the institutional review board, and protocol conformed to ethical guidelines of Declaration of Helsinki. Patient informed consent was obtained. In 17 patients with OLT (13 men, four women; mean age, 48 years; range, 27-64 years), PBV and SPI were measured at Doppler US within 48 hours before or after liver biopsy for clinically suspected acute rejection. Biopsy specimens were assigned scores according to Banff method, and rejection activity index (RAI) was calculated. RAI score of 4 or greater was considered clinically relevant acute rejection. Doppler US parameters were analyzed as absolute values and as percentage point changes with respect to values obtained at last examination before rejection was suspected. Information from two Doppler US parameters was combined; Doppler US composite index was calculated. Statistical tests were conducted to assess accuracy, sensitivity, specificity, and predictive values of Doppler US parameters in diagnosis of graft rejection.

Results: Clinically relevant acute rejection was diagnosed in nine patients. Median time from OLT until histologic diagnosis of acute rejection was 8 days (range, 5-20 days). Rejection was associated with a marked reduction in mean PBV (-43% +/- 5 [standard error of the mean]) and a slight increase in SPI (+12% +/- 16). The calculated Doppler US composite index was strictly related to severity of rejection (P < .001). When applied retrospectively, this index had good accuracy (88%) for prediction of rejection (specificity, 89%; sensitivity, 86%; negative predictive value, 94%).

Conclusions: During the first weeks after OLT, a marked decrease in PBV associated with increased SPI supports suspicion of clinically relevant acute rejection.

Keywords: Acute, Liver, Rejection, Doppler

Organs Failure Prevention for Patients with Hepatorenal Syndrome
Aisulu Rysmakhanova
Department of Internal Medicine, Central Hospital Polyclinic of MIA, Astana city, Kazakhstan

Aims: Hepatorenal Syndrome (HRS) plays an important role in patients with liver cirrhosis. To determine the dynamics of the severity of the condition and prediction of the estimated risk of mortality (ERM) patients with HRS using MARS-therapy and Plasmapheresis.

Methods: The study included a group of 9 patients with HRS in ages from 18 to 66 years. 6 patients of the main group received MARS-therapy and Plasmapheresis. Inside the main group investigated patients were divided into 3 groups (moderate, severe and very severe) depending on the number of points. Assessment of the dynamics of flow multiple organ failure (MOF) performed before treatment and 3-5 days of treatment.

Results: According to the results of the intragroup analysis revealed statistically significant dynamic changes in the main group for the subgroup of moderate severity. The decrease in the average scores in the subgroup indicates positive patient outcomes. Comparison between subgroups and the control group showed no statistical differences in the dynamics of APACHE III. The exception was two subgroups moderate groups where there was a statistically significant difference in the initial state - prior to treatment. This is due to the small sample of patients, where the average score was higher APACHE III in the study group than in the control. At subsequent stages of observation for 3-5 day these differences offset due to the patients. The dynamics of the estimated risk of death in 1st and a 2nd subgroup of the main group shows a statistically significant decreased this indicator.

Conclusions: The use of MARS-therapy and Plasmapheresis treatment may be considered appropriate in someone the complex therapy of patients to preventing the MOF. The appropriate use of MARS-therapy and Plasmapheresis in patients with HRS remains controversial and requires further evidence by the researches.

Keywords: Liver failure, Organs failure, Detoxicy
Production of Steroid Drug Precursor Used in Treatment of Chronic Liver Diseases

Girish Pendharkar, Anjum Syed Danish, Patil Shridhar
School of Life Sciences, Devi Ahilya University, Indore, INDIA

Aims: Use of steroidal drugs in liver dysfunction is reported by different research groups. Corticosteroids are one of them. Reduced inflammation is reported in acute liver failure by glucocorticoid. These drugs blocks receptor proteins in cytoplasm and alter protein synthesis. The complex of steroid drug and receptor interacts with DNA and blocks production of inflammatory biochemical. The production of these important steroidal drugs is done by complex chemical process. Androst-4-ene 3, 17-dione (AD) and 9-hydroxyandrost-4-ene 3, 17-dione (9-OH-AD) are current precursors of corticosteroids. The present study was aimed at production of androstenedione by use of microorganism and screening of efficient substrate carrier.

Methods: Two strains of Mycobacterium species were used for two different biocconversion reactions. For phytoesters to AD conversion Mycobacterium fortuitum subsp. fortuitum NCIM 5239 was used. Optimized medium B was used as incubation medium. For hydroxylation of AD to 9-OH-AD, Mycobacterium sp. NRRL B-8119 was used. Analysis of products was done by

Results: A total of 982 patients were enrolled. The mean age was 54.7 years, and 76.5% was male. Most patients (92.3%) had cirrhosis, and the most common cause of chronic liver disease was alcohol. The prevalence of ACLF based on the AARC and EASL-CLIF definitions was 14.2% and 20.5%, respectively. In AARC ACLF patients, ascites and jaundice as acute deterioration and alcohol, toxic material, and hepatotropic virus as precipitating factors were more frequent than EASL-CLIF ACLF patients. On the other hand, variceal bleeding and bacterial infection as acute deterioration and precipitating factors were more frequent in EASL-CLIF ACLF patients. The 28-day and 90-day mortality of ACLF patients were 23.0% and 39.0% based on AARC definition, and 26.4% and 43.9% based on EASL-CLIF ACLF definition. Patients who met both ACLF definitions showed significantly lower 28-day survival rate than those who met only one ACLF definition (P < 0.05), and significantly lower 90-day survival rate than those who only AARC ACLF definition (P = 0.001), but not EASL-CLIF ACLF definition (P = 0.055). These short-term mortality rates were significantly higher than those without ACLF (all P < 0.001). In patients with ACLF, cirrhosis was not significant factor for short-term mortality. In addition, previous decompensation was also not significant factor, even within a year.

Conclusions: The AARC ACLF patients and EASL-CLIF ACLF patients had different characteristics. However, the patients with ACLF based on both AARC and EASL-CLIF definitions showed significantly higher mortality rate than those without ACLF.
quantitative thin layer chromatography.

**Results:** As compared with control, ethanol and DMF exhibits enhanced biotransformation of AD after 144 h incubation time. But in case of hydroxylation, organic solvents are suppressed the production of 9-OH-AD. Vegetable oils in both bioconversion reactions showed nearly 90-95 mol% conversion of products. Sunflower oils exhibited nearly 88 and 92 mol% conversion of AD and 9-OH-AD respectively.

**Conclusions:** Production of AD and 9-OH-AD could be optimized for industrial production of corticosteroids. Organic solvents and oils may be used as substrate carriers to enhance industrial scale production of live failure drugs.

**Keywords:** Acute liver failure, Corticosteroids, Steroid drugs, Mycobacterium

---

**Bioconversion of steroid substrate into different intermediate drugs.**

---

**Pattern of Liver Disease at Tertiary Level Care in Nepal: Hospital Based Retrospective Study**

Satya Narayan Yadav¹, Sanjit Karla²

¹Institute of Medicine, Tribhuvan University, ²Sarvanga Hospital, Kupondol (Lalitpur), Nepal

**Aims:** - To study distribution and pattern of liver disease in a tertiary care center provides an overview of disease pattern in a community. - To plan and prioritizing strategies to treat the diseases and reduce their burden in the community.

**Methods:** A retrospective study was conducted among patients admitted to the Liver unit, Sarvanga Hospital Lalitpur from April 13, 2018 to October 16, 2018. Demographic profile and disease pattern was studied. Descriptive analysis was used to calculate frequencies and percentage and their relations.

**Results:** Male to female ratio was 2.3:1. The mean age was 41.9 (SD 14.8). Median hospital stay was 8.0 days (Q25-75 6.0-12.0). The top three diseases were alcoholic liver disease 50 (38.5%), viral hepatitis 44 (33.8%), and liver abscess 11 (8.5%). Fifty (38.5%) patients had acute, 74 (56.9%) had chronic liver disease and 6 (4.6%) were malignancy. The main cause of acute disease were infections 41 (82.0%) especially Hepatitis E Virus (HEV). HEV was associated with acute liver failure and pregnancy which was 4 (18.2%) and 2 (12.5%) respectively. Chronic diseases were caused by alcohol 45 (60.8%) followed by infection of hepatitis B and C viruses 11 (14.8%). Cirrhosis was diagnosed in 37 (28.5%) with alcohol as the main cause.

**Conclusions:** Majority had chronic liver disease (CLD), mostly due to alcohol, HBV and HCV. Alcohol was the leading cause of cirrhosis. Prevalence of Hepatitis E was found to be high in acute illness. Therefore, an initiative needs to be taken to decrease alcohol consumption along with HEV, HBV and HCV transmission through community health program.

**Keywords:** Alcohol, Cirrhosis of liver, Hepatitis, Liver diseases

---

**Possibilities of Application of Endoscopic Techniques in the Diagnosis and Treatment of Echinococcosis of the Liver**

Askhat Seitzhanov, B. Kuanyshbaev, Baurzhan

Atyrau City Hospital, Kazakhstan

**Aims:** To improve the quality of diagnostics and treatment of the liver echinococcosis by using endoscopic technologies.

**Methods:** The results of laparoscopic endocystectomy in 78 patients treated for liver echinococcosis compared to cystectomy by laparotomy in 124 patients are presented.

**Results:** Optimal characteristics for laparoscopic endocystectomy were types CL, CE1-CE3 of cystic echinococcosis according to cystic echinococcosis ultrasonic classification by H.A. Gharbi (1981) modified by World Health Organization (2003) with cysts localized in 2–6 liver segments; partial superficial location of cysts; cyst size not less than 5 cm; no cysts in 1, 7 and 8 liver segments or deeply located cysts of any size, as well as cysts of CE4-CE5 types. Of the 78 cases in which laparoscopic endocystectomy was completed successfully, in 4 patients the surgery was continued by a laparotomy access. The reasons for the continuation with laparotomy were unsuccessful attempts for stable hemostasis at resection of liver fibrous capsule excesses (1 case), presence of large fistula between the cyst and components of the biliary system at the bottom of the fibrous cavity (2 patients), and location of the second cyst in the segment unavailable for laparoscopic manipulation (1 case). The frequency of early complications after laparoscopic endocystectomy was...
14.9%. Relapse occurred in 1 (1.1%) patient. Comparative assessment of echinococcosis recurrence risk in different periods (Kaplan–Meier analysis) after laparoscopic interventions and laparotomy, both followed by albendazole treatment, did not identify any statistically significant differences.

**Conclusions:** Endoscopic technology application in the form of video laparoscopy, diagnostics and treatment endovideoscopy of the residual cavity in the intra- and postoperative periods allows improving the diagnostics quality and treatment results of patients with the liver echinococcosis.

**Keywords:** Liver, Echinococcosis, Laparoscopic, Treatment

---

**PE-128**

**Atypical Liver Resections in Liver Alveococcosis**

Rokiya Surova

Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

**Aims:** To evaluate results of surgical treatment of liver alveococcosis in which atypical resection was performed.

**Methods:** We analyzed the results of treatment of 15 patients with alveococcosis of the liver for the period from 2011 to 2017, who had atypical resection of the liver in various volumes.

**Results:** There were 10 men (55, 5%) and 8 women (44, 5%). The age of patients was ranged from 9 to 63 years old. Four patients had a parasite lesion of the right and left lobes of the liver, which produced atypical resections of both lobes. One of them had lesion of both lobes combined with the germination of the duodenal ulcer into the serosa. This patient got an atypical resection of the liver and removal of the parasite with a wedge resection of the duodenum, followed by closure of the resulting defect. The second patient had three lesions, two marginal removed with atypical resection. Alveococcal node, localized in the central segments (first, fourth and eighth), grew into the inferior vena cava, which was not resectable. In percentage terms, the lesion was localized in both lobes in 6 (33,3%), in the right lobe in 9 (50%), in the left lobe in 3 (16,3%) of patients. The duration of the disease ranged from 1 month to 3 years. Six patients got resection of two segments of the liver, and the rest patients were resected in one segment of the liver. Blood loss varied from 150 to 800 ml, and the duration of the operation ranged from 1 hour to 6 hours. There were no postoperative complications (hepatic failure, bile-elimination) in patients with abnormal liver resection. Lethal outcomes also were not observed in this group.

**Conclusions:** Atypical resection is a radical treatment for liver alveococcosis. In case of regional localization, small alveolar nodes or multiple and bilobar liver damage, we consider it expedient to perform an atypical resection of the liver.

**Keywords:** Atypical liver resections, Liver alveococcosis, Small liver resection

---

**PE-129**

**Surgical Aspects Treatment of Liver Echinococcosis**

Baurzhan Kuanyshbayev, M. Altay

Surgical Departments, Regional Medical Center, Kyzylorda City, Kazakhstan

**Aims:** One of the urgent problems at the present stage is the surgical treatment of liver echinococcosis.

**Methods:** In the surgical department of the Kyzylorda Regional Medical Center between 2013-2018 various 108 operations to the patient in connection with echinococcosis liver. 73 patients (67,5%) were women, 35 (32,4%) were men aged 16 to 58. Location in the right lobe of the liver–64 (59.2%), in the left side–34 (31,4%), in both lobes of the liver–10 (9.2%). Hydatid cyst of the liver, recurrent 8 (7,4%). The situation is complicated by fistulas, cystobiliary 17 (15,7%) of the patient. It was manufactured by the following operations: laparoscopic echinococcectomy - 22(20,3%), bisegmentectomy-1 (0,9%), pericystectomy–8 (7,4%), echinococcectomy–77 (71.2%), including: marsupialisation–1 (0,9%), omentopexy–7 (6,4%), abdominal cysts–13 (12%), capitonnage of the residual cavity–56 (51.8%).

**Results:** In the postoperative period, 22 (20.3%) patients had complications. Of these, 13 (59%) in the form of exudative pleurisy, ended with a puncture of the pleural cavity. Suppuration of the residual cavity 7 (31,8%) patients, 2 (9%) patients, had relaparotomy drainage of abscess, 1 (4,5%) patients underwent laparoscopy, drainage of abscess, 4 patients (18,1%) performed puncture of the residual cavity under ultrasound control drainage and Pigtail type. Complications of the biliary tract in 2 (9%), a Pigtail catheter ultrason control. On 8 - 16 weeks after surgery, the bile fistula is closed, the catheter is removed. Hyperthermia in the postoperative period was in 20 (18.5%) patients, they were carried out antibacterial therapy and infusion therapy additionally prescribed fractional plasmapheresis. Postoperative hyperthermia occurred in patients who underwent omentopexy and cyst ablation. There was no mortality.

**Conclusions:** To prevent complications such as abscess of the residual cavity and hyperthermia, it is necessary to choose a radical operation. If it is impossible to perform a radical operation, then it is necessary to carry out capitonnage of the residual cavity with adequate drainage.

**Keywords:** Liver, Echinococcosis, Surgical, Treatment

---

**PE-130**

**A Case of Acute Hepatitis E Mimicking Autoimmune Hepatitis**

Kideok Yoo, Youngnam Kim

Department of Internal Medicine, Cheju Halla General Hospital, Jeju, Korea

www.theliverweek.org
**Aims:** Hepatitis E Virus (HEV), an enterically transmitted virus, occurs mainly in developing countries and endemic areas. However, sporadic cases of acute hepatitis E have been reported in developed countries. Swine seem to function as a reservoir for HEV. We experienced a case of acute hepatitis E in a 41-year-old man. The patient did not have any travel history to an HEV-endemic area.

**Methods:** Here we report a case of acute hepatitis E mimicking autoimmune hepatitis.

**Results:** A 41-year-old man visited hepatology department for jaundice. He was diagnosed with autoimmune hepatitis 2 weeks ago in other hospital. He had been taking prednisolone for 2 weeks for autoimmune hepatitis. He had no medical past history. There was no history of alcohol or herbal medication. He was not performed a liver biopsy. Blood tests performed at other hospitals showed serum bilirubin levels of 10.3 mg/dL. Serum ANA was positive and serum titer was 1:160. Abdominal CT scan performed showed periportal edema, consistent to acute hepatitis. Laboratory findings showed altered liver enzymes with serum aspartate aminotransferase (AST) 89 IU/L, alanine aminotransferase (ALT) 270 IU/L, alkaline phosphatase 101 IU/L, total bilirubin 2.5 mg/dL, IgG 1529 mg/dL. Prothrombin time (INR) was 1.1. The serological tests revealed positive ANA (titer 1:80), ASMA positive with negative tests for anti-LKM1, anti-dsDNA, anti-mitochondrial antibody. Viral serology was negative for HBsAg, anti-HBs, IgM anti-HBc, IgM anti-HAV, anti-HCV with undetectable RNA of HCV. HEV IgM serology was negative for HBsAg, anti-HBs, IgM anti-HBc, IgM anti-HAV, anti-HCV with undetectable RNA of HCV. HEV IgM was positive with HEV IgG was negative. Liver biopsy revealed atypical findings for autoimmune hepatitis. Immunosuppressive therapy was stopped. He recovered after conservative treatment without complication.

**Conclusions:** Hepatitis E should be considered in the differential diagnosis in all cases of unexplained acute hepatitis in developed countries, regardless of travel history. Careful history taking and serologic test is required.

**Keywords:** Acute hepatitis E, Autoimmune hepatitis, Sporadic, Serologic test

---

**PE-131**

**HIV-HCV Coinfection: Prevalence and Associated Risk Factors in the Western Region of Nepal**

Bhoopendra Sharma1, Sanjib Mani Regmi2, Suresh Jaiswal3, Krishna Gurung4, Mamita Khaling Rai2

1School of Health and Allied sciences, Pokhara University, Nepal; 2Department of Microbiology, Gandaki Medical College Teaching Hospital and Research Center Pvt. Ltd., Nepal; 3Department of Microbiology, Prithivi Narayan Campus, Nepal

**Aims:** Both Human Immunodeficiency virus (HIV) and Hepatitis C virus (HCV) are blood borne viruses transmitted primarily through sexual contact and injection-drug use. Because of these similar modes of transmission, adults at risk for HIV infection are also at risk for HCV infection. The rates of HIV-HCV coinfection varies with geographical regions, risk factors, and modes of transmission. This study aimed to explore the prevalence of HIV-HCV coinfection and associated risk factors for HCV in HIV infected individuals in Western Nepal.

**Methods:** This cross-sectional study enrolled 192 HIV positive individuals visiting Antiretroviral Therapy Centre of Western Regional Hospital (WRH), Pokhara, Kaski between June and December, 2017. Consent was taken prior to collection of blood samples. The socio-demographic information and associated risk factors for the viral infection were recorded following a standard format. Blood samples were processed to determine serum anti-HCV antibodies by enzyme-linked immunosorbent assay (ELISA) and electrochemiluminescence immunoassay (ECLIA). Data were statically analysed using SPSS software.

**Results:** The result suggested 4.17% (8/192) prevalence of HIV-HCV coinfection. Although not statistically significant, the sero-prevalence of HCV was highest for male (68/4, 7.14%) than female (2/108, 1.85%). Additionally, sero-prevalence was highest in age group 30-39 years (6/2/0% followed by 40-50 years (1.04%). Intravenous drug use was found to be significantly associated with HIV-HCV coinfection (P < 0.05).

**Conclusions:** Despite effective anti-retroviral therapy, hepatitis and liver-diseases represents major cause of deaths among HIV-HCV coinfected patients suggesting a mandatory screening for HCV in HIV infected individuals. As intravenous drug use is associated risk factor, addressing the risk environment for intravenous drug users could minimize the cases of HIV-HCV coinfection in our community.

**Keywords:** HIV, HCV, Coinfection, Western Nepal
Regional Hospital. The patients were counseled and samples were taken. Samples were processed by ELISA and analyzed by SPSS. HCV, pulmonary TB and extra pulmonary TB were measured for all participants.

**Results:** For HCV 82(91.9%) were negative and 8(8.1%) were positive and for pulmonary TB, 88(97.8%) were negative and 2(2.2%) were positive whereas for extra pulmonary TB, 9(10%) were positive and 81(90%) were negative. In multivariabe analysis, these co-infections were found higher in age group 35-50, male and married. Prevalence of HCV and pulmonary TB showed significant value (p-0.039). Similarly, significant value was also shown in HCV infection among male and IV drug users whereas in TB, significant value was shown among smokers.

**Conclusions:** The result of our research suggests the need of regular screening of the patients to detect these co infections so that it can aid to reduce mortality of HIV infected individuals due to HCV and TB.

**Keywords:** Prevalence, Co-infection, HIV, HCV, TB, ELISA

### PE-134

**The Urinary Tract Infection with Liver Cirrhosis Patient**

Bat-Erdene Dashnyam, Bolortsetseg Sergelen

1. Molor Laboratory, Choibalsan, Mongolia; 2. Dornod Medical Center, Choibalsan, Mongolia

**Aims:** To evaluate the incidence of bacterial infections (BI) in liver cirrhosis (LC), the pathogen agents involved, to define the risk factors and impact on prognosis.

**Methods:** There was a retrospective study that enrolled a total of 25 patients with LC admitted in our clinic between 2018.03-2018.09 (6 months) Clinical, biological and bacteriological data were monitored.

**Results:** 6 patients (24%) were found with urinary tract infection. 4 patients are female, 2 patients are male. Of the 6 cases with urinary tract infection, the etiologic agent was identified in three: E. coli, Klebsiella, Citrobacter.

**Conclusions:** In this study, the rate of urinary tract infections in LC is high, because the study was retrospective. We must actively seek infections in all hospitalized patients with LC.

**Keywords:** Urinary tract infection, Liver cirrhosis

### PE-133

**Morphology and Histopathological Study of a Liver, Having Inflamed Left and Quadrate Lobe**

Pooja Garg, Surajit Ghatak

All India institute of Medical Sciences, Jodhpur, Rajasthan, India

**Aims:** Chronic liver disease is the common cause of death in the developing countries nowadays. The disease increases liver related morbidity and mortality, and often increases the risk of other comorbidities such as type 2 diabetes and cardiovascular disease.

**Methods:** During the routine dissection of undergraduate students at the Department of Anatomy, All India institute of Medical Sciences, Jodhpur India, it was observed in a 74 year old male cadaver the liver was completely covered by the greater omentum. Liver was dissected out to study the morphological and histopathological changes.

**Results:** The weight of the liver was 2.3 kg. The maximum vertical and transverse diameter of the liver was 16.9 cm and 18.2 cm respectively. Diameters of different lobes of liver are mentioned in table no. 1. The right lobe and caudate lobe of the liver were normal. The left lobe and quadrate lobe of the liver were inflamed. The diameters of the left and quadrate lobe of liver were more than the normal parameters. The histopathologiical study of the liver was also done using H&E staining. Fatty liver changes were observed in the histopathology.

**Table 1. Showing the diameter of different lobe of liver**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Lobe of 1</th>
<th>Max. vertical diameter (cm)</th>
<th>Max. transverse diameter (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Right lobe</td>
<td>16.7</td>
<td>8.1</td>
</tr>
<tr>
<td>2.</td>
<td>Left lobe</td>
<td>14.5</td>
<td>7.9</td>
</tr>
<tr>
<td>3.</td>
<td>Quadrate lobe</td>
<td>9.1</td>
<td>7.6</td>
</tr>
<tr>
<td>4.</td>
<td>Caudate lobe</td>
<td>6.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

**Conclusions:** There has been an exponential increase in the global incidence and prevalence of liver disease because of the obesity pandemic. In the absence of therapeutic interventions, most of the cases showed increased morbidity and mortality.

**Keywords:** Histopathology, Morphology, Lobes

### PE-135

**Acute Cholestatic Hepatitis Induced by Epstein-Barr Virus Infection in an Adult**

Kyoung Min Sohn

Department of Gastroenterology, Hansol Hospital, South, Korea

**Aims:** Acute cholestatic hepatitis without features of infectious mononucleosis is a rare presentation of primary Epstein-Barr virus (EBV) infection, with only several cases previously reported in the medical literature.

**Methods:** A 24 years old young man with a febrile illness was noted to have a cholestatic picture of deranged liver function tests. Over the following week a progressive obstructive jaundice developed, with no evidence of cholelithiasis on ultrasound and magnetic resonance cholangiopancreatography. Serological tests for hepatitis A, B, C, E, cytomegalovirus (CMV), leishmaniosis were negative. Specific immunoglobulin M antibodies against EBV were detected in his serum and the diagnosis of EBV associated hepatitis was confirmed by polymerase chain reaction testing.

**Results:** Supportive treatment was implemented and his liver function had normalized 3 months after presentation.

**Conclusions:** EBV is associated with a wide variety of clinical
Laparoscopic Liver Echinococcectomy

Yerlan Umirbekov, Aktobe Medical Center, West-Kazakhstan Medical University, Kazakhstan

Aims: Treatment of parasitic liver cysts remains one of the most urgent problems of surgical hepatology. The only way to treat liver echinococcosis is surgery. Drug therapy is ineffective. New perspectives in the treatment of echinococcosis using the possibilities of videoendoscopic surgical interventions—laparoscopic echinococcectomies. The goal is to improve the results of surgical treatment of patients with liver echinococcosis by reducing the traumatism of operations, the frequency of postoperative complications, relapses and the duration of rehabilitation of patients after surgical treatment.

Methods: In the Department of Surgery of the Aktobe Medical Center, in the period from 2013 to 2018, 21 laparoscopic operations were performed in patients with liver echinococcosis. Among them were 13 men and 8 women aged 19 to 59 years. Usually used 3 trocars. A trocar with a diameter of 10 mm was introduced into the navel. Additional trocars were administered under laparoscopic control in the subcostal area, at the point directly above the hepatic cyst (10 mm trocar) and along the anterior axillary line (5 mm trocar). After that gauzes were injected into the abdominal cavity moistened with a solution of povidone, which was used to cover the area around the cyst. The same gauzes isolated the subphrenic or subhepatic space depending on the localization of the cyst. The next step was puncture of the cyst with a thick needle with complete suction of the cyst contents with vacuum suction. Then, through the same needle (without removing it from the cyst cavity), a 1% povidone solution was injected into the residual cavity. After exposure for 5 minutes, the entire cyst was aspirated again. The treatment was repeated twice. Then the cyst wall in its most thinned place was opened with electrocoagulation scissors. Excess fibrous capsules with thinned hepatic parenchyma were excised. Shells parasites were removed from the cavity of the cyst using an endocontainer. In a case with bile ducts fissure, we coagulated them with an argon plasma coagulator. The walls of the fibrous capsule were treated with povidone solution. The drainage of the residual cavity was performed by specialized silicone drains. Then gauze moistened with a solution of povidone were removed from the abdominal cavity and the subphrenic or subhepatic space was drained.

Results: Laparoscopic surgery of echinococcal liver cysts was possible in all 22 patients without conversion. The average duration of the operation was 50 ± 12 minutes. No were intraoperative complications. The average length of hospital stay was from 5 to 8 days. No were any complication after operations.

Conclusions: Laparoscopic echinococcectomy can be successfully used in the treatment of liver echinococcosis in patients with superficial echinococcal cysts. The absence of laparotomic incision significantly reduces the time of rehabilitation of patients after surgical treatment.

Keywords: Liver cysts, Laparoscopic surgery
Keywords: Rat peritonitis model, Carica papaya leaves, Ultrafiltration, Dialysate glucose

PE-138
Hepatological Profile during Visceral Leishmaniasis
Sukrat Sinha
Department of Zoology, Nehru Gram Bharati University, Allahabad, U.P-211002, India
Aims: We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of Leishmania donovani with 3x10^7 parasites via-intra-cardiac route.
Methods: Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments.
Results: The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-γ was not statistically different between combination vs monotherapy (P = 0.298) but CD2 treatment even alone significantly influenced IFN-γ production than either SAG treatment (P = 0.045) or with CD2 adjunct SAG treatment (P = 0.005) in Ld-S strain as well as in Ld-R strain. The super-oxide generation began enhancing very early on day 10 after SAG treatment with CD2 during which SAG action was at minimum. Unlike SAG treatment, treatment of SAG with CD2 also led to production of nitric oxide and TNF-α, resulting in resulting in most effective clearance of L. donovani from infected macrophages.
Conclusions: Our results indicate that CD2 which can boost up a protective Th1 response which can protect liver from further deterioration during Visceral Leishmaniasis infection.
Keywords: Visceral Leishmaniasis, Immunotherapy, CD2, Liver

PE-139
Assessment of Liver Function among Dengue Patients
Padmavathi Parthasarathy, I. Samiya Begam, Sathiya Priya Brindha, Pregna B Dolia
ACS Medical College and Hospital, Chennai, India
Aims: To assess the liver function to evaluate the effect of dengue virus infection by doing liver function test (LFT) and also to understand the impact of dengue infection in different age groups including males and females.
Methods: This prospective study was conducted on serologically confirmed dengue patients (n = 69) from September to November 2018 at A.C.S medical college & hospital (ACSMC&H), Chennai, India. Blood samples were collected and analysed for LFT which includes Total protein, Albumin, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase in fully automated Erba XL 200 machine.
Results: The Study group classified to three different groups which is Group 1 (<30yrs) (n = 40) mean age (22.4 ± 4.3), group 2 (31-50yrs) (n = 19) mean age (40.8 ± 4.8), group 3 (>50yrs) (n = 10) mean age (60.5 ± 8.4). One way anova showed, Total protein, Albumin, and Alanine aminotransferase are statistically significant (P < 0.05) in all the study groups.
Conclusions: Important problem in adult patients with Dengue fever is Liver injury but clinical manifestations of liver involvement is not common and it is the major contributing factor in morbidity and mortality of patients with Dengue fever hence the monitoring of liver function is so important especially in elderly people. Total protein, Albumin, and Alanine aminotransferase used as early marker to assess the severity of the disease in elderly people.
Keywords: Dengue, Liver function test, Adult population

HDV Viral Load Related Liver Fibrosis Patients Clinical Evaluation Based on M2BPGi Level in Serum
Lkhagva-Ochir TOVUU, Enkhjargal BAYARSAIKHAN
Department of Laboratory Medicine, National Cancer Center of Mongolia
Aims: HBV-HDV coinfection which significantly increases the risk of developing liver cirrhosis and hepatocellular carcinoma (HCC), in Mongolia. HDV-related HCC is understudied, the underlying biological mechanisms associated with liver cancer remains unclear. Mac-2 Binding Protein Glycosylation isomer (M2BPGi) is a novel serological glyco-biomarker for staging liver fibrosis and cirrhosis. We investigate to evaluate the efficiency of serum M2BPGi with chronic hepatitis D infection.
Methods: Serum M2BPGi levels were evaluated in 50 patients with chronic hepatitis D and 25 healthy controls who underwent the hepatologist control in our institution were enrolled in this study. HDV viral load and M2BPGi, PIVKA II level in serum both groups were examined using real time reverse transcription-polymerase chain reaction and ELISA immunoassay. The patients were divided into two groups: high and low groups, based on the HDV viral load. We compared the clinicopathological factors between the high expression and low groups.
Results: M2BPGi serum level was in between healthy controls (0.8 ± 0.49) and hepatitis D patients (6.04 ± 5.8). M2BPGi concentrations also was between in HDV high viral load group 10.8 ± 7.1 (>200 IU/mL, n = 40), HDV low viral load group 1.3 ± 1.4 (<200 IU/mL, n = 10). In the univariate analysis, serum alanine aminotransferase, aspartate aminotransferase, PIVKA II and M2BPGi were determined as the significant risk factors of HDV viral load. Compared with other non-invasive markers, M2BPGi had the greatest specificity for diagnosing cirrhosis and cirrhosis in hepatitis D patients.
Conclusions: Serum M2BPGi could be a non-invasive, predictive new biomarker for liver fibrosis, cirrhosis and progression of HCC among HDV infected patients.

Liver Tuberculosis
Muhammad ZAKRIA1,2
1Surgery, Wapda Medical Complex Lahore, 2Hepatobiliary Surgery, Masood Hospital, Lahore, Pakistan

Aims: Tuberculosis is a disease of third world countries but in fact no country is immune of it. This disease affects almost all parts of the body. Early recognition is very important. Liver rarely presents with tuberculosis. It has to be differentiated from non tuberculosis liver abscess and fibrolamellar variety of hepatocellular carcinoma. If it is recognized early then it can be treated with medicine but some times it requires biopsy to confirm the disease. It usually presents with fever and weight loss. In young age hepatic lesions may not be liver cancer and they should be differentiated from the non cancerous lesions.

Methods: A 26 years old female was presented in emergency department for pain abdomen in the epigastric region. She had fever which was high grade for last few weeks. It was associated with off and on nausea and vomiting. Her lab tests were not significant but radiological reports confirmed lesions in the segment 5 and 6. It was found to be the liver tuberculosis after biopsy.

Results: Antituberculosis therapy for 9 months is very good for the treatment of liver tuberculosis if it is recognized early.

Conclusions: Many times hepatic lesions resembles the malignancy. In this case we had noticed that all the history and radiological investigations were in favour of fibrolamellar variety of hepatocellular carcinoma. In these cases probably liver biopsy play a vital role to manage the disease.

NAFLD, Basic

Hepatocyte-Targeted shNLRP3 Nanobiologics Facilitated Local Suppression of NLRP3 Inflammasome in the Liver and Reduced Nonalcoholic Steatohepatitis

Jingyun Luan, Wei Chen, Dianwen Ju

Department of Microbiological and Biochemical Pharmacy, School of Pharmacy, Fudan University, Shanghai, China

Aims: Emerging evidences have indicated that excessive activation of NOD-like receptor protein 3 (NLRP3) inflammasome triggered by toxic lipids promotes the pathogenesis of nonalcoholic steatohepatitis (NASH). Blockade of NLRP3 inflammasome reduces liver inflammation and fibrosis, but initiates gut microbial dysbiosis that drives NASH progression, which should be attributed to the different functions of NLRP3 inflammasome in different organs. Thus, hepatocyte-targeted delivery therapeutics that allows the local suppression of NLRP3 inflammasome in the liver but devoid of microbial dysbiosis is urgently needed for optimal control of NASH.

Methods: Taking advantage of hepatocyte-specific expression of asialoglycoprotein receptor (ASGPR) and the strong affinity of ASGPR for galactose, we developed galactosylated nanobiologics for hepatocyte-targeted suppression of NLRP3 inflammasome. The therapeutic gene pGPU6-shNLRP3 is encapsulated into closed vesicles produced by DOTAP and cholesterol for Nano-shNLRP3 nanobiologics. DSPE was functioned with galactose via PEG to form DSPE-PEG-Galactose, which was post-inserted into phospholipid bilayer of Nano-shNLRP3 to develop Galactose-Nano-shNLRP3 nanobiologics for hepatocyte-targeting. Moreover, hepatocyte-specificity, distribution, safety and therapeutic efficacy of these nanobiologics were also evaluated.

Results: The data presented here showed that Galactose-Nano-shNLRP3 nanobiologics were specifically internalized by hepatocyte cell lines via the endocytosis mediated by ASGPR. In vivo distribution studies further confirmed the rapid and extensive hepatic accumulation of Galactose-Nano-shNLRP3. The evaluated levels of shNLRP3 in the hepatocytes by Galactose-Nano-shNLRP3 contributed to the hepatic-specific suppression of NLRP3 and efficient prevention of liver inflammation and steatosis. Meanwhile, Galactose-Nano-shNLRP3 were not immunotoxic and did not induce gut dysbiosis.

Conclusions: This work illustrated the potential of Galactose-Nano-shNLRP3 nanobiologics as a promising hepatocyte-targeted therapeutics against NASH through facilitating the local suppression of NLRP3 inflammasome in the liver.

Keywords: NLRP3 inflammasome, Nonalcoholic steatohepatitis, Hepatocyte-targeted, Nanobiologics

NAFLD Screening among Newly Diagnosed Diabetics in Dornod Province, Mongolia

Tsetsegmaa Damdinsuren1, Ryenchindorj Erkhembayar2
1Internal Medicine Department, Dornod Medical Center, Dornod, Mongolia, 2Department of International Cyber Education, Graduate School, Mongolia National University of Medical Sciences, Ulaanbaatar, Mongolia

Aims: Prevalence of diabetics increased dramatically during last two decades in Mongolia. The nationwide studies reported a significant increase in prevalence; 3.1%, 6.5% in 1999, 2010, respectively. Non-alcoholic fatty liver disease (NAFLD) is a chronic medical condition strongly associated with diabetes. Therefore, we aimed to study NAFLD risk among newly diagnosed diabetics in eastern province Dornod, Mongolia.

Methods: We used cross-sectional study design to screen NAFLD
Ameliorating Liver Fibrosis Using the Secretome Released from miR-122 Transfected Adipose-Derived Stem Cells in an Animal Model

Kee-Hwan Kim1, Say-June Kim2

1Department of Surgery, Uijeongbu St. Mary’s Hospital, The Catholic University of Korea; 2Department of Surgery, Seoul St. Mary’s Hospital, The Catholic University of Korea, Korea

Aims: Recently, the exclusive use of mesenchymal stem cell (MSC)-secreted molecules, named as the secretome, rather than cells has been evaluated for overcoming the limitations of cell-based therapy while maintaining its advantages. In this study, we were intended to determine the therapeutic potential of secretome released from miR-122 transfected ASCs.

Methods: We collected the secretory materials released from ASCs that had been transfected with antifibrotic miR-122 (MCM), and compared their antifibrotic effects with naïve secretome (CM). MCM and CM were intravenously administered to the mouse model of thioacetamide-induced liver fibrosis, and their therapeutic potentials were compared.

Results: MCM infusion provided higher therapeutic potential in terms of (a) reducing the collagen content in the liver, (b) inhibiting the proinflammatory cytokines, and (c) reducing the abnormally elevated liver enzymes than did the infusion of naïve secretome. The proteomic analysis of MCM also indicated that the contents of antifibrotic proteins were significantly elevated than naïve secretome.

Conclusions: We thus could conclude that the secretome released from miR-122 transfected ASCs has higher antifibrotic and anti-inflammatory properties than naïve secretome. Because miR-122 transfection into ASCs provides a specific way of potentiating antifibrotic properties of ASC-secretome, it could be considered as an upgraded way of reinforcing the secretome effectiveness.

Association of Coffee and Caffeine Consumption with Fatty Liver Disease, Nonalcoholic Steatohepatitis, and Degree of Hepatic Fibrosis

Darkhan KOPZHASSARULY, Bauyrzhan DARZHIGENOV

Hepatology, Hepatology Center of Almaty, Kazakhstan

Aims: Coffee caffeine consumption (CC) is associated with reduced hepatic fibrosis in patients with chronic liver diseases, such as hepatitis C. The association of CC with nonalcoholic fatty liver disease (NAFLD) has not been established. The aim of this study was to correlate CC with the prevalence and severity of NAFLD.

Methods: Patients involved in a previously published NAFLD prevalence study, as well as additional NASH patients identified in the Hepatology Center of Almaty, were queried about their caffeine intake. A validated questionnaire for CC was utilized to assess for a relationship between caffeine and four groups: ultrasound negative (controls), bland steatosis/not-NASH, NASH stage 0-1, and NASH stage 2-4. A total of 306 patients responded to the CC questionnaire. Average milligrams of total caffeine/coffee CC per day in controls, bland steatosis/not-NASH, NASH stage 0-1, and NASH stage 2-4 were 307/228, 229/160, 351/255, and 252/152, respectively. When comparing patients with bland steatosis/not-NASH to those with NASH stage 0-1, there was a significant difference in CC between the two groups (P = 0.005). Additionally, when comparing patients with NASH stage 0-1 to those with NASH stage 2-4, there was a significant difference in coffee CC (P = 0.016).

Results: Spearman’s rank correlation analysis further supported a negative relationship between coffee CC and hepatic fibrosis (r = -0.215; P = 0.035).

Conclusions: Coffee CC is associated with a significant reduction in risk of fibrosis among NASH patients.

Keywords: Hepatic fibrosis, Chronic liver diseases, Hepatitis C, Coffee caffeine consumption
Chorionic-Plate-Derived Mesenchymal Stem Cells Attenuate Hepatic Steatosis via Restoration of Mitochondrial Function

Yun Bin Lee¹, Se-Mi Jung², Jae Yeon Kim³, Gi Jin Kim³, Jung-Hwan Yoon⁴

¹Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; ²Department of Biomedical Science, CHA University, Seongnam, Republic of Korea

Aims: Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases worldwide, but its pathophysiology is not fully understood due to complexity of the mechanisms involved in the disease. Moreover, the pharmacological therapy for NAFLD is not yet available. We investigated the effects of chorionic-plate-derived mesenchymal stem cells (CP-MSCs) on hepatic steatosis and mitochondrial function.

Methods: HepG2 cells were treated with palmitic acid (PA), and then co-cultured with CP-MSCs. Intracellular lipid accumulation was assessed by oil red O staining and mitochondrial mass was measured by staining mitochondria and quantifying mitochondrial DNA (mtDNA). Male C57BL/6J mice were chronically fed with high-fat diet (HFD). At week 29, mice were injected with either phosphate-buffered saline (NTx) or CP-MSCs (Tx; 1 × 10⁶ cells, 8–10 passages). Four weeks later, liver histology and function were assessed.

Results: PA-induced intracellular lipid accumulation was attenuated when co-cultured with CP-MSCs (Fig. 1A). The mitochondrial mass was reduced by PA treatment and then was restored following co-culture with CP-MSCs (Fig. 1B). Expression of genes involved in regulation of mitochondrial function, such as PGC1 and sirtuins, was dynamically changed by PA treatment and CP-MSC co-culture. Cellular reactive oxygen species (ROS) increases in the cells treated with oxLDL oxidized for 8 hr. Treatment of cells with oxLDL and oxHDL is associated with a significant increase in the concentration of cholesteryl ester hydroperoxides (CEOOH) in LD.

Conclusions: Hepatic steatosis and mitochondrial dysfunction in NAFLD can be ameliorated by transplantation of CP-MSCs. Our study findings suggest the therapeutic potential of CP-MSCs in NAFLD and help understanding alterations in hepatic lipid metabolism which may be restored by CP-MSC transplantation.

Keywords: NAFLD, Stem cells, CP-MSCs, Mitochondria, ROS, SOD

Oxidized Lipoproteins Induce Accumulation of Oxidized Triglycerides and Cholesteryl Ester in Lipid Droplets of Liver Cell

Rojeet Shrestha¹, Zhen Chen², Hitoshi Chiba³, Shu-Ping Hui¹

¹Faculty of Health Sciences, Hokkaido University, Kita-12, Nishi-5, Sapporo 060-0812, Japan; ²Department of Nutrition, Sapporo University of Health Sciences, Nakamura Nishi-4-2-1-15, Higashi-ku, Sapporo 007-0894, Japan

Aims: Non-alcoholic fatty liver disease (NAFLD) is typically characterized by the excessive accumulation of lipid droplets (LD) in the liver and is associated with the presence of metabolic disorders such as diabetes mellitus, obesity, dyslipidemia, hypertension, and oxidative stress. Oxidative modification of LD can induce inflammatory events that can potentially progress to severe liver disease. Since the oxidatively modified lipoproteins carry considerable amount of oxidized lipid that can be taken up by the liver. Therefore, the present study is designed to investigate the role of oxidized lipoproteins in the formation of LD rich in oxidized lipids in liver cells.

Methods: A fasting EDTA blood sample was collected from a healthy human volunteer to isolate VLDL, IDL, LDL and. Oxidized lipoproteins (oVLDL, oIDL, oLDL, oxHDL) were prepared by incubating the lipoprotein fraction with Cu²⁺ for 2, 4 and 8 hours. LD in the HepG2 cells were induced by incubating cells in DMEM medium supplemented with 0.2 mM of each oleic and linolenic acid. Then the cells were treated with the oxidized lipoproteins and incubated for 24 hours. Single LD sample was isolated from the cells using 3D mobile manipulator under brightfield invert microscope. The extracted LD from the cells were analyzed with LTQ Orbitrap mass spectrometry equipped with nano-electrospray ionization.

Results: The amount of triglyceride hydroperoxides (TGOOH) in LD treated with native VLDL and IDL less than 0.5%. The relative amount of TGOOH in LD depends on the degree of oxidation of VLDL and IDL. As high as 5% of TG were oxidized in the cells treated with oxVLDL oxidized for 8 hr. Treatment of cells with oxLDL and oxHDL is associated with a significant increase in the concentration of cholesteryl ester hydroperoxides (CEOOH) in LD.

Conclusions: TGOOH and CEOOH in oxidized lipoproteins can be incorporated in LD in liver cells. The incorporation depends on the degree of oxidation. Accumulation of such oxidized lipid molecules in the LD may be associated with the pathological process.

Keywords: Lipid, Lipid droplet, Non-alcoholic liver disease, Oxidized lipids
Could Cholecystectomy Facilitate or Augment Non-Alcoholic Fatty Liver Disease? Association or Causal Relationship?

Waqar Khalid Saeed
Nishtar Medical College and Hospital, Multan, Pakistan

Aims: Several clinical data strongly suggest an association between cholecystectomy (XGB) and prevalence of non-alcoholic fatty liver disease (NAFLD). But the exact mechanism is unknown, and its causal relationship is also unclear. We tried to investigate the causal relationship between XGB and NAFLD.

Methods: Sham operation and cholecystectomy was performed in two different settings (normal diet condition (study I), and 60% high fat diet (study II)), respectively. Repeated liver biopsy without sacrifice was done at 1, 2, and 4 months. Liver histology, biochemistry, PCR, and western blot for metabolic parameters were compared to sham operation group. Quantitation of bile-acid composition was determined using UPLC-ESI-QTOFMS. The concentration of metabolites was quantified by multiple reaction-monitoring mass spectrometry based on standard curves using authentic standards.

Results: In study 1 (sham vs. cholecystectomy in normal diet), there was no difference in body weight and liver chemistry (ALT, AST, triglyceride and cholesterol levels) at 1, 2, and 4 months. NAFLD activity score (NAS) including hepatic steatosis, inflammation, and ballooning changes was not different between sham and XGB group, except at early stage. Immunohistochemical stain for hepatocyte apoptosis (CK-18, and TUNEL stain), and qPCR for hepatic apoptosis and fat synthesis pathway were not different between control and XGB model in normal diet condition. In study 2 (sham vs. cholecystectomy in 60% high fat diet for 6 months), there were no differences between control and XGB model in NAFLD condition regarding body weight, liver histology, blood chemistry, and molecular study. Hepatic concentration of LCA, CA, UDCA, CDCA, and DCA in control and XGB model was not different at different conditions (normal chow and high fat) at 1, 2, and 4 months.

Conclusions: Cholecystectomy can cause transient liver injury at early stage, but cholecystectomy did not cause and facilitate fat accumulation as well as hepatic inflammation in both normal and obese condition.

Keywords: NAFLD, Cholecystectomy, Cell death

Nonalcoholic Fatty Liver Disease in Severely Obese Adolescent and Adult Patients

Nauryzgul Zhangabai1, Akmaral Dossanova2
1Hepatobililar Surgery, National Research Center for Maternal and Child Health, Kazakhstan; 2Republican Children’s Clinical Hospital “Aksai” KazNMU named after SD Asfendiyarov, Almaty, Kazakhstan

Aims: Nonalcoholic fatty liver disease (NAFLD) is increasingly an indication for liver transplantation in adults. While severe obesity (SO, BMI ≥40 kg m(-2)) in adults is long standing, it is recent in duration in adolescents. With adolescent obesity on the rise, NAFLD is becoming the most frequent liver disease in adolescents. The hypothesis that SO adolescents and adults have different severity of NAFLD because of longer duration of obesity in SO adults was tested.

Methods: Preoperative clinical data, NAFLD activity and NASH (Nonalcoholic steatohepatitis) scores from intraoperative liver biopsies were extracted from a prospective database of consecutively operated SO adolescents and adults (n = 24 each). Fastig preoperative serum inflammatory mediators were evaluated by ELISA.

Results: Other than age, baseline BMI, ethnicity and gender distribution, the incidence and extent of dyslipidemia, hypertension, and metabolic syndrome were comparable between groups. Histologic scores for steatosis and inflammation were similar. Adolescents have significantly higher NASH incidence, hepatocyte injury scores and fibrosis. This was associated with higher serum C-reactive protein and sCD14 levels.

Conclusions: For comparable BMI and metabolic profile, SO adolescents have more advanced liver damage, more severe systemic inflammation, suggesting differences in NAFLD etiologies and more aggressive disease progression in the young obese population.

Keywords: NAFLD, Liver transplantation, Nonalcoholic steatohepatitis, C-reactive protein

Effects of Lactobacillus and Bifidobacterium Strains on Gut Liver Axis in NAFLD Mouse

Sang Jun Yoon, Gi Soo Youn, Min Jea Shin, Dae Hee Han, Hari-priya Gupta, Na Young Lee, Ki Tae Suk, Dong Joon Kim
Department of Internal Medicine, Hallym University Medical Center, Chuncheon, Korea

Aims: Nonalcoholic fatty liver disease (NAFLD) is major global public health problem and its incidence is continually increasing. In our previous study, treatment with Lactobacillus bulgaricus (LB), L. helveticus (LH), Bifidobacterium longum (BL) and B. breve (BB) improved Western diet induced NAFLD. We aimed to evaluate the effect of combination therapy with Lactobacillus and Bifidobacterium strains on gut liver axis in NAFLD mouse.

Methods: We used 6-week aged C57BL/6 mice and divided 6 groups (n = 5/group; normal diet, Western diet, and 4 probiotics test groups (LB+BL, LB+BB, LH+BL, and LH+BB groups, 10⁶ CFU/g for 8 weeks). We compared liver/body weight (L/B) ratio, liver histology (steatosis and inflammation), liver enzymes and inflammatory cytokine (tumor necrosis factor [TNF]-α and interleukin [IL]-1β).

Results: In the analysis of L/B ratio (%), LB+BL (5.1 ± 0.2), LB+BB (4.7 ± 0.5), and LH+BB (5.2 ± 0.5) groups showed signifi-
Results: Methods:

Keywords:

Conclusion: Probiotics treatment with L. bulgaricus, L. casei, L. helveticus, and P. pentosaceus KD7 improved steatohepatitis by modulating gut microbiota composition and inflammatory pathway in gut-liver axis of NAFLD.

Keywords: NAFLD, Gut liver axis, Liver function, Probiotics
**PE-153**

Dipeptidyl Peptidase-IV Inhibitors and Antioxidant Properties of Alkaloids Rich Fraction of Withania Somnifera Improve Liver Dysfunction in Type 2 Diabetic Mellitus  

Anand Krishna  
Devi Ahilya University, Indore, India

**Aims:** A novel approach in the treatment of T2DM, based on incretin hormone which regulated by Dipeptidyl peptidase-IV (DPP-IV). Dipeptidyl peptidase-IV inhibitor (DPP-IV) of Withania somnifera (WS) might have pleiotropic effect due to DPP-IV receptor present on various tissues, including liver. We examined whether DPP-IV inhibitors effect on non-alcoholic fatty liver function in Type 2 Diabetic Mellitus (T2DM) along with antioxidant properties in rat model.

**Methods:** T2DM model was induced in wistar rats with high sucrose diet along with dexamethasone. Biochemical, toxicology and histology variable were evaluated between all the groups, apart from serum DPP-IV inhibition, Insuline, Hba1c, histology of liver tissue were examine. In ex-vivo, hepatic lipid peroxidation, erythrocytes haemolysis was performed.

**Results:** After administration of alkaloids rich fraction of WS, there was a DPP-IV inhibition activity increase in WS (71.39%), as compared to Sitaglinpt (91.16%) with significant reduction in levels of glucose, Insulin, Hba1c, TC, TG. DPP-IV inhibitors also reduced the level of aminotransferases i.e SGOT & SGPT and alkaline phosphatase with improvement of liver tissue histology. WS plant extract have showed better antioxidant capacity to protect lipid peroxidation and reduced erythrocytes haemolysis of RBC.

**Conclusions:** DPP-IV inhibitors improve insulin, Hba1c sensitivity and help to improve the liver dysfunction in T2DM.

**Keywords:** Dipeptidyl peptidase-IV, Lipid peroxidation, Aminotransferases, Diabetic mellitus

**PE-154**

Probiotics Affect Adipose Tissue to Reduce NAFLD  

Dae Hee Han, Gi Soo Youn, Min Jea Shin, Haripriya Gupta, Sang Jun Yoon, Na Young Lee, Dong Joon Kim, Ki Tae Suk  
Department of Internal Medicine, Hallym University Medical Center, Chuncheon, Korea

**Aims:** Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases, comprises a spectrum of diseases ranging from simple steatosis to non-alcoholic steatohepatitis, fibrosis, and cirrhosis. Currently, there are no Food and Drug Administration–approved therapies for NAFLD. Although the molecular mechanisms of probiotics have not been completely elucidated yet, has been shown to be beneficial in NAFLD by the regulation of intestinal microorganisms. The aim of this study is to find how probiotics affect NAFLD.

**Methods:** Six-week male C57BL/6J mice were used in this study. Mice were randomly assigned to normal diet, Western-diet, and 4 Western diet+probiotics groups (n = 10/group). Used probiotics strains are Lactobacillus bulgaricus, L. casei, L. helveticus, Pediococcus pentosaceus KID7. Liver/body weight ratio, and histologic findings (hepatitis and steatosis score) were analyzed. Measurement of serum liver enzyme (ALT, AST), cholesterol, and adipokines. Western blotting, Quantitative real-time PCR and Gut microbiota metagenome were analyzed.

**Results:** In the analysis of liver/body weight ratio, L. bulgaricus (5.1 ± 0.5, P < 0.001), L. casei (5.7 ± 1.0, P < 0.1), L. helveticus (5.2 ± 0.4, P < 0.001), P. KID7 (5.5 ± 0.5, P = 0.009) groups showed significant improvement compared with that of Western group (6.2 ± 0.6). In comparison of histology (hepatitis score/steatosis score), L. bulgaricus (0.7 ± 0.7/0.7 ± 0.7, P < 0.001), L. casei (1.8 ± 0.4/2.1 ± 0.6, P < 0.001), L. helveticus (1.3 ± 0.5/1.7 ± 0.7, P < 0.001) and P. KID7 (1.3 ± 0.5/1.4 ± 0.5, P < 0.001) revealed significant improvement compared with that of Western group (3.1 ± 0.3/2.0 ± 0.0). All strains were effective in improvement of liver enzyme (AST or ALT, P < 0.05), except L. casei, significantly reduced the level of cholesterol (P < 0.05). The expression of RBP4 by western blot was shown that decreased in L. bulgaricus, L. casei, L. helveticus and P. KID7 as compared with western diets. Also it was confirmed by q-PCR that the expression of mRNA was significantly reduced. Levels of TNF-α, IL6 and IL1β were measured by ELISA in serum and all of them were significantly decreased compared with western diet. Gut microbiome analysis revealed that 8 weeks of western diet resulted in enrichment of Firmicutes and Proteobacteriarm Verrucomicrobia in the intestinal microbial community structure at the phylum level and a significant decrease in Bacteroidetes.

**Conclusions:** We found that probiotics affected intestinal microbial composition and decreased cytokines expressed in adipocytes. Restoration of intestinal microbial composition by probiotics lowers the expression of leptin and RBP4 from adipocytes, which lowers hepatitis by lowering the expression of hepatic cytokines.

**Keywords:** NAFLD, RBP4, Probiotics, Microbiome

**PE-155**

The Effect of Orange Water Kefir on Malondialdehyde Level in Liver Tissue of the Hyperlipidemic Rat  

Mochamad Affudin1, Rafik Prabowo1, Miranti Dewi Praman-
Aims: The liver is an organ that plays an important role in various metabolic processes, including lipid metabolism. The accumulation of excess lipids in liver tissue can increase the level of reactive oxygen species (ROS). It can increase lipid peroxidation that marked by malondialdehyde (MDA) levels in the liver tissue. If this compilation occurs continuously, it will increase the risk of non alcoholic liver disease. The previous research shown water kefir and orange, each has been proven to reduce the MDA level. The aim of this research was to determine the effect of orange water kefir intervention on MDA level in liver tissue of hyperlipidemic rat.

Methods: This study used experimental method with post test only control group design. The sample of this study were 15 male rat (Rattus norvegicus) aged 2-3 months and weight 180-250 grams. All groups were acclimatized for one week and fed ad libitum for 8 weeks. Group II and III were given quail egg yolk with dose 5 ml/200 grams of body weight for 4 weeks. For the next 4 weeks, group III was given the orange water kefir with dose of 5 ml/200 grams of body weight. All the intervention were given by the sonde method. Orange water kefir was made in accordance with good manufacturing product (GMP) standards and the procedure to making water kefir. At the end of the study, rats were terminated and the liver organ were examined for MDA level.

Results: Mean of MDA level on each group consecutively were 2.514 ± 0.12268 nmol/dl, 11.8 ± 0.17 nmol/dl, and 4.562 ± 0.12 nmol/dl. The Statistical Analysis with Oneway ANOVA showed significant differences in MDA level between three groups with P = 0.00. While, Bonferroni post-hoc test showed significant comparison between these groups with P = 0.00.

Conclusions: The intervention of orange water kefir was significantly reduce the MDA level of hyperlipidemic rats (P < 0.001).

Keywords: Hyperlipidemia, Malondialdehyde, Orange, Water kefir
from date palm and kefir milk on lipid fraction area of liver tissue \((P > 0.05)\).

**Conclusions:** There was no significant difference of lipid fraction area of liver tissue in the hyperlipidemic rat model after intervention with probiotic beverage consist of date palm and kefir milk.

**Keywords:** Hyperlipidemia, Fatty liver, Lipid fraction area, Kefir milk, Date palm

### PE-157

**EWSR1, a Potential Therapeutic Target in Non-Alcoholic Fatty Liver Disease**

Gil Won Lee¹, Wonhee Hur¹, Sung Min Kim¹, Dong Jun Park¹, Byung-Yoon Kang¹, Jaegyoon Ahn², Sean Bong Lee³, and Seung Kew Yoon⁴

¹The Catholic University Liver Research Center & WHO Collaborating Center of Viral Hepatitis, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; ²Department of Computer Science and Engineering, Incheon National University, Incheon, Republic of Korea; ³Department of Pathology and Laboratory Medicine, Tulane University School of Medicine, New Orleans, LA, USA

**Aims:** Non-alcoholic fatty liver disease (NAFLD) caused by an accumulation of lipid in the liver is a very common chronic disease worldwide. Although considerable progress has been made recently in illuminating the pathogenesis of NAFLD, it remains unclear which mechanisms are associated with the progression of NAFLD. Previous studies have shown that Ewing sarcoma breakpoint region 1 (EWSR1) is an RNA binding protein involved in transcription and splicing, in maintaining mitochondria homeostasis. This study investigated the potential roles of EWSR1 in the progression of NAFLD.

**Methods:** Expression of EWSR1 was analyzed in the liver of NAFLD-induced mice fed with high-fat diet (HFD). Immunofluorescence assay was used to detect lipid accumulation in Oleic acid (OA)-induced mouse embryonic fibroblast (MEF) EWSR1 knock out cell. cDNA microarray analysis of EWSR1 knock out (KO) mouse liver identified genes in lipid biosynthetic and growth control pathways.

**Results:** The EWSR1 expression was increased in HFD-induced NAFLD mice compared with normal diet mice. Lipid accumulation was increased OA-induced EWSR1 KO MEF cell than MEF cell. Microarray expression profiling revealed specific genes, which are mostly involved in fatty acid β-oxidation, glucose and insulin sensitivity were differentially expressed in the liver of EWSR1 KO mice. These results demonstrated, for the first time, that attenuated oxidation-reduction and fatty acid β-oxidation in steatotic liver is associated with an impaired biological activity of EWSR1.

**Conclusions:** These results suggest that EWSR1 expression may act as a key regulator for controlling such things as lipid metabolism in NAFLD, as well as may overcome limitations by improving problems with existing research and development treatments about NAFLD. Further Investigation of the role of EWSR1 in NAFLD pathogenic procession is underway in EWSR1 deficient mice fed HFD.

Supported by grants of the Basic Science Research Program through NRF, NO. 2016R1D1A1B03931395 and BK21.

**Keywords:** Non-alcoholic fatty liver disease, Ewing sarcoma breakpoint region 1, Insulin metabolism, Lipid metabolism

### PE-158

**CJ-14199, a Novel Ileal Bile Acid Transporter Inhibitor for Non-Alcoholic Steatohepatitis**

Jin Woo Jung¹, Hyungjin Jun¹, Dong-Hyun Kim¹, Keun-Ho Lee¹, Byoung Soo Kim¹, Dong-Kyu Kim¹, Soo-Jin Kim¹, Byoung-Seok Moon¹, Shin-Young Ryu¹

¹R&D Center, CJ HealthCare Corporation; ²Molecular Imaging Research Center, Korea Institute of Radiological & Medical Sciences, Korea

**Aims:** In the present study, we demonstrate the in vitro and in vivo pharmacological properties of CJ-14199 and the efficacy of CJ-14199 in mouse NASH models.

**Methods:** In vitro \[^{14}C\]taurocholate uptake inhibition assay was performed using hIBAT- or hLBAT (Liver BAT) overexpressing cell lines. In vivo pharmacological properties of CJ-14199 were determined by measuring fecal bile acid and plasma C4 in normal ICR mice. In vivo efficacy of CJ-14199 was evaluated by...
NAS (Non-alcoholic fatty liver disease Activity Score) and fibrosis area in mouse NASH models. Quantitative whole-body autoradiography (QWBA), absolute bioavailability, and fecal recovery studies were performed in rats using $^{14}$C-CJ-14199.

Results: CJ-14199 inhibited the $^{14}$C-taurocholate uptake in IBAT- or LBAT-overexpressing cells with IC$_{50}$ of 1.83 and 7200 nM, respectively, suggesting ~4000 fold selectivity for IBAT over LBAT. In normal ICR mice, oral administration of CJ-14199 caused an increase of fecal bile acid in a dose-dependent manner, with the increase of plasma C4. In mouse NASH models, CJ-14199 induced significant reduction in NAS and prevented progression of fibrosis. From the QWBA, absolute bioavailability, and fecal recovery studies using $^{14}$C-CJ-14199, CJ-14199 exhibited optimal pharmacokinetics properties as a minimally absorbed locally acting gastrointestinal drugs.

Conclusions: CJ-14199 is a highly selective IBAT inhibitor with the characteristics of locally acting gastrointestinal drugs. The robust efficacy in NASH animal models suggests that CJ-14199 has the potential as a new NASH therapeutics.

Keywords: Non-alcoholic steatohepatitis, NASH, Ileal bile acid transporter inhibitor, IBAT, CJ-14199

---

**Comparison of the Efficacy of Ursodeoxycholic Acid (UDCA) versus Vitamin E plus Vitamin C in Non-Diabetic Patients with Nonalcoholic Steatohepatitis (NASH)**

Tatia Khachide$^{1,2}$, Gocha Barbakadze$^{1,2}$, Manana Jebashvili$^1$, Gela Sulaberidze$^1$, Koba Burnadze$^2$

$^1$Tbilisi State Medical University, Tbilisi, Georgia; $^2$Enmedic Clinic, Tbilisi, Georgia

Aims: Nonalcoholic steatohepatitis (NASH) is a frequent liver disease that can progress to cirrhosis and for which effective therapy is still lacking. Despite an important role of oxidative stress in the pathogenesis of NASH, antioxidant approaches have not been investigated sufficiently. The aim of the study was to compare ursodeoxycholic acid (UDCA) versus vitamin E plus vitamin C in non-diabetic patients with nonalcoholic steatohepatitis.

Methods: Patients with elevated aminotransferase levels and drinking, less than 40g alcohol/week with NASH diagnosis were randomly assigned to receive either UDCA 15 mg/per kg/day (group A) or vitamin E 800 mg/day plus vitamin C 500 mg/day (group B) for 12 months and control group, which did not receive any medical treatment. Lifestyle modification was advised to all groups. The primary study end point was improvement in aminotransaminase levels, secondary end points were improvement in steatosis score and improvement in fibrosis score.

Results: 107 patients were included 35 in the group A, 52 in the group B and 20 in control group, 11 patients dropped out, non because of side effects. Baseline characteristics were not significantly different between groups. After 12 months treatment with vitamin E plus C, as compared with UDCA, was associated with a significant reduction of mean alanine aminotransferase (ALT) levels. Similarly, there was significant reduction of both mean steatosis score and fibrosis score.

Conclusions: Vitamin E plus C combination is an effective, safe and inexpensive treatment option in patients with NASH and may be useful to reduce damage from oxidative stress and slow the process leading to cirrhosis.

Keywords: Nonalcoholic fatty liver disease, Nonalcoholic steatohepatitis, Ursodeoxycholic acid, Vitamin E

---

**Study of Biochemical and Oxidative Stress Markers in the First-Degree Relatives of Persons with Type 2 Diabetes Stratified by Glucose Tolerance Test**

Dhananjay Yadav$^{1,2}$, Meeraambika Mishra$^3$, Seema Rana$^4$, GBKS Prasad$^2$

$^1$Department of Medical Biotechnology, Yeungnam University, Gyeonggan, Republic of Korea; $^2$School of Studies in Biochemistry, Jiwaji University, Gwalior, India; $^3$School of Life Sciences, Sambalpur University, Jyoti Vihar, Burla, Odisha, India; $^4$Department of Home Science, Govt. KRG PG Autonomous College, Gwalior, Madhya Pradesh, India

Aims: The present study has been attempted to compare the relative tolerance to glucose in first-degree relatives of type 2 diabetic patients and estimate the anthropometric, biochemical parameters and markers of oxidative stress in subjects with the different degree of glucose tolerance.

Methods: The study consisted of 34 subjects aged between 20-45 years, with established family history of type 2 diabetes mellitus, who were subjected to oral glucose tolerance test (OGTT). Those without any family history of diabetes served as controls.

Results: Out of the 34 subjects, 5 subjects exhibited high toler-
Association with Low Psoas Muscle Area and Non-Alcoholic Fatty Liver Disease in Patients with Inflammatory Bowel Disease

Min Kyu Kang, Jung Gil Park, Kyeong Ok Kim, Byung Ik Jang
Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Korea

Aims: Recently, decreased muscle mass has been proposed as an additional risk factor in patients with non-alcoholic fatty liver disease (NAFLD), which have been no studies in patients with inflammatory bowel disease (IBD). We aimed to analyze the clinical associations between low muscle mass and NAFLD, independently other risk factors of NAFLD in IBD patients.

Methods: From January 2004 to December 2017, a total 488 IBD patients with the result of computed tomography (CT) were included, which were classified into two groups according to the presence of NAFLD. The volume of muscle was calculated by area of total psoas muscle in third lumbar region on CT per patient’s height$^4$ (m$^2$). Low psoas muscle area (LPMA) was defined as the cases in which the volume of muscle less than 545 mm$^2$/m$^2$ in men and less than 385 mm$^2$/m$^2$ in women.

Results: NAFLD was diagnosed in 49 patients (11.1%) from final 443 IBD patients. Patients in NAFLD group were older (45.1 vs. 38.6 years; $P = 0.006$), had higher level of body mass index (23.0 ± 2.7 vs. 20.8 ± 3.3 kg/m$^2$; $P < 0.001$), more metabolic syndrome (36.7% vs 7.4%; $P < 0.001$), and had higher proportions of LPMA (51.0% vs. 33.0%; $P = 0.019$) than those in non-NAFLD group. In the multivariate analysis, metabolic syndrome (Odds ratio [OR]: 8.633), hyperuricemia (OR: 4.662), small bowel resection (OR: 3.453), and the presence of LPMA (OR: 2.994) were significant risk factors of NAFLD in IBD patients. LPMA was an independent risk factor for NAFLD in patients with IBD, which is adjusted by age, gender, traditional metabolic risk factors, disease severity of IBD, and medication.

Conclusions: LPMA is associated with NAFLD in patients with IBD, independent of metabolic risk factors.

Keywords: Non-alcoholic fatty liver disease, Inflammatory bowel disease, Psoas muscle, Computed tomography

Nonalcoholic Fatty Liver Disease and Sarcopenia Are Independently Associated with Cardiovascular Risk

Eugene Han$^1$, Yong-ho Lee$^2$, Young Dae Kim$^1$, Beom Kyung Kim$^2$, Jun Yong Park$^3$, Do Young Kim$^4$, Sang Hoon Ahn$^5$, Byung-Wan Lee$^6$, Eun Seok Kang$^1$, Bong-Soi Cha$^1$, Kwang-Hyub Han$^1$, Hyo Suk Nam$^4$, Ji Hoe Heo$^1$, and Seung Up Kim$^1$

$^1$Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea; $^2$Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; $^3$Institute of Endocrine Research, Yonsei University College of Medicine, Seoul, Korea; $^4$Department of Neurology, Yonsei University College of Medicine, Seoul, Korea; $^5$Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; $^6$Yonsei Liver Center, Severance Hospital, Seoul, Korea

Aims: Non-alcoholic fatty liver disease (NAFLD) and sarcopenia have a close association with the increased atherosclerotic cardiovascular disease (ASCVD) risks. This study investigated the interactive influence of NAFLD and sarcopenia on ASCVD risks.

Methods: Data from the Korean National Health and Nutrition Examination Surveys 2008–2011 database were analyzed. The sarcopenia index was calculated using dual-energy x-ray absorptiometry. Sarcopenia was defined as the lowest quintile sarcopenia index value (cutoffs: 0.882 for men and 0.582 for women). NAFLD was defined as comprehensive NAFLD score (CNS) >40. Liver fibrosis was assessed using NAFLD fibrosis score (NFS). ASCVD risk was evaluated using ACC/AHA guidelines. ASCVD risk >10% was defined as having a high-risk.

Results: Prevalence of NAFLD and sarcopenia and 31.2% (2,241 of 7,191) and 19.5% (1,400 of 7,191), respectively. The quartile-stratified ASCVD risk scores showed a significant positive association with NAFLD and sarcopenia (all $P$ for trend<0.001). The subjects with both NAFLD and sarcopenia had a higher risk of high-probability in ASCVD risk (odds ratio [OR] = 1.83, $P = 0.014$). They also had a similar trend for high-probability in ASCVD risk (OR = 3.21, $P = 0.004$).

Conclusions: NAFLD and sarcopenia are significantly associated with the increased risk of ASCVD in general population. In addition, NAFLD with liver fibrosis and sarcopenia are significantly associated with the increased risk of ASCVD in subjects with NAFLD.

Keywords: Nonalcoholic fatty liver disease, Sarcopenia, Cardiovascular, Fatty liver
Sarcopenia Is Independently Associated with the Degree of Liver Fibrosis in Patients with Type 2 Diabetes Mellitus

Min Je Sung1, Tae Seop Lim1,2, Mi Young Jeon1,2, Hye Won Lee1,2, Beom Kyung Kim1,3, Do Young Kim1,3, Sang Hoon Ahn1,3, Kwang-Hyun Han1,3, Jun Yong Park1,3, and Seung Up Kim1,3

1Department of Internal Medicine, 2Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 3Yonsei Liver Center, Severance Hospital, Seoul, Korea

Aims: Sarcopenia is significantly associated with degree of liver fibrosis in patients with chronic liver diseases including non-alcoholic fatty liver disease and chronic hepatitis B. We investigated the association between sarcopenia and fibrotic burden in liver in patients with type 2 diabetes mellitus (T2DM).

Methods: Patients with T2DM who received comprehensive medical health check-up between 2010 and 2018 were recruited. Muscle mass was assessed by computed tomography (CT) analysis at the 3rd lumbar vertebra. Fibrotic burden was assessed using fibrosis-4 index (FIB-4). The study population was divided according to quartile stratification of lumbar skeletal muscle index (LSMI) (Q1 to Q4) and patients with lowest quartile (Q1) were considered as having sarcopenia.

Results: In total, 309 patients with T2DM were recruited. Of these, 75 (24.3%) had sarcopenia. Sarcopenic patients were significantly older and had higher FIB-4 and prothrombin time, whereas they had significantly lower alanine aminotransferase, lower body mass index (BMI), and lower LSMI than those of non-sarcopenic patients (all P < 0.05). LSMI and FIB-4 by quartile stratification were significantly correlated (P = 0.003).

BMI and FIB-4 were significantly associated with sarcopenia in univariate analysis (all P < 0.05) and subsequent multivariate analysis found that higher BMI was independently associated with the reduced risk of sarcopenia (odds ratio [OR] = 0.738, 95% confidence interval [CI], 0.654-0.833, P < 0.001), whereas higher FIB-4 was independently associated with the increased risk of sarcopenia (OR = 1.778, 95% CI, 1.154-2.716, P = 0.008). Among the patients with BMI< 25 kg/m^2 (n = 165), sarcopenic patients (n = 54, 32.7%) had significantly higher FIB-4 than that of non-sarcopenic patients (n = 111, 67.3%) (1.66 vs. 1.38, P = 0.004).

Conclusions: Sarcopenia is independently associated with fibrotic burden in patients with T2DM, regardless of BMI. Further studies are required to determine whether interventions to improve muscle mass in this population with T2DM can regress fibrotic burden in liver.

Keywords: Sarcopenia, Liver fibrosis, Chronic liver disease, Muscle mass

Lean Nonalcoholic Fatty Liver Disease and Development of Diabetes Mellitus: A Cohort Study

Dong Hyun Sinn1, Joo Hyun Oh1, Danhee Kang2, Soo Jin Cho3, Seung Woon Paik1, Eliseo Guallar4,5, Juhee Cho2,4,5, Geum-Youn Gwak1

1Department of Medicine, 2Department of Clinical Research Design and Evaluation, SAIHST, 3Center for Health Promotion, 4Center for Clinical Epidemiology, Samsung Medical Center, Sungkyunkwan University, 5Departments of Epidemiology and Medicine and Welch Center for Prevention, Johns Hopkins Medical Institutions, Baltimore, USA

Aims: Body mass index (BMI) is an indicator of metabolic health, but nonalcoholic fatty liver disease (NAFLD), a condition associated with metabolic derangement, is observed in lean individuals. To date, metabolic consequence of lean NAFLD has not been well characterized.

Methods: A total of 51,931 adult men and women without diabetes mellitus (DM), history of liver disease or cancer at baseline who participated in a regular health screening exam between March 2003 and December 2013 were analyzed for incident DM during follow-up. The risk of incident DM for lean participants with NAFLD, overweight/obese participants without NAFLD and overweight/obese participants with NAFLD was compared to lean participants without NAFLD. Fatty liver was diagnosed by ultrasonography, and NAFLD severity was assessed by the NAFLD fibrosis score (NFS).

Results: During 236,446.6 person-years of follow-up (median follow-up of 4.0 years), 5,370 participants developed DM. In fully-adjusted model, the hazard ratios (HRs) were 1.18 (95% CI = 1.03, 1.35), 1.06 (95% CI = 0.98, 1.14), and 1.45 (95% CI = 1.34, 1.57) for lean participants with NAFLD, overweight/obese particip-
Routine Availability of Noninvasive Tests Discriminate Advanced Fibrosis Due to NASH in the Phase 3 STELLAR Trials of the ASK1 Inhibitor Selonsertib

Vincent Wai-Sung Wong1, Quentin M. Anstee1, Eric J. Lawitz2, Naim Alkhouri3, Manuel Romero-Gomez4, Takeshi Okanoue5, Michael Trauner5, Kathryn Kersey6, Georgia Li7, G. Mani Subramanian8, Robert P. Myers9, C. Stephen Djeu9, Ling Han10, Yao Li10, Tuan Nguyen11, Anita Kohli12, Natalie Bzowej13, Ziad Younes14, Shiv Sarin15, Mitchell L. Shiffman16, Stephen A. Harrison17, Zachary Goodman18, Zobair M. Younossi19, Sooji Lee20

1Department of Medicine and Therapeutics, The Chinese Hospital of Hong Kong, Hong Kong; 2Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK; 3Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA; 4Department of Medicine and Therapeutics, The Chinese Hospital of Hong Kong, Hong Kong; 5Hospital Universitario Virgen del Rocio, Sevilla, Spain; 6Saiseikai Saita Hospital, Saita City, Osaka, Japan; 7Division of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria; 8Gilead Sciences, Inc, Foster City, CA, USA; 9The Institute for Liver Health, Chandler, AZ, USA; 10Ochsner Medical Center, New Orleans, LA, USA; 11Gastro One, Germantown, TN, USA; 12Institute of Liver and Biliary Sciences, New Delhi, Delhi, India; 13Bon Secours Liver Institute of Virginia, Richmond, Virginia, USA; 14Pinnacle Clinical Research, San Antonio, TX, USA; 15Inova Fairfax Hospital, Falls Church, VA, USA

Aims: Liver biopsy is currently the reference standard for fibrosis staging, but is an invasive procedure with limitations. There is a major unmet need for accurate, readily available noninvasive tests (NITs) to identify patients with advanced fibrosis due to NASH. Our aim is to describe the performance of NITs using the baseline data from the Phase 3 STELLAR studies of the ASK1 inhibitor selonsertib (SEL).

Methods: The STELLAR studies (NCT03053050 and NCT03053063) enrolled patients with bridging fibrosis (F3) or compensated cirrhosis (F4) due to NASH (NAFLD Activity Score [NAS] ≥3). Baseline liver biopsies were centrally read according to the NASH CRN fibrosis classification and noninvasive markers of fibrosis, including the NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4) index, Enhanced Liver Fibrosis (ELF) test, and liver stiffness (LS) by transient elastography (TE; FibroScan®) were measured. The performance of these tests to discriminate advanced (F3-F4) fibrosis was evaluated using AUROCs with 5-fold cross-validation repeated 100x. Optimal thresholds for F3-F4 fibrosis were selected based on the literature. Data presented are from an interim analysis on 1 May 2018.

Results: A total of 4467 patients (median age 58 years, 55% women, 72% Caucasian, 59% with diabetes) were screened. In the 3220 with evaluable histology, median biopsy length was 2.0 cm, 8% F0, 9% F1, 13% F2, 31% F3, 40% F4, 59% with NAS ≥5. Median values of NFS, FIB-4, ELF, and LS by TE increased with worsening fibrosis (-0.962/1.9/9.21/8.8 kPa in F0-F2 vs 0.342/20.10/16.5 kPa in F3-F4 respectively). AUROCs ranged from 0.75 to 0.80 to discriminate advanced fibrosis (Table). When tests were combined, performance characteristics improved and PPVs ≥98% were possible.

Conclusions: In these large, global phase 3 trials of SEL, routinely available NITs demonstrated acceptable diagnostic performance for the discrimination of advanced fibrosis due to NASH.

Keywords: NASH, Selonsertib, Gilead, Noninvasive test, STELLAR, ASK1 inhibitor, MAFLD

Clinical Utility and Application of Noninvasive Tests in Selecting Patients with Advanced Fibrosis Due to NASH in the Phase 2 ATLAS Trial


1Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong; 2University of California San Diego, La Jolla, CA, USA; 3Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA; 4University of Sydney, Sydney, NSW, AUS; 5Gilead Sciences, Inc, Foster City, CA, USA; 6Inova Fairfax Hospital, Falls Church, VA, USA; 7GI Specialists of Georgia, Marietta, GA, USA; 8Florida Research Institute, Lakewood Ranch, FL, USA; 9Delta Research Partners, Bastrop, LA, USA; 10Pinnacle Clinical Research, Austin, TX, USA; 11Swedish Medical Center, Seattle, WA, USA

Aims: Liver biopsy is a barrier to clinical trial enrollment in NASH. We describe the utility of noninvasive tests (NITs) to en-
roll patients with advanced fibrosis (F3-F4) due to NASH.

Methods: The ATLAS study (NCT03449446) enrolled patients based on: 1) a biopsy showing F3-F4 fibrosis per the NASH CRN classification (the biopsy cohort); or 2) in the absence of a prior biopsy, an ELF test ≥9.8 and liver stiffness (LS) by transient elastography (TE; FibroScan) ≥14.0 kPa using the XL probe (the NIT cohort). Patients in the NIT cohort had baseline biopsies and were randomized regardless of results. Analyses are based on an interim data cut.

Results: Of the 645 screened patients with evaluable fibrosis stage (median age 59 years, 62% women, 61% with diabetes, median BMI 33.7 kg/m²), 395 were enrolled. Fifty-five (14%) qualified based on NIT criteria; F3-F4 fibrosis was confirmed in 87% (48/55) (4% F0, 4% F1, 5% F2, 22% F3, 65% F4). Patients in the biopsy cohort with F3-F4 fibrosis had demographics, liver biochemistry, and serum fibrosis markers similar to those in the NIT cohort, but with higher LS by TE (Table). The proportions of patients with NAS ≥4 (87% vs 86%) and cirrhosis (65% vs 53%; P = 0.09) did not differ between the NIT and biopsy cohorts. Within the NIT cohort, biopsy length was shorter in patients with F0-F2 vs F3-F4 (1.3 vs 2.2 cm; P = 0.18). Patients with F0-F2 fibrosis also had lower BMI (31.0 vs 34.4 kg/m²; P = 0.11), less diabetes (43% vs 75%), and less lobular inflammation and ballooning.

Table: Baseline Laboratory and Histological Features

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Serum Fasting</th>
<th>Biopsy Cohort F0-F2</th>
<th>NIT Cohort F0-F2</th>
<th>NIT Cohort F3-F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (U/L)</td>
<td>32</td>
<td>39</td>
<td>39</td>
<td>47</td>
</tr>
<tr>
<td>TLT (g/dL)</td>
<td>3.3</td>
<td>3.0</td>
<td>3.2</td>
<td>2.3</td>
</tr>
<tr>
<td>ELF (kPa)</td>
<td>6.9</td>
<td>10.8</td>
<td>10.1</td>
<td>10.6</td>
</tr>
<tr>
<td>LS by TE (kPa)</td>
<td>9.9</td>
<td>15.3</td>
<td>15.9</td>
<td>15.9</td>
</tr>
<tr>
<td>Lobular inflammation grade 2</td>
<td>22 (35%)</td>
<td>23 (45%)</td>
<td>3 (5%)</td>
<td>29 (83%)</td>
</tr>
<tr>
<td>Ballooning grade 2</td>
<td>20 (34%)</td>
<td>24 (41%)</td>
<td>4 (7%)</td>
<td>39 (13%)</td>
</tr>
</tbody>
</table>

Data are median or n (%)..

Conclusions: In this Phase 2 trial of patients with NASH, a combination of ELF and LS by TE identified the target population in 87% of patients. Enrollment based on NITs should be considered for future NASH studies to reduce reliance on biopsy.

Keywords: NASH, NAFLD, Noninvasive test, ATLAS trial, Fibrosis to all-cause, cardiovascular, and liver-related mortality. We aimed to investigate association between atrial fibrillation and advanced liver fibrosis in patients with NAFLD.

Methods: From January 2010 to December 2017, 6293 NAFLD patients aged 35 years and older were enrolled. All electrocardiograms were diagnosed after a review by a skilled cardiologist. The stage of liver fibrosis is assessed by new adjusted, non-invasive scoring model including NAFLD fibrosis score (NFS) and Fibrosis-4 (FIB-4) index, which was determined as the both low and high cut-off value (COV).

Results: Of 6293 patients with NAFLD, 59 (0.9%) were diagnosed with AF. The AF patients were older (52.0 vs. 64.6 years, P = 0.001), had higher BMI (25.2 vs. 26.6 kg/m², P = 0.001) and waist circumference (84.0 vs. 89.9 cm, P = 0.001) compared to non-AF patients. AF was an independent risk factor for advanced fibrosis, assessed by both COVs of NFS (adjusted for obesity, hypertension, high sensitivity C reactive protein, lipid profile, and sex, ORs = 2.48 to 3.38, P < 0.01 in the low-COV group, ORs = 10.79 to 14.55, P < 0.01 in the high-COV group, respectively. In addition, AF was an independent risk factor for advanced fibrosis, assessed by both COVs of FIB-4 (adjusted for obesity, hypertension, high sensitivity C reactive protein, lipid profile, and sex, ORs = 2.54 to 2.86, P < 0.01 in the low-COV group, ORs = 3.64 to 5.97, P < 0.05 in the high-COV group, respectively).

Conclusions: AF may be an independent risk factor for advanced liver fibrosis in patients with NAFLD.

Keywords: Atrial fibrillation, Advanced liver fibrosis, Non-alcoholic fatty liver disease

PE-168

Prevalence of Pre-Diabetes, Diabetes, Abdominal Obesity and Hypertension among the Service Communities of Bhilai City of India

Nutan Yadav¹, Deepak Kumar²

¹Dindayal Upadhyay University Gorakhpur, UP, India; ²Pt. Ravishankar Shulda University Raipur India

Aims: The main objective of this study was to estimate the prevalence of diabetes, pre-diabetes and obesity among service community of Bhilai city.

Methods: The subjects for the study were randomly selected and were belonging to service community. The study was carried out on about 500 subjects who voluntarily participated in the study. The prevalence of pre-diabetes, diabetes, and hypertension were determined by American diabetes association criteria and central obesity was measured by body mass index (BMI) which was calculated from height and weight of the subjects employing the standard formula.

Results: The present study revealed that the incidence of diabates among the employees of police community is about 10%. The incidence is significantly high among females as compared

PE-167

Atrial Fibrillation Is Associated with Advanced Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease

Min Kyu Kang, Jung Gil Park

Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Korea

Aims: Although non-alcoholic fatty liver disease (NAFLD) has been reported to be independently associated with increased incidence of atrial fibrillation (AF), the association of advanced liver fibrosis with AF in NAFLD patients has not been established. Advanced liver fibrosis in patients with NAFLD is related

June 20-22, 2019 | BEXCO, Busan, South Korea
Nonalcoholic Steatohepatitis Is Associated with a Higher Risk of Advanced Colorectal Neoplasm

Sungwoo Ryu, Jimin Han, Dong Hyeon Lee, Sae Kyung Joo, Yong Jin Jung, Byeong Gwan Kim, Won Kim

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul, Korea

Aims: Nonalcoholic fatty liver disease (NAFLD) is known to increase the risk of adenomatous colonic polyps. However, the role of screening colonoscopy in patients with biopsy-proven NAFLD in detecting advanced colorectal neoplasm is not clearly evidence-based. Therefore, we investigated whether the histological severity of NAFLD is associated with advanced colorectal neoplasm.

Methods: This study included patients ≥40 years old who underwent routine colonoscopy between 2013 and 2018 within a biopsy-evaluated prospective NAFLD cohort. Advanced colorectal neoplasm was defined as an adenomatous polyp greater than 10 mm in diameter and/or with villous histology and/or with high-grade dysplasia or adenocarcinoma.

Results: Among the 472 patients with biopsy-proven NAFLD who underwent colonoscopy, the prevalence of advanced colorectal neoplasm was 10.2% (n = 48). Patients with advanced colorectal neoplasm had a higher stage of hepatic fibrosis than those with a low-grade adenomatous polyp (P = .005). Multivariable logistic regression analysis revealed that the presence of histologically confirmed hepatic steatosis was an independent risk factor for adenomatous colorectal polyp (odds ratio [OR], 3.89; 95% confidential interval [CI], 1.41–10.7; P = .009) and the presence of nonalcoholic steatohepatitis (NASH) was an independent risk factor for advanced colorectal neoplasm (OR, 9.33; 95% CI, 1.14–76.3; P = .037).

Conclusions: The presence of biopsy-proven NASH was significantly associated with an increased risk of advanced colorectal neoplasm among patients with NAFLD. This finding may alert physicians to conduct screening colonoscopy in patients with NASH to detect advanced colorectal neoplasm early.

Keywords: Nonalcoholic fatty liver disease, Nonalcoholic steatohepatitis, Advanced colorectal neoplasm, Fibrosis, Hepatocellular ballooning
The Liver Week 2019

The Liver Week 2019

A decline in kidney function. It suggests that significant and sustained weight loss may improve long-term kidney outcomes in patients with NAFLD.

Keywords: Chronic kidney disease, Non-alcoholic fatty liver disease, Weight reduction, Non-alcoholic steatohepatitis

PE-171

The Invasive and Noninvasive Assessments for Liver Fibrosis in Korean Nonalcoholic Fatty Liver Disease Patients

So Yeon Kim1, Sang Young Han1, Sang Yi Moon1, Yang-Hyun Baek1, Sung Wook Lee2, and Jin Sook Jeong3

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Hu Hospital, Busan, Republic of Korea; 1Division of Gastroenterology and Hepatology, Department of Internal Medicine, On Hospital, Busan, Republic of Korea; 2Division of Gastroenterology and Hepatology, Department of Internal Medicine, Dong-A University Hospital, Busan, Republic of Korea; 3Department of Pathology, Dong-A University Hospital, Busan, Republic of Korea

Aims: The only way to definitively confirm nonalcoholic steatohepatitis (NASH) is a liver biopsy. However, due to its invasive nature, the noninvasive tests have been developed. The prevalence of nonalcoholic fatty liver disease (NAFLD) is a median of 20% in the Korean population and NAFLD has become an important public health issue in Korea. However, there were few studies related to diagnosis of NASH on Korean NAFLD patients in previous studies.

Methods: We prospectively analyzed a total of 59 patients (mean age: 48 ± 14 years, female: 28) with NAFLD who performed liver biopsy at Dong-A university hospital from November, 2017 to January, 2019. Clinical characteristics, the results of liver biopsy and noninvasive testing, such as AST to platelet ratio index (APRI), fibrosis-4 (FIB-4) index and NAFLD fibrosis score were recorded. We divided patients into 2 groups (steatosis group and steatohepatitis group). Metabolic parameters of 2 groups were analyzed.

Results: The number of steatohepatitis diagnosed by liver biopsy is 40 (68%) and the number of liver fibrosis patients diagnosed by APRI, FIB-4 index and NAFLD fibrosis score is 29 (49%), 20 (34%) and 32 (54%), respectively. The AUROC curves of APRI, FIB-4 index and NAFLD score were 0.849 (95% Confidence interval [CI] : 0.740-0.957), 0.695 (95% CI : 0.545-0.762) and 0.515 (95% CI : 0.365-0.665), respectively. Steatohepatitis group (16 patients) showed high insulin resistance (70% vs 38%, P=0.024), metabolic syndrome (75% vs. 38%, P=0.008), central obesity (93% vs. 25%, P<0.001) and fasting glucose level (65% vs. 31%, P=0.022), compared to steatosis group (40 patients).

Conclusions: We cautiously consider to do liver biopsy or noninvasive assessment for liver fibrosis in NAFLD patients with metabolic syndrome, obesity or diabetes mellitus, even if nonalcoholic fatty liver diagnosed by ultrasound.

Keywords: Steatohepatitis, NAFLD, Liver fibrosis, Liver biopsy

PE-172

The Grade of Nonalcoholic Fatty Liver Disease Is an Independent Risk Factor for Gallstone Disease

Young-Kyu Kim, Kyu Hee Her

Department of Surgery, Jeju National University Hospital, Republic of Korea

Aims: There are some reports about association between nonalcoholic fatty liver disease (NAFLD) and gallstone disease (GD) because of sharing risk factors. However, there is no report about an association between grades of NAFLD and GD. Therefore, the aim of this study was to know whether grade of NAFLD could be an independent risk factor affecting GD in a Korean population.

Methods: This study enrolled a total of 7,886 subjects who completed a questionnaire and underwent ultrasound and medical checkup at the Health Promotion Center of Jeju National University Hospital in Korea from January 2009 to December 2017. Grade of fatty liver and presence of gallstones were investigated by abdominal ultrasound. The body Mass index, biochemical parameters were checked, and age, metabolic syndrome and sex were collected based on their medical records. Univariate and multivariate analyses were performed to identify risk factors affecting GD.

Results: The estimated prevalence of NAFLD and GD were 40.5% and 4.5% respectively. In the univariate analysis, risk factors affecting GD were the age, NAFLD, metabolic syndrome and fasting glucose level. In the multivariate analysis, NAFLD (OR: 1.43, 95% CI: 1.20-1.70), metabolic syndrome (OR: 1.38, 95% CI: 1.18-1.61) and fasting glucose level (OR: 1.20, 95% CI: 1.04-1.40) were independent risk factors affecting GD.

Keywords: Steatohepatitis, NAFLD, Liver fibrosis, Liver biopsy
ol, aspartate aminotransferase, alanine aminotransferase. In the multivariate logistic regression analysis, independent risk factors were older age and higher grade of NAFLD.

Conclusions: Older age and higher grade of NAFLD are independent risk factors affecting GD. There is a strong correlation between grade of NAFLD on abdominal ultrasonography and GD.

**PE-173**

**Appropriateness of Liver Biopsy for Nonalcoholic Fatty Liver Disease during Laparoscopic Cholecystectomy for Gallstone Disease**

Kyung Sik Kim1, Sang-Hyub Han1, Ji Hae Nahm2, Do Young Kim1, Seung Woo Park3, Young Nyun Park4

1Department of Hepatobiliary and Pancreatic Surgery, 2Department of Pathology, 3Department of Internal medicine, Severance Hospital, Yonsei University College of Medicine, 4Department of Surgery, Armed Forces Capital hospital, Republic of Korea

**Aims:** Obesity is well known as a risk factor for gallstone disease and is also a risk factor for fatty liver. Although, liver biopsy is particularly useful in patients without definite clinical manifestations, liver biopsy is invasive and is not recommended except in special case. However, hepatic biopsy is not a relatively risky procedure during laparoscopic cholecystectomy. Therefore, we investigated the clinical characteristics in biopsy proven non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in gallstone disease patients during laparoscopic cholecystectomy for gallstone disease.

**Methods:** We retrospectively reviewed 288 medical records with gallstone disease who underwent laparoscopic cholecystectomy with liver biopsy from 2006 to 2017 and biopsy involved the fatty liver. A univariate and multivariate logistic regression were performed to evaluate the association between clinical factors and fatty liver.

**Results:** Ninety-six (33.3%) patients were diagnosed as fatty liver. Mean BMI of the patients was 24.5 kg/m² (24.1-25.0). In univariate analysis, 6 clinical factors involved the fatty liver. BMI, Hb, ALP, AST, DM, and Liver disease. However, 4 clinical factors were involved in the multivariate logistic regression model. (BMI: OR = 1.210 (1.111-1.318), P < 0.001; ALP: OR = 0.991 (0.984-0.998), P = 0.018; DM: OR = 2.618 (1.135-6.204), P = 0.024; and Liver disease: OR = 2.193 (1.667-3.049), P < 0.001). The liver biopsy could be recommended in high BMI patients with DM or Liver diseases.

**PE-174**

**Risk Factors for Incident Nonalcoholic Fatty Liver Disease and Liver Fibrosis in Breast Cancer Survivors**

Hwi Young Kim1, Woosung Lim2, Byung-In Moon2, Hye Ah Lee3

1Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Republic of Korea; 2Department of Surgery, College of Medicine, Ewha Womans University, Seoul, Republic of Korea;
3Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; 4Clinical Trial Center, Ewha Womans University Mokdong Hospital, Seoul, Republic of Korea

**Aims:** Data on nonalcoholic fatty liver disease (NAFLD) in patients with breast cancer are scarce. We aimed to investigate clinical features and risk factors of NAFLD in breast cancer survivors.

**Methods:** In this prospective, single-center cohort study, we started screening breast cancer patients from August 2018, who had been followed after appropriate anticancer treatments including surgery, radiotherapy, and chemotherapy in the Cancer Center for Women in our institution. Patients in remission (defined as ‘breast cancer survivors’) with fatty liver on ultrasound at baseline or during follow-up evaluations were referred to the Liver Center in the same institution. Exclusion criteria were i) significant alcohol consumption; ii) other causes of liver diseases, such as viral or autoimmune; iii) evidence of recurrent breast cancer or serious comorbidities (other malignancies, cardiopulmonary diseases, etc.). As of March 2019, a total of 231 patients who gave informed consents were enrolled, and a cross-sectional analysis was conducted.

**Results:** Mean age was 53.3±8.2 years. Body mass index (BMI) was 25.2±3.4 kg/m², and waist circumference was 89.3±8.7 cm. Median time period from first visit to consultation was 30.4 months (interquartile range [IQR], 16.6-51.5). For hormonal therapy, 147 patients were taking tamoxifen (63.6%) for 36.5 months (median; IQR, 18.4-54.1) and 50 were on letrozole (21.6%) for 20.0 months (median; IQR, 13.3-51.8), respectively. Metabolic syndrome (MetS) was found in 83 patients (35.9%). Homeostasis model assessment-insulin resistance (HOMA-IR) was 2.14 (median; IQR, 1.52-2.96). Serum AST/ALT were 25.0 IU/L (IQR, 21.0-23.0 IU/L (IQR, 16-33), respectively. Liver stiffness (LS) by transient elastography was 4.2 kPa (median; 2.4-14.6). Controlled attenuation parameter (CAP) was 281.5 dB/m (median; IQR, 243-320). At baseline, 103 patients had NAFLD at baseline (44.6%), and 128 patients developed NAFLD during follow-up (‘incident NAFLD’, 55.4%). Patients with incident NAFLD were more commonly on tamoxifen (72.4% vs. 17.3%, P = 0.011), had lower baseline BMI (24.5 vs. 26.1 kg/m², P < 0.001), and were less commonly associated with MetS (28.1% vs. 45.6%, P = 0.006) compared to those with baseline NAFLD. Patients with baseline NAFLD had lower appendicular skeletal muscle mass (ASM)-to-BMI ratio (0.61 vs. 0.65, P = 0.001) as well as ASM% (24.9% vs. 26.0%, P = 0.003). LS was not significantly different between patients with baseline NAFLD vs. those with incident NAFLD (4.8 kPa vs. 4.4 kPa, P = 0.057). In multiple linear regression analyses, risk factors for higher LS were i) HOMA-IR (P < 0.001), ASM-BMI (P = 0.034), percentage fat (P = 0.020) in overall patients; ii) HOMA-IR (P < 0.001), ASM-BMI (P = 0.018), percentage fat (P = 0.028) in patients with BMI≥25; iii) HOMA-IR (P < 0.001) in patients with BMI<25.

**Conclusions:** Incident NAFLD in breast cancer survivors was associated with lower BMI and tamoxifen use, whereas preexisting NAFLD was associated with lower muscle mass and MetS. HOMA-IR was associated with lower muscle mass and MetS.
**PE-175**

Features of the Prevalence of Risk Factors for Non-Alcoholic Fatty Liver Disease among Residents of the City of Bishkek (Kyrgyzstan)

Sabirov Ibragim, Bebezov Bakhadyr, Surov Edird
Kyrgyz-Russian Slavic University, Kyrgyzstan

**Aims:** Assess the prevalence of NAFLD risk factors among residents of the city of Bishkek (Kyrgyzstan).

**Methods:** In the course of screening, 2389 people who applied for various reasons to family medicine centers in Bishkek, according to the exclusion criteria, 1005 people took part in the study, including 678 (68%) women and 327 (32%) men aged 17 to 96 years old. To achieve this goal, with the informed consent of the patients, the following parameters were measured: waist circumference, biochemical blood test (AST, ALT), data from the anamnesis (smoking, diabetes mellitus) and liver ultrasound.

**Results:** The data presented in the table.

<table>
<thead>
<tr>
<th>Sign</th>
<th>Men (n = 327)</th>
<th>Women (n = 678)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young age (25-44y)</td>
<td>78 (24%)</td>
<td>90 (13%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Mid age (45-59y)</td>
<td>165 (50%)</td>
<td>408 (60%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Elderly age (65-74y)</td>
<td>69 (21%)</td>
<td>132 (20%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Old age (75-90y)</td>
<td>15 (4%)</td>
<td>48 (7%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Waist (m ≥102 cm; w ≥88 cm)</td>
<td>102 (22%)</td>
<td>348 (77%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>ALT (&gt;38 U/l)</td>
<td>237 (23%)</td>
<td>455 (45%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>AST (&gt;41 U/l)</td>
<td>114 (11%)</td>
<td>183 (18%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>204 (20%)</td>
<td>87 (9%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>180 (18%)</td>
<td>387 (39%)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

**Conclusions:** Middle-aged women prevailed among the patients (40%). In individuals with NAFLD, the leading risk factor was abdominal obesity (44.5%), with a high level of AST (29%) and a high level of ALT (68%).

**Keywords:** NAFLD, Metabolic syndrome, Waist circumference, Biochemical blood test

**PE-176**

Serum Biomarkers to Differentiate Non-Alcoholic Steatohepatitis, Advanced Fibrosis, and Severe Steatosis from Mild Form of Non-Alcoholic Fatty Liver Disease

Ha Seok Lee, Sung Won Chang, Sehwa Kim, Min-jin Lee, Young-Sun Lee, Sang Jun Suh, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yoon, Soon Ho Um, Kwan Soo Byun
Department of Internal Medicine, Korea University College of Medicine, Korea

**Aims:** With increasing prevalence worldwide, diagnosis and determining of severity for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) is becoming more important. In this study, we evaluated a diverse set of biomarkers to differentiate NASH, advanced fibrosis, and severe steatosis from mild form of NAFLD.

**Methods:** This is a single-center prospective cross-sectional study of patient with biopsy-confirmed NAFLD. The patients were undertaken laboratory test, liver biopsy, and eighteen kind of serum biomarkers. Sera were stored at -80°C and measured using the Lumixx Multiplex platform. We tried to find specific biomarkers associated with NASH, advanced fibrosis, and severe steatosis using linear regression model.

**Results:** A total of 88 patients were enrolled. Among 88 participants (42% male, median age 52.5 years), 51.1% had NASH, 19.3% had advanced fibrosis (stage 3-4), and 20.5% had severe steatosis (stage 3). There was no statistically significant biomarker associated with NASH. In advanced fibrosis, however, sCD40L was statistically significant predictor (OR = 0.927; 95% CI 0.869-0.990, P = 0.023). In severe steatosis, sCD40L (OR = 1.075; 95% CI 1.014-1.140, P = 0.015), PAI-1 (OR = 1.019; 95% CI 1.014-1.140, P = 0.007), and aPAI-1 (OR = 1.035; 95% CI 1.008-1.063, P = 0.011) showed significant results.

**Conclusions:** We failed to find out specific biomarkers to differentiate NASH. However, sCD40L showed significant relevance about advanced fibrosis. sCD40L, PAI-1, and aPAI-1 showed significant about severe steatosis. Further investigations should be conducted to find out novel biomarkers to replace liver biopsy.

**Keywords:** Biomarker, NAFLD

**PE-177**

The High Occurrence of Non-Alcoholic Steatohepatitis with Fibrosis in Patients with Moderate Fatty Liver Accompanied by Metabolic Syndrome

Dong Hoon Lee, Soo Hyung Ryu, Yun Jae Shin, Bo Kyung Lee, Young Sun Na, Boeun Kim, Onhwa An, Tae Young Park, Jeong Seop Moon
Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea

**Aims:** The prevalence of steatohepatitis, which can progress to cirrhosis and hepatocellular carcinoma, among patients with non-alcoholic fatty liver disease (NAFLD) has been known to be about 20%. We evaluated the occurrence of steatohepatitis and fibrosis in liver biopsy specimens of patients with NAFLD accompanied by metabolic syndrome.

**Methods:** We retrospectively analyzed nine NAFLD patients who underwent percutaneous liver biopsy at the fatty liver clinic of Seoul Paik Hospital from August 2018 to February 2019. They were recommended to reduce body weight with diet program and exercise to treat NAFLD at our fatty liver clinic. All of them were diagnosed with fatty liver equal to or more than mild to
moderate grade by ultrasonography. Also, all of them had at least one of the metabolic syndrome conditions such as hypertension, diabetes mellitus (DM), and hyperlipidemia. A total of 9 HCC patients (M:F=2:7; Age: 50.6 ± 13.4 years; BMI: 30.2 ± 5.9 kg/m²; serum ALT level 45(27-222 IU/L); Grade of fatty liver, mild to moderate: moderate to severe = 4:1:4) were subjected. One had hypertension only, one DM only, two both of hypertension and DM, four hyperlipidemia, and the last one had all of them.

**Results:** All nine patients had steatohepatitis in liver biopsy specimens. Seven patients had moderate grade and two showed severe lobular inflammation. Eight of nine showed the development of fibrosis in the liver. Two had 1/4 stage fibrosis, two of 2/4, and four of 3/4. Transient elastography (TE) was performed in 7 patients, of which TE level was lower than expected in patients with fibrosis of more than stage 3. There was no relationship between the severity of fibrosis and the level of TE. There was no difference in the severity of inflammation grade and fibrosis stage according to the grade of fatty liver, the existence of fatty pancreas and atherosclerosis, the percentage of body fat, and BMI.

**Conclusions:** The patients with equal to or more than mild to moderate fatty liver accompanied by metabolic syndrome have a very high chance to develop steatohepatitis and fibrosis. Therefore, more strict body weight reduction by diet program is needed in these patients.

**Keywords:** Non-alcoholic fatty liver disease, Fatty liver, Fibrosis, Metabolic syndrome

---

**PE-178**

*The Value of Controlled Attenuation Parameter in Fibrosis Prediction by Liver Stiffness in Nonalcoholic Steatohepatitis*

Saein Kim, Jung Il Lee, Hyun Woong Lee, Kwan Sik Lee

Department of Internal Medicine, Gangnam Severance Hospital Yonsei University College of Medicine, Seoul Republic of Korea

**Aims:** Liver stiffness measurement (LSM) tends to overestimate fibrosis stage in nonalcoholic fatty liver disease (NAFLD). Controlled attenuation parameter (CAP), provided by LSM device, has been introduced for noninvasive quantification of hepatic steatosis. This study aimed to determine the role of CAP values in predicting liver fibrosis stages by LSM in nonalcoholic steatohepatitis (NASH).

**Methods:** One hundred eighty-four patients with biopsy proven NASH had LSM and CAP evaluated at baseline. Among them, 130 patients had 1-year follow-up LSM and analyzed for the changes of LSM after pioglitazone or ursodeoxycholic acid (UDCA) treatment.

**Results:** When CAP values were grouped by tertiles, lower tertile ranged 223-310, middle 311-339, and higher 340-400 dB/m. In Kleiner fibrosis stage F0-1, LSM values increased at higher CAP tertile (P = 0.001), and in F2, at middle and higher tertiles (P = 0.027). No differences across CAP tertiles were noticed in F3-4 (P = 0.752). Receiver operating characteristic curves for LSM cutoff in diagnosis of F2 identified 8.05 kPa for lower CAP tertile, 9.35 kPa for middle, and 10.55 kPa for higher tertile. When changes in proportion of high LSM (F2) were assessed among pioglitazone and UDCA treated patients using different LSM cutoffs by CAP tertiles, pioglitazone treated patients demonstrated decrease in proportion of high LSM when UDCA group failed to show significant changes.

**Conclusions:** LSM in NASH may overestimate stages of liver fibrosis especially in patients with high CAP values. Interpretation of LSM in association with simultaneously measured CAP scores may provide more helpful information sparing unnecessary liver biopsy.

**Keywords:** Fibroscan, Controlled attenuation parameter, Nonalcoholic steatohepatitis, Liver fibrosis

---

**PE-179**

*Predictors of Sarcopenia in Obese Korean Population*

Min Je Sung1, Hye Won Lee1,2, Beom Kyung Kim1,2, Jun Yong Park1,2, Do Young Kim1,2, Sang Hoon Ahn1,2, Kwang-Hyub Han1,2, and Seung Up Kim1,2

1Department of Internal Medicine, 2Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 3Yonsei Liver Center, Severance Hospital, Seoul, Korea

**Aims:** Sarcopenia is not only associated with obesity, but also with cardiometabolic diseases and liver fibrosis. We investigated the prevalence of sarcopenia and its predictors in obese subjects.

**Methods:** Living-related liver donors and subjects who received a comprehensive medical health check-up were recruited. Obesity was defined as body mass index (BMI) ≥ 25 kg/m². Muscle mass was assessed using computed tomography (CT) at the 3rd lumbar vertebra. Cardiometabolic disease risk was assessed using Atherosclerotic Cardiovascular Disease 10-year risk (ASCVD) and fibrotic burden was assessed using the fibrosis-4 index (FIB-4). The study population was divided by quartile stratification of the lumbar skeletal muscle index (LSMI) (Q1 to Q4) and patients with lowest quartile (Q1) were considered as having sarcopenia.

**Results:** Among 466 obese subjects (86 donors and 380 subjects with health check-up), 53 (11.4%) had sarcopenia. Subjects with sarcopenia were significantly older (mean 53.3 vs. 66.6 years) and had higher ASCVD score (mean 14.95 vs. 23.29), FIB-4 (mean 1.57 vs. 1.16), prevalence of hypertension (62.3 vs. 46.0%) and diabetes (45.3 vs. 31.0%), whereas they had significantly lower BMI (mean 26.4 vs. 27.4 kg/m²), estimated glomerular filtration rate (mean 81.7 vs. 93.4 ml/min/1.73m²), and LSMI (mean 43 vs. 56 cm²/m²) than those of subjects without sarcopenia (all P < 0.05). Multivariate analysis found that higher BMI (odd ratio [OR] = 0.592, 95% confidence interval [CI] 0.440-0.797, P = 0.001) was independently associated with a reduced risk of sarcopenia, whereas higher ASCVD score (OR =
1.042, 95% CI 1.018-1.066, \( P = 0.001 \) and FIB-4 (OR = 1.715, 95% CI 1.053-2.794, \( P = 0.030 \)) were independently associated with an increased risk of sarcopenia.

**Conclusions:** Sarcopenia is significantly associated with lower BMI, higher fibrotic burden, and higher cardiovascular risk in obese Korean population.

**Keywords:** Sarcopenia, Obesity, Liver disease, Metabolic disease, Body mass index

---

**Putative Relationship between Changes in Body Composition and Metabolic Characteristics under Lifestyle Intervention in Patients with Nonalchoholc Fatty Liver Disease**

**Methods:** Patients who were diagnosed with NAFLD were prospectively enrolled since July 2016 in this single-center prospective cohort study. Diagnosis of NAFLD was based on the presence of fatty change in the liver ultrasound in the absence of significant alcohol intake or evidences of other chronic liver diseases (e.g., viral, autoimmune or metabolic, etc.). Anthropometric, laboratory and radiologic data were collected, including vibration-controlled transient elastography (VCTE) and body composition analysis (BCA) at the time of enrollment. Patients visited to the clinic regularly for comprehensive interview and laboratory tests every 3-6 months and underwent VCTE and BCA on a yearly basis, under individualized lifestyle intervention including reduced calorie intake and moderate-intensity exercise.

**Results:** As of March 2019, 63 patients out of the entire prospective cohort (n = 272) were included in the analysis who completed follow-up evaluation including paired measurements of VCTE and BCA. Median age was 48.9 years, and 44 patients were male (69.8%). Baseline body mass index (BMI) was 26.5 kg/m² (median; interquartile range [IQR], 24.5–29.9); 20 patients had BMI<25 (nonobese, 31.8%), and 43 had BMI ≥25 (obese group). Baseline body mass index (BMI) was 26.5 kg/m² (median; IQR, 24.5–29.9); 20 patients had BMI<25 (nonobese, 31.8%), and 43 had BMI ≥25 (obese group; \( P < 0.001 \)). There was a significant difference in BMI, higher fibrotic burden, and higher cardiovascular risk in the nonobese group rather than the obese group.

**Conclusions:** In this preliminary report of a prospective cohort study, changes in BMI under lifestyle intervention led to decrease in LSM, along with reciprocal changes in percentage fat and relative skeletal muscle mass, along with components of metabolic syndrome in NAFLD patients. Improvement in the insulin resistance was more profound in the nonobese group rather than the obese group.

**Keywords:** Nonalcoholic fatty liver disease, Lifestyle intervention, Body composition, Insulin resistance

---

**Dickkopf-1 from Hepatocellular Carcinoma Cells Promotes the Angiogenic Potential of Endothelial Cells by Activating the VEGFR-2 Signaling Pathway**

**Methods:** The cell lines Huh7 and Hep3B, with low and high biological function of DKK-1 in angiogenesis of hepatocellular carcinoma (HCC) is not well documented. We investigated the phenotypical changes of vascular endothelial cells after interaction with HCC cells expressing DKK-1 using two-dimensional (2D) and three-dimensional (3D) co-culture systems. The biological function of DKK-1 in angiogenesis of hepatocellular carcinoma (HCC) is not well documented. We investigated the phenotypical changes of vascular endothelial cells after interaction with HCC cells expressing DKK-1 using two-dimensional (2D) and three-dimensional (3D) co-culture systems.
Protective Effect of Bioengineered Silver Nanoparticles against Diethylnitrosamine Induced Hepatocarcinogenesis via Knockdown of Oxidative Stress and Inflammation by Regulating NF-κB Pathway

Ekta Yadav

Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences (SHUATS), Prayagraj, India

Aims: Current study was designed to biofabricate, characterize and evaluate protective effect of Trianthema portulacastrum (TP) extract mediated silver nanoparticles (AgTPNPs) against diethylnitrosamine (DEN) induced hepatocarcinoma in rat model.

Methods: Liver damage in rats was induced with a single dose of DEN (200 mg/kg) as well as double dose of phenobarbital. Simultaneously, animals were administered with AgTPNPs at two dose levels (10 and 20 mg/kg p.o.) for 16 weeks. At the end of study, serum biomarkers, hematological status, antioxidants enzymes, proinflammatory cytokines, i.e., tumor necrosis factor-α, interleukin-6, interleukin-1β, and nuclear factor kappa beta (NF-κB), were examined to assess the protective effect of AgTPNPs. Additionally, gene expression (Akr1b10, Foxp1 and ING3) concerned with hepatocarcinoma as well as was as histological studies were also undertaken to assess the outcomes of current study.

Results: AgTPNPs were synthesized by co-precipitation method and different characterization techniques confirmed the formation of spherical crystalline nanoparticles with size range of 50-80 nm. FTIR results showed the existence of possible bioactive functional groups of phytoconstituents in the synthesized AgTPNPs. Results demonstrated that DEN significantly induced the hepatocellular carcinoma in each group, which was significantly reversed (P < 0.001) by AgTPNPs in a concentration dependent manner. A significant reduction in level of serum hepatic and non-hepatic marker enzymes, oxidative stress and different inflammatory markers via direct and indirect inhibition of NF-κB expression were observed in rats administered with AgTPNPs. Regarding gene expression, AgTPNPs treated group exhibited significant elevation in Akr1b10 and ING3 expression whereas reduction in Foxp1 gene expression level as compared to control group. Histopathological study further favored the restructuring effect on destructed hepatic tissue.

Conclusions: Collectively, results demonstrated that AgTPNPs potentially ameliorated the damaging effects of DEN induced hepatocellular carcinoma and it can be utilized as an effective nano technology based anticancer approach.

Keywords: Liver Cancer, Biofabricate, Nanoparticles, Histological
Alpha-Fetoprotein Inhibition Enhances the in Vitro and in Vivo Anti-Tumor Effects of Sorafenib on Hepatocellular Carcinoma

Jin Sook Kim¹, Kyung Tae Kim², Joong Won Park²*¹

¹Division of Clinical Research, ²Division of Cancer Branch, ³Center for Liver and PancreatoBiliary Cancer, National Cancer Center, Goyang, Korea, Republic Of Korea

**Aims:** Sorafenib is the standard systemic therapy for patients with advanced hepatocellular carcinoma (HCC); however, the drug has moderate response rate and duration, and low disease control rate. Moreover, the survival rate, after administration of sorafenib, is lower in patients with high serum alpha-fetoprotein (AFP) levels. Thus, we hypothesized that AFP inhibition increases the anti-tumor effect of sorafenib on HCC in *in vitro* and *in vivo* models.

**Methods:** AFP-producing Huh-7 cell line was used in this study. The cells were transfected with AFP siRNA for 72 hours followed by treatment with sorafenib (2 µmol/L) for 24 hours. Hoechst 33342 staining was used to analyze cell number using cytation3. Propidium iodide staining was used to assess cell cycle state using flow cytometry. Immunoblotting assay was used to determine apoptosis. Patient-derived xenograft (PDX) models were used to evaluate augmentation effects of AFP inhibition on sorafenib. PDX models were divided into 5 groups for treatment with the following: control; non-target siRNA; AFP siRNA; sorafenib; AFP siRNA + sorafenib. siRNA was intratumorally injected every 3 days and sorafenib (10 mg/kg) was administered orally by gavage once daily. At the end of study, the body weights of the mice were recorded, and the mice were sacrificed their tumors were harvested for analysis.

**Results:** The 3D anatomy can be visualised in high quality which results in good perception of the third dimension (depth). Tumour assignment to liver segments was significantly correlated to the level of training (P < 0.05). There was a significant increase (P < 0.001) in the precision of tumour localisation by 51% and resection proposal from 2D through 3D reconstructions by 13%-21%. Quantitative differences of the simplified Couinaud’s classification of the liver segments compared to the true vascular anatomy of up to 40% were found.

**Conclusions:** The impact of individual 3D-reconstruction on surgical planning has been proven to be significant and increases precision quantitatively.

**Keywords:** 3D reconstruction, Liver segment, Tumors, Vascular tree

---

Successful Single-Stage Extended Right Hemihepatectomy with Low Anterior Resection of the Rectum in Patients with Colorectal Cancer with Liver Metastases

A. Smagulov, Shahmarat Ospanov, Bolat Tleuliev

Surgery Department, Qyzylorda Regional Cancer Center, Kazakhstan

**Aims:** Colorectal cancer (CRC) occupies the 4th place in the structure of cancer morbidity in Kazakhstan. From 35 to 57% of patients with colorectal cancer with primary treatment have metastases to the liver. However, active surgical treatment of metastatic liver invasion allows achieving 5-year survival in 27-47% of patients.

**Methods:** We present the clinical observation of successful surgical treatment of rectal cancer with liver metastases with simultaneous execution of extended right hepatectomy and “low” anterior rectal resection. Patient 1, 52 years old, male. From anamnesis: the above complaints are noted within 6 months. Ultrasonography of the abdominal cavity revealed a focal lesion in the right lobe of the liver, with a colonoscopy: in the middle-ampullar rectal section, a tumor up to 5 cm in length is located 8 cm above the anus, which closes the colon lumen of the gut by 2/3; the result of a biopsy: moderately differentiated adenocarcinoma. By PET – no other metastatic problems.

**Results:** Was performed extended right hepatectomy (cholecystectomy) and “low” anterior rectal resection. After operation...
Significance of Plasma Levels of Soluble Programmed Death-1 and Soluble Programmed Death-Ligand 1 in Hepatocellular Carcinoma

Gwang Hyeon Choi, Jung Wha Chung, Yun Suk Choi, Da woon Jeong, Soomin Ahn, Eun Sun Jang, Jin-Wook Kim, Sook-Hyang Jeong

Departments of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea; Departments of Internal Medicine, Wonkwang University Sanbon Hospital, Wonkwang University College of Medicine, Republic of Korea; Departments of Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea

Aims: In contrast to tissue expression of programmed death-1 (PD-1) and its ligands (PD-L1), plasma levels of soluble programmed death-1 (sPD-1) and soluble PD-L1 (sPD-L1) were not clearly defined in hepatocellular carcinoma (HCC). This study aimed to investigate plasma levels of sPD-1 and sPD-L1, and to evaluate their relationship with clinical factors and overall survival in HCC patients.

Methods: Using plasma samples obtained from the prospectively enrolled HCC patients (n = 242) and age- and sex-matched healthy controls (n = 91), the plasma levels of sPD-1 and sPD-L1 were measured by commercial ELISA.

Results: The 242 HCC patients showed a mean age of 60.8 years, male in 80.6%, HBsAg-positive in 70.2%, Child-Pugh class A in 84.7%, and BCLC 0/A in 57.0%. The plasma sPD-1 was detected in 35.2% of healthy control (median level, 244; IQR, 92–1948 pg/mL) and in 34.7% of HCC patients (median level, 472; IQR, 177–1660 pg/mL; P = 0.25). In healthy control group, sPD-1 level was higher in male than in female patients (P = 0.03). The plasma sPD-L1 was detected in almost all the subjects, and not different between healthy control and HCC group (median 371 versus 332 pg/mL; P = 0.13). The proportion of Child-Pugh class B was higher in detectable-sPD-1 group (22.6%) than in the non-detectable-sPD-1 group (14.4%, P = 0.04), and higher in the high-sPD-L1 group (19.8%) than in the low-sPD-L1 group (9.9%, P = 0.04). Otherwise, there was no clinical factor significantly associated with sPD-1 level and sPD-L1 level. During mean follow-up of 3.5 years, the overall survival was not different between the non-detectable- and detectable-sPD-1 group, and between the low- and high-sPD-L1 group.

Conclusions: Though, detectable sPD-1 level or high sPD-L1 level were associated with poor liver function in HCC patients, either level may not be a useful biomarker for the diagnosis or prognosis of HCC.

Keywords: Plasma level, Soluble programmed death-1, Soluble programmed death-ligand 1, Hepatocellular carcinoma

PE-187

Significance of Plasma Levels of Angiopoietin-2 and Vascular Endothelial Growth Factor in Hepatocellular Carcinoma

Gwang Hyeon Choi, Jung Wha Chung, Yun Suk Choi, Da woon Jeong, Soomin Ahn, Eun Sun Jang, Jin-Wook Kim, Sook-Hyang Jeong

Departments of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea; Departments of Internal Medicine, Wonkwang University Sanbon Hospital, Wonkwang University College of Medicine, Republic of Korea; Departments of Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea

Aims: This study aimed to investigate the profiles of plasma levels of Angiopoietin-2 (Ang-2) and vascular endothelial growth factor (VEGF), and to elucidate their association with the overall survival in hepatocellular carcinoma (HCC) patients.

Methods: Using the plasma samples obtained from the prospectively enrolled HCC patients (n = 242) and age- and sex-matched healthy controls (n = 91), the plasma levels of Ang-2 and VEGF were measured by commercial ELISAs.

Results: The HCC patients showed a mean age of 60.8 years, male in 80.6%, HBsAg-positive in 70.2%, Child-Pugh class A in 84.7%, and BCLC 0/A in 57.0%. Compared to healthy controls, HCC patients showed a significantly higher Ang-2 level (median 487 versus 1684 pg/mL, P < 0.001) and higher VEGF level (median 4.2 versus 26.5 pg/mL, P < 0.001). Using the median level as a cutoff, the high-Ang-2 group (n = 120) showed a significantly poorer performance, poorer liver function, more aggressive tumor features, and lower survival than the low-Ang-2 group. In contrast, the high-VEGF group (n = 120) showed a significantly poorer performance and more aggressive tumor features than the low-VEGF group, but liver function and survival were not different from the low-VEGF group. On multivariate analysis, the high-Ang-2 level was an independent factor (HR [hazard ratio] 2.51; 95% CI [confidence interval] 1.60–3.94; P < 0.001) associated with the overall survival, along with Child-Pugh class B (HR 3.51; 95% CI, 2.21–5.59; P < 0.001) and TNM stage 3 or 4 (HR 5.41; 95% CI 3.31–8.85). Moreover, the AUROC of Ang-2 (0.749) for the survival prediction, was higher than that of alpha-fetoprotein.
(0.717) or PIVKA-II (0.743).

**Conclusions:** Plasma level of Ang-2 in HCC was an independent factor for overall survival, showing a higher AUROC than alpha-fetoprotein, while VEGF plasma level was not associated with survival in HCC. Further validation study is warranted.

**Keywords:** Plasma level, Angiopoietin-2, Vascular endothelial Growth factor, Hepatocellular carcinoma

---

**Cytotoxicity of Human Hepatic Intrasinusoidal CD-56bright Natural Killer Cells against Hepatocellular Carcinoma Cells**

Shin Hwang³, Jaeseok Han², Ji-Seok Baek², Eunyoung Tak³, Gyun Won Song¹, Sung-Gyu Lee¹, Dong-Hwan Jung¹, Gil-Chun Park¹, Chul-Soo Ahn¹, and Nayoung Kim³

¹Division of Liver Transplantation and Hepatobiliary Surgery, Department of Surgery, University of Ulsan College of Medicine, Seoul, Korea; ²Department of Convergence Medicine & Asan Institute for Life Sciences, Asan Medical Center, University of Ulsan College of Medicine, Korea

**Aims:** Hepatic intrasinusoidal (HI) natural killer (NK) cells from liver perfusate have unique features that are similar to those of liver-resident NK cells. Previously, we have reported that HI CD56bright NK cells effectively degranulate against SNU398 hepatocellular carcinoma (HCC) cells. Thus, the aim of this study was to further investigate the phenotype and function of HI NK cells.

**Methods:** Healthy living donor right lobe graft was washed with 1 L of histidine-tryptophan-ketoglutarate solution, and liver perfusate was collected. Various fluorescence-labeled Abs were used for flow cytometry. K562, Huh7, or SNU398 cells as target cells were seeded in round-bottom 96-well plates at 7000 cells/well. CytoTox 96 Non-radioactive cytotoxicity assay was performed.

**Results:** We found that HI CD56bright NK cells degranulated much less to Huh7 cells. HI CD56bright NK cells expressed NKG2D, Nkp46, TNF-related apoptosis-inducing ligand (TRAIL), and FAS ligand (FASL) at higher levels than CD56dim cells. SNU398 cells expressed more NKG2D ligands and FAS and less PD-L1 than Huh7 cells. Blockade of NKG2D, TRAIL, and FASL significantly reduced the cytotoxicity of HI NK cells against SNU398 cells, but blockade of PD-L1 did not lead to any significant change. However, HI NK cells produced IFN-γ well in response to Huh7 cells.

**Conclusions:** The cytotoxicity of HI CD56bright NK cells was attributed to the expression of NKG2D, TRAIL, and FASL. These results suggest the possible use of HI NK cells for cancer immunotherapy and pre-screening of HCC cells to help identify the most effective NK cell therapy recipients.

**Keywords:** Hepatic intrasinusoidal NK cells, Liver-associated NK cells, Cancer immunotherapy, Cytotoxicity
Serum Level of Growth Differentiation Factor 15 Reflects the Aggressiveness of Hepatocellular Carcinoma Including Metastasis

Soon Kyu Lee, Jong Young Choi, Jung Hyun Kwon, Jung Won Jang, Chang Wook Kim, Si Hyun Bae, Seung Kew Yoon, Mi-La Cho

1Division of Hepatology, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea; 2Division of Hepatology, Department of Internal Medicine, Incheon St. Mary's Hospital, The Catholic University of Korea; 3Division of Hepatology, Department of Internal Medicine, Uijeongbu St. Mary's Hospital, The Catholic University of Korea; 4Division of Hepatology, Department of Internal Medicine, Eunpyeong St. Mary's Hospital, The Catholic University of Korea; 5The Rheumatism Research Center, Catholic Research Institute of Medical Science; The Catholic University of Korea, Korea

Aims: Growth differentiation factor (GDF15) is one of the transforming growth factor β superfamily and increased in several cancers including hepatocellular carcinoma (HCC). However, the level of GDF15 according to the characteristics of HCC has not been investigated. We examined the serum level of GDF15 in HCC patients and correlated with the clinical tumor characteristics.

Methods: A total of 80 patients diagnosed with HCC between 2013 and 2017 were analyzed in our study. In 80 enrolled patients, 20 patients for each modified UICC stage (I-IV) were included. The 15 healthy patients were also included as control group. The serum level of GDF15 and programmed death-1 ligand 1 (PD-L1) were checked at the time of initial diagnosis of HCC. The level of GDF15 were analyzed with tumor characteristics including tumor stage, size, presence of portal vein thrombosis (PVT) and metastasis.

Results: The mean age of 80 HCC patients were 59.9 years and 54 patients (67.5%) were HBV-related HCC. The median level of GDF15 and PD-L1 were 782.7 pg/mL (range, 624.1-909.1) and 35.4 pg/mL (range, 15.7-63.4), respectively. The serum level of GDF15 were significantly higher in HCC patients than healthy control (P < 0.001). However, PD-L1 level were significantly lower in HCC patients (P = 0.001). Moreover, advanced stage (III-IV) had higher level of GDF15 than stage I-II (P < 0.05) and PD-L1 level were not differ between tumor stage. The size of tumor had a significantly positive correlation with the level of GDF15 (r = 0.50, P < 0.001). The patients with metastasis or PVT had higher GDF15 level with significance (P < 0.003; P = 0.001, respectively).

Conclusions: The obtained results allow to conclude that video surgery of large volume on the liver has great prospects in clinics where there is sufficient experience of such surgical interventions in an open manner.

Keywords: Laparoscopic, Hemihepatectomy, Liver, Tumors

Hydralazine Stimulates HIF-1-Dependent but Inhibits HIF-2-Dependent Gene Expression in Liver Cancer Cells

Ranbir Singh, Dharmender Singh

Department of Applied Sciences, Raja Mahendra Pratap Post Graduate College, Haridwar, Uttarakhand, India

Aims: Hypoxia-inducible factors (HIFs) are transcriptional regulators that mediate the cellular response to low oxygen. Although HIF-1 is usually considered as the principal mediator of hypoxic adaptation, several tissues and different cell types express both HIF-1 and HIF-2 isoforms under hypoxia or when treated with hypoxia mimetic chemicals such as Hydralazine. However, the similarities or differences between HIF-1 and HIF-2, in terms of their tissue- and inducer-specific activation and function, are not adequately characterized.

Methods: To address this issue, we investigated the effects of true hypoxia and hypoxia mimetics on HIF-1 and HIF-2 induction and specific gene transcriptional activity in two hepatic cancer cell lines, Huh7 and HepG2.

Results: Both hypoxia and Hydralazine caused rapid induction of both HIF-1α and HIF-2α proteins. Hypoxia induced erythropoietin (EPO) expression and secretion in a HIF-2-dependent way. Surprisingly, however, EPO expression was not induced when cells were treated with Hydralazine. In agreement, both HIF-1 and HIF-2-dependent promoters (of PGK and SOD2 genes, respectively) were activated by hypoxia while Hydralazine only activated the HIF-1-dependent PGK promoter. Unlike Hydralazine, other hypoxia mimetics such as DFO and DMOG activated both types of promoters. Furthermore, Hydralazine impaired the hypoxic stimulation of HIF-2, but not HIF-1, activity and Hydralazine-induced HIF-2α interacted poorly with USF-2, a HIF-2-specific co-activator.

Conclusions: These data show that, despite similar induction of HIF-1α and HIF-2α protein expression, HIF-1 and HIF-2 specific gene activating functions respond differently to different stimuli and suggest the operation of oxygen-independent and gene- or tissue-specific regulatory mechanisms involving additional transcription factors or co-activators.

Keywords: Liver, Cancer
**PE-192**

**Targeting HDAC2 Elicits Synergistic Anti-Cancer Effects of Sorafenib in Hepatocellular Carcinoma**

Hyung Seok Kim, Hee Doo Yang, Sang Yeon Kim, Minjung Na, Gyungdeck Yang, and Suk Woo Nam

Gene Expression & Comprehensive Knowledge-based Omics Research Laboratory, Department of Pathology, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

**Aims:** Hepatocellular carcinoma (HCC) is the fifth frequently diagnosed cancer and is the second leading cause of cancer death worldwide. Many groups have suggested possible clinical applications for liver cancer therapy but sorafenib, an orally-available kinase inhibitor, is the only standard systematic therapies for treatment of hepatocellular carcinoma. However, survival benefit of sorafenib is unsatisfactory due to high level heterogeneity of individual response. We previously reported that histone deacetylase 2 (HDAC2) was deregulated in HCC, and thereby contributed to liver tumorigenesis by enhancing mitotic and metastatic potential of transformed cells. Targeted-disruption of HDAC2 suppressed in vitro and in vivo tumorigenic potential of HDAC2 in liver cancer. The goal of this study was to investigate whether both sorafenib treatment and HDAC2 inhibition elicit synergistic anti-tumor effect against HCC cells.

**Methods:** A series of inhibitors, activators and siRNAs was utilized to validate regulatory mechanisms for HDAC2-targeting in hepatocellular carcinogenesis.

**Results:** Here, we showed that sorafenib effectively blocked ERK/MEK and AKT signaling pathway upon EGF stimulation in liver cancer cell lines. Also, we found that valproic acid (VPA), a selective inhibitor of histone deacetylase family I, and sorafenib treatment synergistically evoked liver cancer cell growth retardation. This effect was recapitulated by HDAC2 knockdown with sorafenib treatment and exhibited synergistic effect on apoptotic cell death of liver cancer cell lines, Hep3B and Huh7, compared to single treatment of sorafenib.

**Conclusions:** Our data suggest that combined sorafenib treatment with HDAC2 targeting may provide more benefits toward HCC therapy providing a novel approach for future application in patients with advanced HCC.

**Keywords:** Histone deacetylase 2, Sorafenib, Valproic acid, Hepatocellular carcinoma

**PE-193**

**Association of Telomerase Reverse Transcriptase Gene Expression with Clinical Phenotype of Hepatocellular Carcinoma**

Jin Seoubl Kim1, 2, Hye Seon Kim1, 2, Hee Chul Nam1, 2, Pil Soo Sung3, 4, Si Hyun Bae3, 4, Jong Young Choi3, 4, Seung Kew Yoon3, 4, Jeong Won Jang1, 2

1Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2The Catholic University Liver Research Center, Korea

**Aims:** Cancer driver genes and major pathways leading to liver carcinogenesis have yet to be elucidated. As a gatekeeper mutation, telomerase reverse transcriptase (TERT) was recently identified to have a fundamental role in multi-step hepatocellular carcinogenesis. This study aimed to investigate the association between TERT gene set analysis and clinical phenotype of HCC.

**Methods:** The protein-protein interaction (PPI) networks were established for TERT through the STRING database, after which potential genes related to HCC or apoptosis were finally detected. We examined the expression of the selected gene set by qRT-PCR in tissue samples of 153 patients with HCC (111 paired surgical and 42 non-surgical specimens). The data were correlated with tumor stage, recurrence, and progression of HCC.

**Results:** From the PPI network, seven TERT gene sets for HCC, such as CCT5, TUBA1B, mTOR, RPS6KB1, AKT1, WHAZ, YWH-AQ, and TERT, were identified and analyzed for gene expression by qRT-PCR. Among these, TERT was the most significant differentially expressed gene; the expression of TERT is upregulated in tumor than non-tumor tissues, with its increasing expression with tumor stage progression. Patients with a high expression of TERT had significantly higher rates of recurrence and worse progression-free survival than those with a low TERT expression. Upregulation of TERT expression was significantly associated with male patients.

**Conclusions:** TERT gene expressions are associated with clinical phenotype of HCC, in terms of the development, recurrence, and disease progression of HCC. Our data indicate that TERT pathway might serve as a useful surrogate for the follow-up of HCC patients.

**Keywords:** Telomere, Hepatocellular carcinoma, Biomarker, Progression

**PE-194**

**Investigating Role of Cinnamon Bioactive Compounds Towards Hepatic Carcinoma Marker in Diabetes State Using Computational Interaction Approach**

Chakresh Kumar Jain

Jaypee Institute of Information Technology NOIDA, INDIA

**Aims:** Investigating role of Cinnamon bioactive compounds towards hepatic carcinoma marker in diabetic state using computational interaction approach. The aberration in c-Met kinase (PDB ID: 2RFN) is because of overexpression and mutation and to trigger the carcinogenic pathways associated with HCC reported in approximately 50% of patients and also exhibited the relations with insulin-like growth factor receptor 1. Thus the c-Met inhibition may be one of the potential therapeutic approach and may play important role in the control or inhibition of HCC. Traditionally in indina system *Cinnamomum cassia* as
a spice has been used in food preparation and therapeutically reported to have anti cancer activities in literature. The active compound Cinnamaldehyde, cinnamic acid, and cinnamyl alcohol have been found in *Cinnamomum cassia*.

**Methods:** Here in this work investigate the computational in-silico study using autodock tool with Cinnamaldehyde and observed the interaction with c-met pdb id 2RFN. (1) first download the PDB structure of c met protein from RCSB web portal PDB ID 2RFN (2) Performed the docking experiment using autodock vina ver 1.1.2 (blind docking) on biological assembly 1 out of two of the molecule in the structure with all default parameter (3) the results has been noticed and interaction is studied.

**Results:** The docking score was found -4.1 K Cal/mol.

**Conclusions:** We performed the basic interaction of the selected compound and found good interaction can be further validated simulation study. This gives an idea of about the insight of mechanism of action of these compound.

**Keywords:** C Met, Docking, Diabetes, Cinnamomum cassia

---

**Adipose Tissue-Derived Mesenchymal Stem Cells Inhibit Hepatocellular Carcinoma Cells via Secretion of Interferon (IFN)-Beta and Tumor Necrosis Factor-related Apoptosis-Inducing Ligand (TRAIL) in Vitro**

Soonjae Hwang1,2, Sung Hoon Kim3, Jin Suk Lee1,2, Young Woo Eom1

1Cell Therapy and Tissue Engineering Center, Yonsei University Wonju College of Medicine, Wonju, 26426, South Korea, 2Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, 26426, South Korea, 3Department of General Surgery, Yonsei University Wonju College of Medicine, Wonju, 26426, South Korea

**Aims:** Adipose tissue-derived mesenchymal stem cells (ASCs) are emerging as promising anti-agents to inhibit hepatocellular carcinoma because the interferon (IFN)-beta and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) secreted by ASCs inhibit certain cancer cells through decreasing tumor cell growth and inducing apoptosis separately. However, it was not investigated that ASCs inhibit hepatocellular carcinoma cells through IFN-beta and TRAIL in vitro. Therefore, it was hypothesized that ASCs suppress hepatocellular carcinoma cell through IFN-beta and TRAIL.

**Methods:** In order to test the hypothesis, Huh7 and Hep3B human hepatocellular carcinoma cells were co-cultured with ASCs for 5 days. After co-culture with ASCs, the Huh7 and Hep3B cells were examined for cell viability using MTT assay. In addition, Huh7 and Hep3B cells were individually treated with concentrated media (CM) obtained from supernatant of cultured ASCs for 4 days with or without neutralizing antibody to IFN-beta and/or TRAIL. It was observed that cell viability of the Huh7 and Hep3B cells treated with ASC-CM was decreased. Huh7 and Hep3B cells co-treated with ASC-CM and neutralizing antibody to IFN-beta or TRAIL showed increased cell viability compared to Huh7 and Hep3B cells treated with ASC-CM alone.

**Conclusions:** We conclude that ASC may play a role in inhibiting hepatocellular carcinoma through IFN-beta and TRAIL.

**Keywords:** Adipose tissue-derived mesenchymal stem cell, Hepatic cancer, IFN-beta, TRAIL

---

**Results:** Results of experiments showed that cell viability of Huh7 and Hep3B cells indirectly co-cultured with ASCs was decreased compared to control group. In addition, Huh7 and Hep3B cells were individually treated with concentrated media (CM) obtained from supernatant of cultured ASCs for 4 days with or without neutralizing antibody to IFN-beta and/or TRAIL. It was observed that cell viability of the Huh7 and Hep3B cells treated with ASC-CM was decreased. Huh7 and Hep3B cells co-treated with ASC-CM and neutralizing antibody to IFN-beta or TRAIL showed increased cell viability compared to Huh7 and Hep3B cells treated with ASC-CM alone.

**Conclusions:** We conclude that ASC may play a role in inhibiting hepatocellular carcinoma through IFN-beta and TRAIL.

**Keywords:** Adipose tissue-derived mesenchymal stem cell, Hepatic cancer, IFN-beta, TRAIL
Radiofrequency Ablation of Metastatic Liver Tumors
A. Kozhakhmetov, A. Zheksenbaev
Endovascular Surgery Department, Aktau Regional Hospital, Kazakhstan

**Aims:** Metastatic liver cancer is one of the most dangerous conditions during the course of cancer. The most common liver metastases occur in colorectal cancer, breast cancer, stomach. Currently, the method of radiofrequency ablation (RFA) is increasingly used as an alternative to surgery. This method of local exposure allows the thermal destruction of the tumor under the influence of high-frequency radio emission. The RFA method is used both in the presence of a solitary focus in the liver, and in single foci located in one lobe of the liver, and in both lobes. The technique is used both for small metastases up to 3 cm in size and for large formations up to 5 cm in size.

**Methods:** RFA of liver metastatic foci was performed in 6 patients, including 3 men and 4 women. To conduct RFA was used the generator of the company "Medtronic (COVIDIEN)" and single needle electrodes "Cool-Tip" with a length of 25 cm, with working parts of 30 mm. Ultrasonic testing was carried out on the scanner HITACHI ARIETTA V70, the positioning of the electrode in the center was carried out using convex probe with a scanning frequency of 3.5 MHz. We used percutaneous access to the hearth by the method of free hand. All RFA sessions were performed in the mode of "Impedance control", in which the impact power is automatically adjusted depending on the resistance of the tissue and is 150-170 watts. The duration of the application was standard and averaged 12 minutes.

**Results:** In dynamic observation within 12 months after RFA continued growth was detected in 3 cases, stabilization of metastatic process in the liver was observed in 4 cases. It is noted that the size of metastatic foci, not exceeding 2 cm, in no case was not recorded continued growth. Continued growth was identified in those cases where the size of metastatic foci greater than 3, see Method PET-CT demonstrated the highest informativeness among all control methods.

**Conclusions:** The Findings suggest that RFA is an effective method of treatment of patients with metastatic liver cancer of various primary locations. The main advantage of this technique is minimally invasive, and as a result, short periods of hospitalization.

**Keywords:** Liver, Tumors, HCC, RFA

Transarterial Chemoembolization for Primary and Metastatic Liver Tumors
A. Akbayev, Zh. Ryspanbetov
Endovascular Surgery Department, Taraz Regional Oncology Center, Kazakhstan

**Aims:** To assess effectiveness of chemoembolization of hepatic artery (CEHA) in treatment of patients with metastatic colorectal cancer, and also to determine the optimal interval in combination of CEHA with other treatment methods.

**Methods:** The study includes analysis of the results of treatment of 30 patients with resectable metastases of colorectal cancer in the liver. The first group included 15 patients with resection made 1 week after CEHA. The second group consisted of 15 patients in whom resection operation was made 2 weeks after CEHA with subsequent assessment of morphological changes in metastases.

**Results:** Therapeutic pathomorphism was recorded in 25/30 patients. In the first group, therapeutic pathomorphism was observed in 13/15 patients. In 11/13 patients, the 2nd degree of therapeutic pathomorphism was recorded. In 2/13 patients – the 1st degree. In the second group, therapeutic pathomorphism was observed in 12/15 patients. In all patients the 2nd degree of therapeutic pathomorphism was recorded. No significant differences in the degree of therapeutic pathomorphism were recorded on the 7th and 14th day after regional chemotherapy (P = 0.436).

**Conclusions:** Hepatic artery chemoembolization is an effective method of treating patients with metastases of colorectal cancer in the liver. In use of chemoembolization of hepatic artery in combination with other surgical methods, the seven-day time interval is optimal.

**Keywords:** CEHA, Liver, Treatment, Tumor

Activated Human Hematopoietic Stem Cells Exhibit Antitumor Activity toward Hepatocellular Carcinoma in Vitro
Marlen Doskali, Yuka Tanaka, Shuji Akimoto, Hideki Ohdan
Hiroshima University Hospital, Department of Gastroenterological and Transplant Surgery, Japan

**PE-197**

**PE-198**
Aims: Hepatocellular carcinoma (HCC) recurrence rate after liver transplantation (LT) consists of 10%-20% and remains the leading cause of cancer-related death. We have successfully applied an adoptive immunotheraphy to liver cirrhotic patients with HCC in a phase I trial after LT. In our study we have shown that Interleukin (IL)-2/OKT3 stimulated lymphocytes, containing much of NK (natural killer)/NKT cells, from donor liver graft, have a vigorous anticancer effect. However, a single treatment with activated lymphocytes might lead to limited effects. We aimed to develop a new therapeutic approach for the efficient expansion of such innate components of cellular immunity obtained from the circulated hematopoietic stem cells (HSCs).

Methods: Human HSCs were cultured for 14 days in the presence of 5% AB-serum X-VIVO15 medium containing IL-7, IL-15, Flt3L (Fms-related tyrosine kinase 3 ligand), stem cells factor (SCF). Furthermore, the expanded cells were briefly (72 hours) pre-activated with IL-12 and IL-2 before the harvest. The phenotype and characterization of activated cells were identified by flow cytometric analysis and the cytotoxicity against tumor was determined by ¹¹¹Cr release assay.

Results: After being cultured for 17 days the proportion of cell fractions in the expanded HSCs varied among individuals. The average proportion of CD56^+CD3^-, CD56^-CD3^+ and CD56^-CD3^- was 15.4% (range, 3.1%-39.7%), 10% (range, 2.2%-37%) and 58.4 (range, 17.9%-91.8%), respectively. The brief pre-activation of expanded HSCs exhibit enhanced expression of IFN-γ, TNF-α, Granzyme B and TNF-related apoptosis-inducing ligand (TRAIL) on their surface. Furthermore, these cells showed vigorous anti-cancer ability in vitro, at an effector-target cell ratio of 40:1. NK cells destroyed 63% (±10.1) of HepG2, an HCC cell line.

Conclusions: These findings suggest that repeated adoptive immunotherapy using activated human HSCs might be a promising approach for inducing innate immunity to decrease the incidence of cancer recurrence after liver transplantation.

Keywords: Liver, Cancer, Transplantation
Methods: HCC cell line HepG2 cells were cultured. In order to investigate the effect of metformin on HepG2 cells according to glucose level, cells were cultured in 5mM glucose and 25mM glucose medium. 3-(4, 5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assays were performed to determine the effect of metformin on the cell proliferation. Apoptosis was measured by a cell death detection enzyme-linked immunosorbent assay and a caspase-3 activity assay. Expression levels of various proteins, with or without specific small interfering ribonucleic acid-induced gene disruption, were measured by Western blot analysis.

Results: Metformin induces apoptosis of HepG2 cells and reduces cell viability. However, the efficacy of metformin-induced apoptosis was reduced in the hyperglycemic environment (25mM glucose). Metformin reduced IGF-1R activity in HCC cells and decreased IRS-1, PI3K, and Akt activities in IGF-1R pathway, leading to increased TSC-2 activity and decreased mTOR activity. When AMPK siRNA was also used to block AMPK function, metformin caused HepG2 cell apoptosis. In addition, in the normal environment, metformin increased AMPK Thr 172 activity and decreased AMPK Ser 485 activation. However, AMPK Ser 485 activity was increased in hyperglycemic environment as well as AMPK Thr 172.

Conclusions: The inhibitory effect of metformin on HCC cells induces a decrease in IGF-1R activity by metformin and thus pro-
Liver Cancer Stem Cell Model with Lung Metastasis
Developed in the Microenvironment of Hepatocellular Carcinoma

Said M Afify, Ghmkin Hassan, Amira M Osman, Anna Sanchez Calle, Hend M Nawara, Md Jahangir Alam, Hager M Mansour, Hagar Ali Abu Quora, Juan Du, Maram H Zahra, Akimasa Seno, Yoshiaki Iwasaki, Masaharu Seno

Aims: Liver cancer considered malignant tumor in or on the liver, which contain different subpopulations, the root of these different subpopulations called cancer stem cells (CSCs). Liver CSCs have been regarded as the cells with specific stem cell-like features in the liver cancer tissue which responsible for tumor initiation growth, progression and metastasis. Lung metastasis considered the most extra-hepatic metastasis of liver cancer. Therefore, the use of metformin is helpful in the treatment of liver cancer, especially in hyperglycemia.

Methods: Mouse iPSCs cells were converted for 4 week to liver CSC-like cells in the presence of 50% Huh7cm. The medium was changed every day with fresh medium. The survived cells (5x10^6 cells) were injected into the liver of BALB/c nude mice. After 4 weeks malignant tumor was existed in the liver. During the operation, we detected metastatic nodules on the lung. We removed metastatic nodule and the primary tumor. Histopathologic examination and primary culture done for the primary tumor as well as the metastatic nodule. Expression of stem cell markers (Nanog, Oct3/4, Sox2, and Klf4) and CSC markers (CD44, CD90 and ALDH1) were confirmed by rt-qPCR in both the mIPS-Huh7cm cells, mIPS-Huh7cmP cells and Lung Metastatic nodule (LMN cells). Also, we compared the expression of mechanical marker (fibronectin, vimentin and N-Cadherin) and epithelial marker (E-Cadherin).

Results: We observed that the primary cells from the malignant tumor are rich in CSCs with high expression and expression of metastatic marker compared to converted and LMN cells. These results give us information about the metastatic potential of primary tumor cells which inter to circulation then metastatic to lung.

Conclusions: mIPS-Huh7cm cells considered as CSCs with metastatic potential in vivo. This model will be very important to understand the molecular mechanisms of metastasis.

Keywords: Cancer stem cells, Cancer research, Liver cancer
as well. Future studies considering other aspects that may influence the effectiveness of screening should follow.

**Keywords:** Screening, Liver cancer, Death

**PE-203**

**Cytochrome P450 4A11 Expression in Tumor Cells: A Favorable Prognostic Factor for Hepatocellular Carcinoma Patients**

Hyuk Soo Eun\(^1\), Sang Yeon Cho\(^2\), Byung Seok Lee\(^3\), Sup Kim\(^4\), In-Sang Song\(^5\), Kwangik Chun\(^6\), Cheong-Hae Oh\(^7\), Min-Kyung Yeo\(^8\), Seok Hyun Kim\(^9\), and Kyung-Hee Kim\(^10\)

\(^1\)Departments of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea; \(^2\)Department of Internal Medicine, Chungnam National University School of Medicine, Daejeon, Korea; \(^3\)Department of Internal Medicine, Chungnam National University School of Medicine, Daejeon, Korea; \(^4\)College of Medicine, Chungnam National University School of Medicine, Daejeon, Korea; \(^5\)Department of Microbiology, Infection Control Convergence Research Center, Medical Science, Radiation Oncology, Chungnam National University School of Medicine, Daejeon, Korea; \(^6\)Departments of Surgery, Chungnam National University Hospital, Daejeon, Korea; \(^7\)Department of Surgery, Chungnam National University School of Medicine, Daejeon, Korea; \(^8\)Departments of Pathology, Chungnam National University Hospital, Daejeon, Korea; \(^9\)Department of Pathology, Chungnam National University School of Medicine, Daejeon, Korea

**Aims:** Elevated cytochrome p450 (CYP) 4A gene expression has been linked to the aggravation of various cancers and affects various regulated metabolites. In hepatocellular carcinoma (HCC), the clinicopathological value of CYP4A has not yet been explored, although CYP4A is expressed at high levels in the liver. The goal of this study was to evaluate the clinicopathological value of CYP4A11 expression in HCC.

**Methods:** We performed immunohistochemical analysis of CYP4A11 and correlated the results with clinicopathological features of HCC (n = 155). Western blotting and reverse transcription–polymerase chain reaction against CYP4A11 and CYP4A22 were also performed for 15 and 20 pairs of fresh-frozen primary HCC and non-neoplastic liver tissue, respectively. Moreover, we analyzed the underlying mechanism by comparing the high and low CYP4A11 mRNA expression groups using gene set enrichment analysis.

**Results:** CYP4A11 expression level was higher in non-neoplastic hepatocytes than those in HCC cells (P < 0.001), and CYP4A11 expression positively correlated with favorable prognostic factors, including tumor size, histological grade, and pathological tumor stage (P = 0.007, P = 0.005, and P = 0.007). Multivariate analysis revealed that CYP4A11 expression was an independent prognostic factor of overall and disease-free survival (P = 0.002 and P = 0.033). Based on gene set enrichment analysis, high CYP4A11 mRNA expression negatively correlated with the expression of cell cycle-related genes.

**Conclusions:** These findings support the notion that CYP4A11 expression is a favorable prognostic factor of HCC and suggest potential predictive diagnostic and prognostic roles of CYP4A11 expression in HCC.

**Keywords:** Cytochrome P450 CYP4A11, Diagnosis, Hepatocellular carcinoma, Prognosis

**PE-204**

**Profiling Cytochrome P450 Family 4 Gene Expression in Human Hepatocellular Carcinoma**

Hyuk Soo Eun\(^1\), Sang Yeon Cho\(^2\), Byung Seok Lee\(^3\), In-Ock Seong\(^4\), Kyung-Hee Kim\(^5\)

\(^1\)Department of Internal Medicine, Chungnam National University Hospital, Daejeon 34952, Republic of Korea; \(^2\)Departments of Internal Medicine, Chungnam National University School of Medicine, Daejeon 35015, Republic of Korea; \(^3\)Departments of Pathology, Chungnam National University School of Medicine, Daejeon 35015, Republic of Korea

**Aims:** Cytochrome P450 family 4 (CYP4) enzymes are known as microsomal omega (ω)hydroxylases that metabolize fatty acids, eicosanoids, vitamin D and carcinogens. Thus, CYP4 enzymes may influence tumor development and progression. The aim of the present study was to evaluate the CYP4 expression profile in hepatocellular carcinoma (HCC) and its clinical relevance.

**Methods:** The present study obtained CYP4 mRNA expression data for 377 HCC cases from The Cancer Genome Atlas cohort and performed Kaplan Meier survival, Gene Ontology functional enrichment, and gene set enrichment analysis (GSEA). In addition, the level of CYP4F2 protein expression was evaluated in matched pairs of HCC and non tumor tissue samples and the results were correlated with the clinicopathological characteristics of HCC (n = 113).

**Results:** HCC survival analyses indicated better overall survival in patients with high CYP4F2, CYP4F12 and CYP4V2 mRNA expression levels; the results for histologic grade and Tumor-Node-Metastasis stage supported these data. GSEA revealed high levels of CYP4F2, CYP4F12 and CYP4V2 mRNA expression to be negatively correlated with expression of cell cycle-related genes. CYP4F2 protein expression was higher in non-neoplastic liver tissue than in HCC tissue and positively correlated with favorable pathological tumor stage (I versus II-IV) (P = 0.022) and was a good independent prognostic factor for overall survival (P = 0.004).

**Conclusions:** These findings demonstrate that the expression levels of genes CYP4F2, CYP4F12 and CYP4V2 are favorable prognostic factors in HCC and suggest the potential predictive diagnostic and prognostic roles of CYP4F2, CYP4F12 and CYP4V2 gene expression in HCC.

**Keywords:** Cytochrome P450 family 4, Hepatocellular carcinoma, Diagnosis, Prognosis
**PE-205**

Quantified Hepatic Stiffness by MR Elastography Is a Marker for Early Recurrence in Patients with HCC within the Milan Criteria

Hyo Jung Cho1, Bo Hyun Kim2, Hye Jin Kim2, Jini Huh2, Jai Keun Kim2, Jei Hee Lee1, Chul Won Seo2,3, Young-Hwan Ahn1, Jinhee Jung1, Jung Woo Eun1, Soon Sun Kim1, Sung Won Cho1, and Jae Youn Cheong1

1Department of Gastroenterology, 2Department of Radiology, Ajou University School of Medicine, Suwon, South Korea; 3Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, South Korea

**Aims:** Magnetic Resonance Elastography (MRE) is a non-invasive tool for measuring hepatic stiffness (HS) with high diagnostic accuracy. In this study, we tried to investigate whether quantified HS by MRE could predict the prognosis of patients with hepatocellular carcinoma (HCC) within the Milan criteria.

**Methods:** This study was designed as a retrospective study. The HCC patients within Milan criteria with available pre-treatment quantified HS by MRE were reviewed and those who achieved complete remission (CR) after hepatic resection, radiofrequency ablation, or trans-arterial chemoembolization were included. Cox regression and Kaplan-Meier analyses were performed to identify risk factors associated with recurrence or survival.

**Results:** A total of 110 HCC patients who underwent hepatic resection (n = 75), RFA (n = 11) or TACE (n = 24) were included. Higher liver stiffness (> 4.5 kPa; (hazard ratio [HR] = 3.65; 95% confidence interval [CI] = 1.63–8.18; P = 0.002) was identified as an independent risk factor for predicting early HCC recurrence. In the subgroup analysis for patients who underwent curative treatment (including hepatic resection and RFA), higher HS was also identified as an independent risk factor for predicting early HCC recurrence (HR = 5.95; 95% CI = 2.14-16.53; P = 0.001). There was no significant variable associated with liver transplantation-free-survival.

**Conclusions:** Pre-treatment HS measured by MRE is a potential biomarker for predicting early tumor recurrence in the patients with HCC within the Milan criteria after CR.

**Keywords:** Magnetic resonance elastography, Hepatocellular carcinoma, Hepatic stiffness, Recurrence

**PE-206**

Antiviral Treatment Status at Hepatocellular Carcinoma Development Affects Overall Survival in Chronic Hepatitis B Patients

Tae-Se Kim, Dong Hyun Sinn, Wonseok Kang, Geum-Youn Gwak, Yong-Han Paik, Moon Seok Choi, Joon Hyeok Lee, Kwang Cheol Koh, and Seung Woon Paik

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

**Aims:** Despite potent antiviral therapy for hepatitis B virus (HBV), some patients still develop hepatocellular carcinoma (HCC). Whether characteristics and prognosis of HCCs developed in such patients differ from those developed in antiviral treatment-naïve patients is unknown. We aimed to compare the prognosis of patients who developed HBV-related HCC while on long-term antiviral therapy and those who developed HBV-related HCC while treatment-naïve.

**Methods:** A total of 189 patients (127 without antiviral treatment history and 62 with more than 5 years of antiviral treatment history) diagnosed with modified UICC stage I HBV-related HCC between 2011 and 2013 were analyzed.

**Results:** During a median 5 years of follow-up, mortality was observed in 17 patients (9%). The overall survival was better in treatment-naïve patients compared to patients who have received antiviral therapy for more than 5 years (5-year overall survival rates: 93.2% vs 83.3%, respectively, P = 0.015). There was no significant difference in recurrence free survival between two groups (5-year recurrence free survival rates: 59.3% vs 61.8%, respectively, P = 0.612). In contrast, ALBI score at 12 months after HCC diagnosis improved in treatment-naïve patients (-0.03 ± 0.37) while it aggravated in patients who have been under antiviral therapy for 5 years or more (0.10 ± 0.26) (P = 0.006). Liver failure without HCC progression as a cause of morality was observed only in patients who have received antiviral therapy for more than 5 years (4 of 10 patients, 40% vs. 0%).

**Conclusions:** Worse survival in patients who develop HBV-related HCC after long-term antiviral therapy can be attributed to less potential for liver function improvement compared to those who develop HCC while treatment-naïve. More attention should be given to changes in liver function when treating patients who develop HCC despite long term antiviral therapy.

**Keywords:** Hepatocellular carcinoma, Antiviral treatment status, Overall survival, Liver function

**PE-207**

Hepatitis C Virus Genotype Affects the Survival of Patients with Hepatocellular Carcinoma

Bo Ra Kim1,2, Sang Soo Lee2,3, Hye Kyong Park1, Chang Bin Im1, Changjo Im1, Ra Ri Cha1, Wan Soo Kim1, Jae Min Lee1,2, Hyun Jin Kim1,2, Tae Hyo Kim1,2, Woon Tae Jung1,2, Ok-Jae Lee1,2

1Department of Internal Medicine, Gyeongsang National University School of Medicine and Gyeongsang National University Hospital, Jinju, Republic of Korea; 2Department of Internal Medicine, Gyeongsang National University School of Medicine; 3Department of Gastroenterology, Gyeongsang National University School of Medicine, Jinju, Republic of Korea

**Aims:** Hepatitis C virus infection is associated with an increased risk of hepatocellular carcinoma (HCC). Previous studies have shown that the survival of patients with HCC varies depending on the Hepatitis C Virus (HCV) genotype. However, the influence of HCV genotype on the survival of HCC patients treated with curative intent has not been fully elucidated. The purpose of this study is to investigate the impact of HCV genotype on survival of HCC patients treated with curative intent.

**Methods:** This was a retrospective cohort study of patients with HCC treated with curative intent at a single center over a 10-year period. The influence of HCV genotype on survival was evaluated using Kaplan-Meier survival analysis and Cox proportional hazards regression analysis.

**Results:** A total of 233 patients with HCC treated with curative intent were included in the analysis. The overall survival rate at 5 years was significantly lower in patients with HCV genotype 1a (14.0%) compared to patients with HCV genotype 1b (43.0%) (log-rank test, P = 0.001). After adjusting for covariates, the hazard ratio for HCV genotype 1a compared to HCV genotype 1b was 5.84 (95% CI: 2.10-15.83) (Cox regression, P = 0.001).

**Conclusions:** This study provides evidence that the HCV genotype significantly affects the survival of HCC patients treated with curative intent. Further research is needed to elucidate the mechanism by which HCV genotype influences the survival of HCC patients.
Factors Associated with Postprogression Survival in Advanced Hepatocellular Carcinoma Patients with Post-Sorafenib Progression Not Eligible for Regorafenib

Hye Yeon Kim1,2, Chang Wook Kim1,2, Sang Wook Choi1,2, Do Seon Song1, U Im Chang1, Jin Mo Yang1, Sung Won Lee1, Hae Lim Lee1, Nam Ik Han1, Sun Hong Yoo1,2, Jung Hyun Kwon1,2, Soon Woo Nam2, Pil Soo Sung1,2, Jeong Won Jang1,2, Si Hyun Bae1,2, Jong Young Choi1,2, Seung Kew Yoon1,2

1Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2The Catholic University Liver Research Center, Republic of Korea

Aims: We aimed to investigate the prognostic factors associated with postprogression survival (PPS) in advanced hepatocellular carcinoma (HCC) patients who showed radiological progressive disease (PD) following sorafenib monotherapy, and were not eligible for 2nd-line regorafenib treatment.

Methods: Total of 223 patients who were confirmed with radiological PD following sorafenib monotherapy from September 2008 to December 2017 were enrolled. We define those with Child-Pugh class A, ECOG PS 0 or 1 at progression, and who had tolerated sorafenib as candidates eligible for 2nd line regorafenib therapy.

Results: Among 223 patients with PD after sorafenib treatment, 126 (56.5%) patients met eligibility criteria for regorafenib treatment at first radiological confirmation of PD. The median PPS of the candidates for regorafenib treatment (12.1 months) was statistically longer (P = 0.001) than that of the non-candidates (3.2 months). Prognostic factor associated with good PPS in non-candidates for regorafenib therapy was absence of macrovascular invasion [hazard ratio = 0.5 (95% confidence interval 0.33-0.76)] at initial radiological PD.

Conclusions: Absence of macrovascular invasion at initial radiological PD following sorafenib may predict good PPS in advanced HCC patients who had progressed after sorafenib monotherapy and were not eligible for 2nd-line regorafenib treatment.

Keywords: Prognosis, Hepatocellular carcinoma, Sorafenib, Progression

---

Diagnostic Value of Protein Induced by Vitamin K Absence in Hepatocellular Carcinoma Patients with Normal Alpha-Fetoprotein Level

Cong Long Nguyen1,*, Truong Khanh Vu1, Minh Diep Luu1, Nghe Tinh Nguyen1, Thanh Nam Nguyen1, Manh Duy Vu1

1Hepato-Gastroenterology Department, Bach Mai Hospital, Vietnam; 2Thai Binh Medical College, Thai Binh, Vietnam

Aims: The aim of this study was the evaluation of the changes of protein induced by vitamin K absence (PIVKA-II) levels in hepatocellular carcinoma patients having normal Alpha-fetoprotein (AFP) levels.

Methods: A total of 83 patients diagnosed of hepatocellular carcinoma (HCC) based on histopathology with the normal level of AFP (≤20ng/mL) were tested by PIVKA-II (a cut-off value of 40 mAU/ml), and then classified the stage of liver cancer based on size, number of tumors, Child-Pugh score, vascular invasion and BCLC classification.

Results: A total 83 patients were enrolled and performed liver biopsy for the diagnosis of HCC. The average age of patients was 58 ± 9.6 years and the 69 patients (83.1%) were men. The mainly cause of HCC was HBV infection in 68 patients (81.9%), in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively. All patients having the normal AFP level, the proportion of patients with concentration of PIVKA-II increased in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively. All patients having the normal AFP level, the proportion of patients with concentration of PIVKA-II increased in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively. All patients having the normal AFP level, the proportion of patients with concentration of PIVKA-II increased in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively. All patients having the normal AFP level, the proportion of patients with concentration of PIVKA-II increased in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively. All patients having the normal AFP level, the proportion of patients with concentration of PIVKA-II increased in BCLC stages A, B, C and D of 43.4%, 37.4%, 13.3%, and 6%, respectively.
the PIVKA-II level was significantly higher in the vascular invasive group than in the non-vascular invasive group (P = 0.03).

**Conclusions:** PIVKA-II was a maker that could improve the diagnostic of hepatocellular carcinoma in patients with normal AFP value.

**Keywords:** PIVKA-II, Hepatocellular carcinoma, AFP, Live cancer

---

### PE-210

**Comparing Characteristics, Treatment Outcomes of Non-B Non-C Virus and Hepatitis Virus-Related Hepatocellular Carcinoma**

Dong Duc Hoang

Thai Nguyen University of Medicine And Pharmacy, Vietnam

**Aims:** To compare the clinical characteristics, treatment outcomes of hepatocellular carcinoma (HCC) due to viral B, C hepatitis and non-B, non-C patients.

**Methods:** This prospective study involved 118 patients divided into the viral HCC group (76 patients) and non B,C HCC (NBC-HCC) group (42 patients). All patients were underwent one session of transcatheter chemoembolization (TACE) procedure. Two groups of patients were compared in rate of baseline characteristics. An AFP response was defined as a decrease in AFP at least 50% after treatment. Imaging response was evaluated according to the modified Response Evaluation Criteria in Solid Tumours (mRECIST).

**Results:** The differences of the age, gender, Child-Pugh score, BCLC score, tumor location, number of tumor, size of tumor, branch portal vein thrombosis before treatment between the viral-HCC group and NBC-HCC group were not statistically significant (P > 0.05 for all). Changes in mean of size of the tumor and AFP level both group after treatment were significant, P < 0.05. Comparing achievement of stagnant arterial flow, in viral-HCC group rate of complete occlusion was 61.8%, in NBC-HCC group was 59.5%, P = 0.6. 40.8% patients with AFP response were identified in viral-HCC group, this rate in NBC-HCC group was 71.4%, P = 0.001. Tumor response rate in viral-HCC was not significantly different from NBC-HCC (72.4% and 78.6%, P = 0.6).

**Conclusions:** NBC-HCC patients presented same clinical characteristics as compared with viral HCC. Despite the state, NBC-HCC patients had better outcome in AFP response than virus-related HCC.

**Keywords:** Hepatocellular carcinoma, Viral hepatitis, Transarterial chemoembolization

---

### PE-211

**Lenvatinib Is Independently Associated with the Reduced Risk of Progressive Disease When Compared to Sorafenib in Patients with Hepatocellular Carcinoma**

Kyung Hyun Kim\(^1\), Beom Kyung Kim\(^2,3\), Jun Yong Park\(^2,3\), Sang Hoon Ahn\(^1,3\), Kwang-Hyub Han\(^1,3\), Do Young Kim\(^1,3\), and Seung Up Kim\(^1,3\)

\(^1\)Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; \(^2\)Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Republic of Korea; \(^3\)Yonsei Liver Center, Severance Hospital, Seoul, Republic of Korea

**Aims:** Treatment outcome of lenvatinib is not inferior to that of sorafenib in treating patients with unresectable hepatocellular carcinoma (HCC). We compared treatment outcomes of lenvatinib and sorafenib and identified independent predictors of progressive disease (PD) at early time-point in patients with unresectable HCC.

**Methods:** Patients with unresectable HCC treated with lenvatinib (n = 10, 26.3%) or sorafenib (n = 28, 73.7%) between October 2018 and December 2019 were retrospectively recruited. The treatment response was assessed using the modified RECIST criteria.

**Results:** Patients treated with lenvatinib were likely to have ECOG 1 (vs. 0) performance (30.0% vs. 10.7%), larger maximal tumor size (mean 6.9 vs. 3.3 cm), and less macroscopic portal vein invasion (80.0% vs. 32.1%) than those treated with sorafenib (all P < 0.05). During the follow-up (median 2.0 months), 17 (44.7%) patients experienced PD. The proportion of Child-Pugh class B (vs. A) and multiple tumors were significantly higher in patients treated with lenvatinib than those treated with sorafenib (all P < 0.05). On multivariate analysis, lenvatinib was independently associated with the reduced risk of PD (odds ratio=0.098, 95% confidence interval, 0.010–0.952, P = 0.045), whereas multiple tumor was independently associated with the increased risk of PD (odds ratio=14.665, 95% CI, 1.670–128.787, P = 0.015). The progression-free survival tended to be longer in patients treated with lenvatinib than those treated with sorafenib (4.1 vs. 2.0 months, P = 0.059 by log-rank test).

**Conclusions:** Lenvatinib was better is progress-free survival than sorafenib in unresectable HCC. Large-scale study is required for validation in Korean cohort.

**Keywords:** Hepatocellular carcinoma, Lenvatinib, Sorafenib
unknown. The aim of this study was to identify the risk and risk factors of recurrence among patients who did not experience recurrence for long period.

**Methods:** A total of 1451 consecutive patients (median: 55 years old, male: 79.0%, hepatitis B virus: 76.7%) with good liver function (Child-Pugh class A) who were diagnosed with early stage HCC, and received radiofrequency ablation or resection as initial treatment between 2005 and 2010 were analyzed. Among them, 477 patients were alive and without recurrence at 5-years.

**Results:** During a median follow-up period of 8.1 years, 961 patients (66.2%) experienced HCC recurrence. The cumulative recurrence rates at 2-year and 5-year were 39.2% and 57.8%, respectively. Of the 477 patients who were alive and without recurrence at 5-years, 122 patients (25.5%) experienced recurrence. For them, the next 5-year cumulative recurrence rate was 30%. While sex, albumin-bilirubin grade, alphafetoprotein (AFP) level, tumor number, maximal tumor diameter and treatment modality at diagnosis were associated with early recurrence (within 2 years), sex, fibrosis-4 (FIB-4) score, and AFP levels were associated with further HCC recurrence among patients who did not experience recurrence for more than 5-years.

**Conclusions:** HCC recurrence rate was substantially high even after five years of no-recurrence period after HCC treatment. HCC patients warrant continued HCC surveillance even after five years of no-recurrence period, especially for men, high FIB-4 score, and elevated AFP levels at 5-years.

**Keywords:** Hepatocellular carcinoma, Recurrence, Early stage, No-recurrence period

---

### PE-213

**Indications for Endoscopic Screening and Prophylaxis of Esophageal Varices in Patients with Hepatocellular Carcinoma Invading Portal Vein**

Jihye Lim1, Ha Il Kim1, Ju Hyun Shim1,2, Jonggi Choi1,2, Danbi Lee1,2, Kang Mo Kim1,2, Young-Suk Lim1,2, Han Chu Lee1,2, Young-Hwa Chung1,2, Yang Sang Lee1,2, and Dong Jin Suh1

1Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; 2Asan Liver Center, Asan Medical Center University of Ulsan College of Medicine, Seoul, Korea; 3KMP Healthcare Seoul Clinic, Korea

**Aims:** Given the short life expectancy of patients with hepatocellular carcinoma (HCC) and portal vein tumor thrombosis (PVTT) probably yielding increased portal pressure, we aimed to identify risk factors for high-risk esophageal varices and potential predictors for variceal bleeding, in order to determine indications for variceal screening and prophylaxis in such patients.

**Methods:** This study included 255 asymptomatic patients with HCC-PVTT registered in a hospital-based cancer registry of Asan Medical Center. All patients experienced upper endoscopy for variceal screening and had no prior history of variceal hemorrhage or endoscopic prophylaxis. We examined clinico-endoscopic risk factors of high-risk varices, defined as large/medium varices or small varices with red-color sign, in the entire patients, and subsequently, significant predictors for variceal hemorrhage in a subset of 106 patients with any grade of varices.

**Results:** Of the 255 patients screened by endoscopy, 60 (23.5%) had high-risk varices; and 149 (66.2%) did not have varices, with 31 (12.2%) having solitary or combined gastric varices. Most of patients had Child-Pugh class A liver function; one-third did infiltrative tumors; and one-fifth did metastatic lesions. In terms of patterns of PVTT, Vp2, Vp3, and Vp4 disease existed in 87 (34.1%), 65 (25.5%), and 103 (40.4%) respectively. As initial therapy for HCC, chemoembolization (67.5%) was most common, and radiotherapy for PVTT was done in 32.5% of the patients. Vp4 grade and low platelet count were independently correlated with high-risk varices. A total of 18 bleeders (7.1%) with 11 high-risk (18.3%) and 7 low-risk (3.6%) varices occurred during the median follow-up of 13.8 months. Multivariate Cox analysis revealed that infiltrative HCC and red-color sign on varices were significant predictors of variceal bleeding over time, as were not beta-blockers, radiotherapy, sorafenib treatment and the degrees of Vp, coagulopathy and hepatic function. Neither high-risk varices nor variceal bleeding did not affect survival of patients (log-rank test, P = 0.179 and P = 0.867, respectively).

**Vp2:** segmental branches of portal vein or above, Vp3: lobe large branches of portal vein, Vp4: the main trunk of portal vein or superior mesenteric vein or inferior vein cava.

**Conclusions:** Our data indicate that variceal screening should be considered in patients with HCC-PVTT extending to the major PVTT, and prophylactic variceal ligation may be needed in selected patients.

**Keywords:** Esophageal varix, Variceal bleeding, Hepatocellular carcinoma, Portal vein tumor thrombus

---

### PE-214

**Alpha-Fetoprotein L3 Level, Not an L3 Fraction, Is an Useful Marker for the Diagnosis of Hepatocellular Carcinoma**

Han Ah Lee, Hyun Gil Goh, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Sang Jun Suh, Young Kuk Jung, Ji Hoon Kim, Yeon Seok Seo, Hyung Joon Yim, Jong Eun Yeon, Kwan Soo Byun, Soon Ho Um

Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

**Aims:** Though serum lens culinaris agglutinin-reactive fraction of α-fetoprotein (AFP-L3) level has been proposed as a potential diagnostic marker of hepatocellular carcinoma (HCC), it is still controversial whether AFP-L3 level has higher accuracy than other markers.

**Methods:** Total 411 patients who underwent AFP and AFP-L3 tests were included. AFP-L3 level was estimated with the following formula: AFP-L3 level (ng/mL) = serum AFP level (ng/mL) × L3 fraction (%).


**Results:** Among total 411 patients, 150 (36.5%) patients had no underlying liver disease, 150 (36.5%) patients had chronic liver disease without HCC, and 111 (27.0%) patients had HCC. Except for patients with no underlying liver disease, chronic hepatitis B was the most common underlying liver disease (155 patients, 37.7%). All patients had imaging test, 66 (16.1%) patients had no space-occupying lesion (SOL), 111 (27.0%) patients had HCC, 20 (4.9%) had dysplastic nodule, 214 (52.0%) patients had benign nodules. The area under the receiver operating characteristics curve (AUROC) of AFP-L3 level, AFP level, and AFP-L3 fraction were 0.812 (95% confidence interval [CI], 0.771-0.848), 0.768 (95% CI, 0.724-0.808) and 0.797 (95% CI, 0.755-0.835). AUROCs of AFP-L3 level were significantly higher than AFP level for the diagnosis of HCC (P < 0.001).

There were no significant differences between the AUROCs of AFP level and AFP-L3 fraction (P = 0.1645), and those of AFP-L3 level and AFP-L3 fraction (P = 0.2886). With the cut-off value of 5.1 ng/mL, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of AFP level were 73.0%, 65.7%, 44.0% and 86.8%. While, with the cut-off value of 2.5 ng/mL, the sensitivity, specificity, PPV and NPV of AFP-L3 level were 72.1%, 80.3%, 57.6% and 88.6%.

**Conclusions:** AFP-L3 level, rather than L3 fraction, is more useful marker for the diagnosis of HCC than serum AFP level. **Keywords:** Lens culinaris agglutinin-reactive fraction of α-fetoprotein, Hepatocellular carcinoma, Tumor marker

---

**Clinical Manifestations and Prognosis of Non-Cirrhotic and Cirrhotic Hepatocellular Carcinoma Patients with Chronic Hepatitis B**

**Jung Hwan Yu, Jongbeom Shin, Young-Joo Jin, Jin-Woo Lee**

Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, Incheon, South Korea

**Aims:** The differences of the clinical features and survival outcomes between cirrhotic and non-cirrhotic HCC patients with hepatitis B virus (HBV) infection remain to be determined. We evaluated clinical characteristics and prognosis of non-cirrhotic HBV-associated HCC patients compared with cirrhotic patients.

**Methods:** Between January 2005 and December 2015, 1,345 patients were diagnosed to have HCC at our hospital. Of these, 860 HBV-associated HCC patients with cirrhosis (cirrhotic group, n = 519, 60.3%) or without cirrhosis (non-cirrhotic group, n = 341, 39.7%) were retrospectively analyzed. Propensity score matching (PSM) was used to adjust for differences between the two groups.

**Results:** The non-cirrhotic group had lower Child-Turcotte-Pugh (CTP) classes, greater tumor sizes, and were less likely to have portal vein thrombosis than the cirrhotic group. Age and gender were not significant different between the two groups. Cumulative overall survival (OS) rates at 2, 4, 6, and 8 years after treatment were significantly higher in the non-cirrhotic group (67.2%, 57.1%, 43.2%, and 38.3% vs. 58.3%, 41.3%, 33.2%, and 27.8%, respectively, p-value < 0.001). However, no significant intergroup difference in OS rates was observed after PSM (p-value = 0.680). Significant predictive factors of OS were CTP class, tumor size, tumor number, and curative-intended treatment for the cirrhotic group.

**Conclusions:** After PSM, cumulative OS rates were no difference between HBV-related HCC patients with and without cirrhosis, and they were clearly dependent on CTP class, regardless of the presence of cirrhosis itself both in cirrhotic and non-cirrhotic patients.

**Keywords:** Hepatitis B, Cirrhosis, Hepatocellular carcinoma

---

**Albumin-Bilirubin Grade Can Subclassify Patients with a Child-Pugh Score of 5 Treated with Sorafenib for Hepatocellular Carcinoma**

**Hye Yeon Kim,1,2 Chang Wook Kim,1,2 Sang Wook Choi,1,2 Do Seon Song,1,2 U Im Chang,1,2 Jin Mo Yang,1,2 Sung Won Lee,1,2 Hae Lim Lee,1,2 Nam Ik Han,1,2 Sun Hong Yoo,1,2 Jung Hyun Kwon,1,2 Soon Woong Nam,1,2 Seawon Hwang,1,2 Pil Soo Sung,1,2 Jeong Won Jang,1,2 Si Hyun Bae,1,2 Jang Young Choi,1,2 Seung Kew Yoon,1,2**

1Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 2The Catholic University Liver Research Center, Republic of Korea

**Aims:** The Albumin-Bilirubin (ALBI) grade is a recently developed index to assess hepatic reserve and prognosis in patients with hepatocellular carcinoma (HCC). We aimed to investigate the prognostic value of ALBI grade in advanced HCC patients who received sorafenib.

**Methods:** From September 2008 to October 2017, a total of 786 consecutive patients with advanced HCC who received sorafenib monotherapy were retrospectively included from six University hospitals in Korea. Serum albumin and bilirubin values were used to determine ALBI grade. Overall survival was stratified by ALBI grade using the Kaplan-Meier method. A Cox proportional hazard model was used to identify independent factors for influencing overall survival.

**Results:** Hepatitis B virus-related HCCs comprised 75.4% (593/786) of enrolled patients. Among 786 enrolled patients, 161 (20.5%), 555 (70.6%), and 70 (8.9%) were classified as ALBI grade 1, 2, and 3, respectively, in baseline. Majority of the patients with ALBI grade 1 (150/161, 93.1%) had a Child-Pugh score of 5. Among patients with ALBI grade 2, 30.9% (172 patients) had a Child-Pugh score of 5 and 52.3% (290 patients) had a Child-Pugh score of 6. The median OS was 16.5, 10.1, and 7.4 months for ALBI grade 1, 2, and 3, respectively (P < 0.001). Cox regression analysis showed that baseline ALBI grade strongly influenced the mortality of HCC patients receiving sorafenib. Among patients with a Child-Pugh score of 5, overall survival was significantly different between patients with
Differentiation between Hepatocellular Carcinoma and Other Hepatic Malignancy in Cirrhosis: Performance of LI-RADS 2018

Yeun-Yoon Kim1,3, Myeong-Jin Kim1, Eun Hwa Kim2, Yun Ho Roh1, Chansik An1

1Department of Radiology, Biostatistics Collaboration Unit, Department of Biomedical Systems Informatics, Severance Hospital, Yonsei University College of Medicine; 2Department of Radiology, Samsung Medical Center, Korea

Aims: To evaluate the diagnostic accuracy of Liver Imaging Reporting and Data System (LI-RADS) v2018 for differentiating between hepatocellular carcinoma (HCC) and other hepatic malignancy (OM) in patients with liver cirrhosis.

Methods: From 2008 to 2017, 55 patients with untreated OM and liver cirrhosis were eligible for this retrospective case-control study (mean age, 58 ± 10 years; 45 men and 10 women). Controls consisted of 165 treatment-naïve patients with HCC and liver cirrhosis (mean age, 58 ± 10 years; 134 men and 31 women). Two radiologists blinded to the final diagnosis independently and retrospectively determined the presence of LR-M features and major HCC features (nonrim arterial phase hyperenhancement, nonperipheral washout, and enhancing capsule). The diagnostic performances of each imaging feature, LR-M criteria, and LR-5 criteria were calculated and compared by using the generalized estimating equation method.

Results: Individual LR-M features had sensitivity of 9–71% and specificity of 83–97% for diagnosing OM. Major features of HCC had sensitivity of 62–83% and specificity of 69–89% for diagnosing HCC. The LR-M criteria had sensitivity of 89% (95% confidence interval [CI], 81–97) for diagnosing OM, with specificity of 48% (95% CI, 40–56). The LR-5 criteria had a sensitivity of 74% (95% CI, 67–81) for diagnosing HCC, with a specificity of 89% (95% CI, 81–97). The accuracy of LR-5 criteria was higher than that of LR-M criteria (78% [95% CI, 72–83] vs. 58% [95% CI, 52–65], P < .001).

Conclusions: The LR-5 and LR-M criteria provide comparable performances for differentiating between hepatocellular carcinoma and other hepatic malignancy with LI-RADS v2018.

Keywords: Cirrhosis, Diagnosis, Liver cancer, Magnetic resonance imaging

Epidemiological and Clinical Features of Patients with HCC in Mongolian and Russian Population

Baatarkhuu. O1,2, Tsogolmaa Oidov3, Igor Malov2, Evgeniy Savilov4, Sergey Malov2, Rodion Rasulov, and Victoriaya Voronchenko2, Ariunaa Kh4, Sanduijav R, and Baasanjav N5,7

1Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 2Irkutsk State Medical University, Russian Federation; 3Irkutsk State Medical Academy of Continuing Education, Russian Federation; 4National Cancer Center, Ulaanbaatar, Mongolia; 5Ach Medical University, Ulaanbaatar, Mongolia; 6Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia; 7Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Aims: Among all oncological diseases, liver cancer is the 3rd in Mongolian and 5th in Russian most common. We sought to describe the clinical and epidemiological characteristics and outcomes of HCC patients from Mongolia and Russia.

Methods: The studies were carried out in the cross-border regions of Mongolia and Asian part of Russia in the Lake Baikal region (Irkutsk region). 349 patients with hepatocellular carcinoma (HCC) of the Caucasian and Mongolia races were enrolled in the study.

Results: HCC incidence (2015) shows more unfavorable trends in the territory of Mongolia (7.45 per 100,000 total population) compared to Asian region of Russia (8.45 per 100,000). Patients from Mongolia often have a history of jaundice and acute hepatitis, HCC patients in Mongolia are related with HBV or HCV in 94.4% and 76.0% in Russia. Out of the etiological factors HCC is more often associated with the hepatitis B virus in Mongolia (34.4%) than in the Asian part of Russia (17.1%). At the same time, in Caucasians, HCC developed primarily on the background of liver cirrhosis.

Conclusions: Mongolia in terms of the incidence of HCC belongs to the hyper endemic regions of the world. In this country, among the risk factors, HBV continues to play a big role. Due to the high incidence and late diagnosis in both countries, there is a need to develop a national strategy for early diagnosis and treatment of patients with HCC.

Keywords: Liver cancer, Epidemiology, Mongolia, HCC

Management of Hepatocellular Carcinoma in Mongolia

Ariunaa Khabsbazar1,3, R. Sanduijav2, Baasanjav N3,5, and O. Baatarkhuu1,4,5

1Department of Chemotherapy, National Cancer Center, Ulaanbaatar, Mongolia; 2Mongolian National University of Medical Sciences; 3Ach Medical University, Mongolia; 4Mongolian association for the Study of Liver Diseases; 5Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Aims: This study will evaluate the efficacy of selective internal
radiation therapy (SIRT) using SIR-Spheres® yttrium-90 resin microspheres compared to sorafenib in the treatment of patients with locally advanced hepatocellular carcinoma (HCC).

Methods: Total 360 patients were enrolled to the study from 27 sites of Asia-Pacific 11 countries. The National Cancer Center of Mongolia was one of the sites this study and we were recruited a total 39 patients into the study from March 2011 to June 2016 in Mongolia. This multicenter, phase III, randomized-controlled clinic trial, we randomly assigned patients with advanced hepatocellular carcinoma who had not received surgical therapy for HCC to receive sorafenib (at a dose of 400mg twice daily) or yttrium-90 resin microspheres by the transarterial route.

Results: Among the 39 patients recruited in Mongolia, 19 received at least one dose sorafenib and 20 received SIRT treatment in Singapore; these patients were included in the safety analysis. Adverse events that were reported for patients receiving sorafenib were predominantly grade 1 or 2 in gastrointestinal, constitutional and dermatologic in nature. The most frequently reported drug-related adverse events in patients treated with sorafenib were hypertension, hand-foot skin reaction, diarrhea, alopecia, fatigue. Common procedure-related adverse events were usually mild (grade 1/2) and included nausea and vomiting (27.7% all grades) and abdominal pain (22.1% all grades), with very few grade 3.

Conclusions: We found that patients treated SIRT had significantly fewer total numbers of adverse events (p 0.0964) when compared with those treated with sorafenib.

Keywords: HCC, Management, Mongolia

PE-220
Evaluation of the American Joint Committee on Cancer (AJCC) 8th Edition Staging System for Hepatocellular Carcinoma in 1,034 Patients with Curative Resection
Sang Yun Ha1, Sujin Park1, Sangjoon Choi1, Dong Hyun Sinn1, Jong Man Kim2
1Department of Pathology and Translational Genomics, Samsung Medical Center; Sungkyunkwan University School of Medicine, Seoul, Korea; 2Department of Internal Medicine, Samsung Medical Center; Sungkyunkwan University School of Medicine, Seoul, Korea

Aims: Recently, 8th edition staging system of the American Joint Committee on Cancer (AJCC) was released with change in T stage. We validated the prognostic value of the new AJCC staging system in comparison to the previous 7th edition.

Methods: Total 1,034 patients who had undergone curative resection as the initial treatment for hepatocellular carcinoma (HCC) at Samsung Medical Center, Seoul, Korea, between 2008 and 2012, were enrolled in this study. Pathology T stage was determined by AJCC 7th and 8th edition, respectively. Recurrence free survival (RFS) was estimated using the Kaplan-Meier method and compared by log-rank test. The analysis of the time dependent receiver-operating-characteristic (ROC) curves for censored survival data was used to compare the capability of the two models to predict tumor recurrence.

Results: The median follow up period was 64.9 months (range: 0.8-112.5 months). The 1-, 3- and 5-year RFS rates were 77.7%, 61.8% and 56.4%, respectively. Among 477 T1 patients by 7th edition, 157 were re-classified as T1a, and 320 as T1b by 8th edition. Stage migration was observed in 65 patients (6.3%); from T2 to T1a in 45 patients and from T3 to T4 in 20 patients. AJCC 7th edition and 8th edition showed similar predictive ability, and the 2 year AUC value were comparable in 7th and 8th edition (0.693 vs. 0.690). RFS was not different between T1a and T1b by 8th edition (P = 0.256). For solitary tumors ≤2 cm (T1a by 8th edition), those with microvascular invasion (n = 54) had shorter RFS than those without it (n = 171) (P = 0.016), although there is no such distinction in 8th edition. Tumors involving a major branch of portal vein or hepatic vein (T4 by 8th edition and T3b by 7th edition, n = 20) showed shorter RFS than multifocal tumors at least one of which is >5 cm (T3 by 8th edition and T3a by 7th edition, n = 40) (P = 0.017), supporting the change in 8th edition. RFS was comparable between solitary tumors ≥2 cm with vascular invasion (n = 375) and multifocal tumors ≤5 cm (n = 92), which were classified as a single category T2 in both 7th and 8th editions. For multifocal tumors ≤5 cm, survival showed no difference according to presence of vascular invasion.

Conclusions: The AJCC 8th edition staging system for HCC showed comparable predictive performance to the 7th edition. It is desirable in future revision to consider sub-stratification of solitary tumors ≤2 cm (T1a) depending on the presence of vascular invasion, which is not included in 8th edition. Further studies are required to validate these findings.

Keywords: Hepatocellular carcinoma, Prognosis, Stage, AJCC

PE-221
Application of Multimodal Image Fusion Technology in the Diagnosis and Treatment of Intrahepatic Cholangiocarcinoma
Chihua FANG
Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, China

Aims: To explore the value of multimodal image fusion in pre-operative planning and intraoperative navigation of intrahepatic cholangiocarcinoma (ICC).

Methods: Clinical data of 11 patients with intrahepatic cholangiocarcinoma who underwent multimodal image fusion technology from January 2018 to September 2018 in the Department of Hepatobiliary, Zhujiang Hospital were retrospectively analyzed. CT enhanced scan and MRI enhanced scan with gadoxetate disodium (Gd-EOB-DTPA) of the upper abdomen were respectively performed, and 3D models of individualized
An Astonishing Familiar Cluster of Intrahepatic Cholangiocarcinoma (ICC) in Wilson’s Disease (WD)

Giovanni BRANDI1, Alessandro RIZZO1, Andrea PALLONI1, SimonAVOVAR1, Francesca ABBATTI1, Stefania DE LORENZO1, Giorgio FREGA2, Francesco VASURI4, Annalisa ASTOLFI4, Valentina INDIO4, Francesco TOVOLI4, Matteo CESCON4

1Department of Experimental, Diagnostic and Speciality Medicine, S. Orsola Malpighi Hospital, University of Bologna, Bologna, “F. Addarii” Institute of Oncology and Transplantation Pathology, S. Orsola Malpighi Hospital, University of Bologna, Bologna, “Giorgio Prodi” Cancer Research CenterUniversity of Bologna, Bologna, Italy, Division of Surgery and Transplantation, S. Orsola Malpighi Hospital, University of Bologna, Bologna, Italy

Aims: According to literature, the rate of hepatobiliary malignancies in WD is low; occasional cases of hepatocellular carcinoma (HCC) have been reported with even rarer incidence of ICC. We report the case of a family with WD in which two siblings, Mr F and Mr G, developed ICC at the ages of 56 and 60 respectively while their sister was affected by WD without liver malignancies. The two malignancies were treated with surgical resection and the patient is currently without any evidence of recurrence of the disease after four years.

Conclusions: While the reasons for the low incidence of ICC in WD remains obscure, we underline the exceptional findings of two ICC in two siblings in absence of additional definite risk factors, one of which showed complete response to chemotherapy.

Serologic Detection of Autoantibodies from Patients with Cholangiocarcinoma by Proteomic Approach

Mohammad Zahid MUSTAFA1, Zunera TANVEER1, Eric BALLOT1, Jean Charles DUCLOS VALLEE1

1Center for Advanced Studies in Virology and Biotechnology (CASVAB), University of Balochistan, Quetta, Pakistan; 2Department of Physiology, Bolan University of Medical and Health Sciences, Quetta, Pakistan; 3Département d’Immunologie Biologique, AP-HP Hôpital Saint Antoine, 75012, Paris, France; 4Inserm, Unité 1193, Université Paris-Saclay, 94800, Villejuif, France

Aims: Autoantibodies can be used clinically for cancer detection which can be identified by proteomic analysis of tumor associated antigens (TAAs) that are potentially involved in malignant transformation. The purpose of the present study was to detect the autoantibodies in sera of patients with cholangiocarcinoma by serological proteomic approach for early cancer diagnosis.

Methods: Serum samples were obtained from 9 patients with CC and from 5 healthy volunteers. The European Cell Culture Bank provided cholangiocarcinoma cell lines (CCSW1 and CCLP1). Proteins were separated using 2 DE. Then proteins were transferred on to nitrocellulose membrane and proteins were detected using enzyme conjugated secondary antibody and ECL substrate (enhanced chemiluminescent) generated signals were visualized by X-films. Silver staining was used to see the migration pattern on gels.

Results: 2-D electrophoresis maps of CC cell lines shown different protein distributions. After silver staining, an average of 160-180 spots were detected from CCSW1, mainly between pH 4 and 8, with molecular weight ranging from 40 to 90 kDa. With CCLP1, between 80 and 100 spots were distributed in acidic parts of the map with MW from 20 to 90 kDa. By comparative blotting analysis, four common immunoreactive spots were found in CCSW1 blots with and two out of nine CC patient sera but not with control sera, whereas two common immunoreactive spots were found only with control sera. With CCLP1, no common spot observed in immunoblots with CC sera.

Conclusions: The detected immunoreactive protein spots might correspond to the autoantibodies produced to the homologous tumor associated antigens.
Predictive Factors and Treatment Outcome for Recurrent Intra-Hepatic Cholangiocarcinoma

Yauren CHANG1, Chun-Yi TSAI1, Shang-Yu WANG1,2, Kun-Ming CHAN1, Wei-Chen LEE2, Tse-Ching CHEN2, Yi-Yin JAN1, Chun-Nan YEH1,2, Ta-Sen YEH1,2

1General Surgery, Chang Gung Memorial Hospital, Linkou, 2Pathology, Chang Gung Memorial Hospital, Linkou, Taiwan, 3Liver Research Center, Chang Gung Memorial Hospital, Chang Gung University, Taoyuan, Taiwan

Aims: Intrahepatic cholangiocarcinoma (ICC) had devastating outcome owing to advanced stage at diagnosis and high recurrence after hepatectomy. There is no consensus on treatment for recurrent ICC. We aim to explore predictive factors and treatment outcome for recurrent ICC.

Methods: 160 out of 216 ICC (71.4%) patients experiencing recurrence underwent curative resection from 1977 to 2014. We categorized the recurrent pattern into intra-hepatic involvement (group A, n = 75), locoregional involvement (group B, n = 80), and distant metastasis (group C, n = 65).

Results: Larger tumor size and vascular invasion independently predict ICC recurrence. For group A patients, gross pathological morphology and vascular invasion were the two independent predictive factors. For group B patients, larger tumor size was the only independent predictive factor. For group C patients, larger tumor size and hepatolithiasis were the two independent predictive factors. Further subdivision disclosed patients with merely intrahepatic recurrence had superior overall survival (OS) compared with those beyond intrahepatic recurrence (P < 0.0001). Twenty-seven out of 160 patients underwent repeat hepatectomy or/with metastatectomy for recurrence (16.8%), who had superior OS to the rest 133 patients received other treatment modalities (85.6 versus 20.9 months, P < 0.001). Twelve group A patients and 11 group B patients underwent surgery had significantly favorable post-recurrence OS, when compared with those did not (61.6 versus 14.7 and 29.2 versus 8.2 months, respectively, P < 0.05).

Conclusions: Aggressive tumor behavior determines high risk of recurrence, however, intrahepatic recurrence may have favorable prognosis. Furthermore, aggressive hepatectomy or/ with metastatectomy in selected patients may provide survival benefit in highly selected patients.

Efficacy of Sorafenib Alone and in Combination with Rapamycin Inhibitors for Post-Liver Transplant Recurrence of Hepatocellular Carcinoma: A Single Center Experience

Ji Hoon Park1, Jae Seung Lee1, Jae Geun Lee1,2, Beom Kyung Kim1,2, Seung Up Kim1,2, Dong Jin Joo1,2, Do Young Kim1,2, Sang Hoon Ahn1,2, Myoung Soo Kim1,2, Soon Il Kim1,2, Kwang-hyub Han1,2, and Jun Yong Park1,2

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; 2Yonsei Liver Center, Yonsei University Health System, Seoul, Korea; 3Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

Aims: We investigated the efficacy of sorafenib alone and in combination with a mammalian target of rapamycin (mTOR) inhibitor for the patients with recurrent hepatocellular carcinoma (HCC) after liver transplantation (LT).

Methods: 38 patients, who used tacrolimus as an immunosuppressive agent, diagnosed with recurrent HCC after LT and initiated sorafenib between 2008 and 2019, were retrospectively analysed. Kaplan-Meier analyses were used to calculate progression-free survival (PFS) and overall survival (OS).

Results: The median age of 33 males and 5 females was 53.7 years. 35 (92.1%) and 2 (5.3%) patients had chronic hepatitis B and C, respectively. The median OS from LT was 837.5 days. The median OS and PFS from sorafenib initiation were 453 and 178 days, respectively. 21 patients (55.3%) added mTOR inhibitor with tacrolimus at the time of initiating sorafenib. There was no significant difference of baseline variables whether mTOR inhibitor user or not, except male gender (12 [70.6%] in mTOR inhibitor plus sorafenib user vs. 21 [100%] in sorafenib treatment, P = 0.012). The treatment outcomes of sorafenib in combined mTOR inhibitor users were not significantly better compared to sorafenib treatment; the median OS and PFS from sorafenib initiation were 659 (vs. 398) and 230 (vs. 120) days, respectively (All P > 0.05).

Conclusions: In a single center experience, combined treatment with sorafenib and mTOR inhibitor was not superior comparing to tacrolimus-mono therapy when perform sorafenib treatment for recurrent HCC after LT.
Initial Real-Life Experience of Nivolumab Treatment for Patients with Advanced or Metastatic Hepatocellular Carcinoma after Sorafenib Failure

Jin Won Chang, Jae Seung Lee, Beom Kyung Kim, Seung Up Kim, Do Young Kim, Sang Hoon Ahn, Kwang-Hyub Han, and Jun Yong Park

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; Yonsei Liver Center, Yonsei University Health System, Seoul, Korea

Aims: In the checkmate 040 trial, Nivolumab, an anti-PD-1 antibody showed durable response and long-term survival in patients with advanced hepatocellular carcinoma (HCC). We studied this retrospective analysis to evaluate the treatment efficacy and safety of nivolumab in advanced or metastatic HCC after sorafenib failure.

Methods: We retrospectively reviewed the records of HCC patients who had nivolumab treatment at Severance Hospital in Seoul, Korea, between November 2017 and January 2019. Nivolumab 3 mg/kg was administered. Nivolumab treatment was given every two weeks until progression or intolerable toxicity or death. Response evaluation was done based on mRECIST.

Results: A total of 67 patients entered into this study. We excluded 25 patients who did not perform response evaluation, because of follow-up loss, too short follow-up duration, death. All patients received nivolumab as second-line therapy after sorafenib. The median treatment dose was 8.9 doses. Median overall survival was 9.0 months. The median progression free survival was 3.4 months. One case who had lung metastasis, was complete response, 5 cases partial response, 13 cases stable, and 23 cases progression. The overall response rate (ORR) was 14.3% and disease control rate (DCR) was 45.2%. The most frequent adverse event was Jaundice (21.4%), followed by edema (19%) and nausea (9.5%) and fatigue (9.5%).

Conclusions: In early real-life experience, nivolumab treatment demonstrated clinically meaningful anti-tumor activity and a manageable safety profile in patients with sorafenib-refractory advanced or metastatic HCC.

Keywords: Nivolumab, Hepatocellular Carcinoma, Sorafenib

Hepatocellular Carcinoma in Old Age – Are There Any Benefits of Resection of Liver in Old Age?

In Sik Shin, Deok Gie Kim, Sung Whan Cha, Seong Hee Kang, Sung Hoon Kim, Moon Young Kim, Soon Koo Baik

Department of Surgery, Internal Medicine, Yonsei University Wonju College of Medicine, Wonju Severance Christian Hospital, Wonju, Korea

Aims: Hepatocellular carcinoma (HCC) is a common cause of death in population. There are some treatment option including surgical resection of HCC, radiofrequency ablation (RFA), or liver transplantation. The number of elderly patients with HCC has been increasing with longer life expectancy of the population. Older people have coexisting medical conditions that can adversely affect surgical outcomes and these become the reason of alternative way including chemotherapy. We compared about the surgical treatment outcomes between older age groups and younger groups.

Methods: We performed 234 hepatic resection in patients with HCC from Mar. 2012 to Dec. 2018. We reviewed retrospectively medical records of patients. Patients divided to two groups. Old age group is more than 70 years old patients and young patients group is less than 70 years old. We compared preoperative, operative characteristics and postoperative outcomes between both groups.

Results: Young age group is 184 patients and old ages is 50 patients. Young patients group had more HBV hepatitis than old age group (61.4% vs 26%), but other indices showed few differences. Two groups had similar number of major resection (26.1% vs 20%), but the operation time was a little bit shorter in old age group. The bleeding during procedure (600cc vs...
500cc, median value, \( P = 0.285 \)) and transfusion (both \( 0 \) cc, median value, \( P = 0.337 \)). The Disease Free Survival (DFS) was 46, 49 each (\( P = 0.518 \)) and Overall survival (OS) was same as 76 (\( P = 0.517 \)). The major postoperative complications were 23(12.6%) and 9 (18.4%) each (\( P = 0.351 \)).

Conclusions: There were no difference between older age groups and younger age groups. Although several risk factors for postoperative morbidity and mortality increase with age, aggressive treatment strategy can achieve long term survival for HCC.

Keywords: Hepatocellular carcinoma, Old age, Surgical approach, Aggressive treatment

### PE-229

**Postoperative Infectious Complications Decrease Overall and Recurrence-Free Survival in Patients Undergoing Liver Resection for Hepatocellular Carcinoma**

Jiong-Jie YU,1 Zhen-Li LI,1 Qian ZHONG,2 Lei LIANG,3 Chao LI,3 Ming-Da WANG,3 Wan Yee LAU,1 Yong-Yi ZENG,1 Ya-Hao ZHOU,1 Jun HAN,1 Feng SHEN,1 Tian YANG1

1Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, 2Department of Anesthesiology, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, China, 3Faculty of Medicine, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China

Aims: This study aimed to evaluate if postoperative infectious complications impact long-term survival after liver resection for HCC.

Methods: A total of patients undergoing curative liver resections for HCC were retrospectively analyzed from a multi-institutional database. Independent risk factors of postoperative infectious complications were identified. After excluding patients with postoperative early deaths (< 90 days), the long-term overall survival (OS) and recurrence-free survival (RFS) were compared between patients with and without postoperative 30-day infectious complications.

Results: Among 2442 patients identified, 332 had postoperative 30-day infectious complications. Age > 60 years, diabetes mellitus, obesity, cirrhosis, intraoperative blood transfusion, operative time > 180 min and major hepatectomy were identified as the independent risk factors of postoperative infectious complications. In univariable analyses, median OS and RFS of patients with postoperative infectious complications were significantly poorer than those of patients without (86.8 vs. 43.2, and 54.3 vs. 22.6 months, both \( P < 0.001 \)). After adjustment for other prognostic variables, multivariable Cox-regression analyses identified that postoperative infectious complications were independently associated with decreased OS (hazard ratio: 1.199, 95% CI: 1.021-1.660, \( P = 0.027 \)) and RFS (hazard ratio: 1.187, 95% CI: 1.027-1.372, \( P = 0.021 \)).

Conclusions: Postoperative infectious complications decrease long-term OS and RFS in patients undergoing curative liver resection for HCC. To reducing the incidence of infectious complications, preoperative optimization, surgical procedure and postoperative care should be carefully planned.

### PE-230

**Real-Time Navigation for Laparoscopic Hepatectomy Using Image Fusion of Preoperative 3D Surgical Plan and Intraoperative Indocyanine Green Fluorescence Imaging**

Chihua FANG

Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, China

Aims: This study aims to evaluate the feasibility and effectiveness of a novel laparoscopic hepatectomy navigation system (LHNS) that incorporates preoperative three-dimensional models and indocyanine green fluorescence imaging (IGFI) to achieve real-time surgical navigation.

Methods: Forty-eight patients undergoing laparoscopic hepatectomy from January 2017 to December 2018 were selected. 23 patients were performed under the guidance of LHNS, and 25 were treated with laparoscopic hepatectomy. The operative condition and clinical prognosis were analyzed retrospectively.

Results: There was no significant difference in preoperative characteristics between the two groups. There was no statistical difference between the two groups in the operation and clinical results. The hepatic tangent line was clearly displayed by LHNS in 20 cases; however, the boundary projection was unclear in 2 cases and the boundary was not clearly displayed in 1 case with IGFI. In addition, unexpected bleeding caused by injury to important pipelines was avoided by the projection of three-dimensional models of blood vessels during incision of hepatic parenchyma.

Conclusions: The LHNS we developed provides a new intraoperative image guidance method for laparoscopic hepatectomy. The results of our comparative analysis confirmed the feasibility and clinical utility of LHNS in identifying intrahepatic anatomy, determining the scope of hepatectomy and guiding hepatic parenchymal disconnection in real time. LHNS is expected to become a new real-time navigation system for laparoscopic hepatectomy.

### PE-231

**Three-Dimensional Visualization Evaluation and VR Study of Giant Liver Cancer with Blood Vessels as the Axis**

Chihua FANG

Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, China

Aims: The study was to evaluate if postoperative infectious complications play a relevant role. The aim of this study was to evaluate if postoperative infectious complications impact long-term survival after liver resection for HCC. To reducing the incidence of infectious complications, preoperative optimization, surgical procedure and postoperative care should be carefully planned.
Aims: To explore the clinical application value of three-dimensional visualization of blood vessels as the axis and virtual reality technology in giant liver cancer.

Methods: The thin-layer CT image data of 13 patients who were diagnosed as giant primary liver cancer by medical history, imaging and laboratory tests were collected for three-dimensional reconstruction, and then transformed into VR model. The anatomical relationship between the tumor and its surrounding important structures was analyzed. The preoperative evaluation, typing and surgical planning based on blood vessels as the axis were carried out to guide intraoperative navigation. The consistency was verified by the intraoperative rapid pathological examination.

Results: 13 patients successfully achieved 3D reconstruction and VR model transformation. According to the 3D visualization classification of blood vessels as the axis, 13 cases were as follows: 3 cases of type I a grade 1, 2 cases of type I a grade 2; 1 case of type II a grade 2; 1 case of type II b grade 3; 2 cases of type II c grade 3; 4 cases of type II a grade 3.

Conclusions: Three-dimensional visualization and VR technology can provide comprehensive information on the anatomical structure of liver cancer lesions and blood vessels, which is of great value in the application of giant liver cancer surgery.

---

PE-232

Application of Three-Dimensional Visualization, VR Technology Combined with ICG Molecular Fluorescence in Hepatectomy under Non-Vascular Occlusion for Centrally Located Hepatocellular Carcinoma

Chihua FANG

Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, China

Aims: To explore the application value of three-dimensional visualization, VR technology combined with ICG molecular fluorescence in hepatectomy under non-vascular occlusion for centrally located hepatocellular carcinoma.

Methods: Clinical data of one patient with centrally located hepatocellular carcinoma undergoing mesohepatectomy in the Department of Hepatobiliary, Zhuhang Hospital Affiliated to Southern Medical University in July 2018 were retrospectively analyzed. Three-dimensional visualization and VR technology were adopted and intraoperative use of FIGFI was combined with hepatectomy under non-vascular occlusion.

Results: According to the three-dimensional visualization, the volume of the whole liver, the tumor, the pre-resected liver and the residual liver was 1423.54ml, 405.35ml, 524.48 ml and 899.06 ml respectively. The residual liver volume accounts for 63.15% of the standard liver volume. The tumor was about 11.1*11.5*8.54 cm. VR model showed that the tumor was located in segments VI, V and VIII. Three-dimensional visualization with blood vessels as the axis was classified as 3-class, II b-type. The centrally located hepatocellular carcinoma was classified as type III, which was to be treated by mesohepatectomy. Mesohepatectomy under non-vascular occlusion was performed during operation. The preoperative 3D visualization and VR model were consistent with the intraoperative findings, and the preoperative planning was consistent with the actual operation. There were no obvious postoperative complications.

Conclusions: Three-dimensional visualization and VR technique combined with ICG molecular fluorescence can assist hepatectomy under non-vascular occlusion for centrally located hepatocellular carcinoma.

---

PE-233

Is the Outcome after Hepatectomy for Hepatocellular Carcinoma Different from That of Classic Hepatocellular Carcinoma and Mass-Forming Cholangiocarcinoma? A Case-Matched Analysis

Damiano GENTILE1, Matteo DONADON1, Luca DI TOMMASO1, Angela PALMISANO1, Matteo CIMINO1, Jacopo GALVANIN1, Bruno BRANCIFORTE1, Guido TORZILLI1

1Hepatobiliary and General Surgery, Humanitas University, Humanitas Clinical and Research Center; Department of Pathology, Humanitas University Humanitas Clinical and Research Center, Italy

Aims: Hepatocellular carcinoma (HCC-CC) is a rare tumor. The aim of this study was the analysis of the outcome comparing such tumor with classic hepatocellular carcinoma (HCC) and mass-forming cholangiocarcinoma (MFCCC).

Methods: Our prospectively maintained database was queried, and 20 patients with HCC-CC were identified. A 2:1 match was performed with 40 patients operated in the same period for HCC, and with 40 operated for MFCCC. Only T1 or T2 patients N0 M0 were considered. Primary endpoint was the overall survival (OS) and disease-free survival (DFS).

Results: Median tumor diameter of HCC-CC group was 3.8 cm (range 1.3-5), and single tumor was detected in 13. After a median follow-up of 33.8 months (range 6-77), the 1-, 3-, and 5-year OS rates were 90%, 65%, and 50% respectively. The 1-, 3-, and 5-year DFS rates were 65%, 45%, and 20% respectively. Both OS and DFS did not differ significantly among the three histotypes.

Conclusions: Patients with HCC-CC showed similar rates of OS and DFS to those patients with classic HCC and MFCCC. Further evaluations of differences in tumor features and biology are necessary to better characterize the prognosis of patients with HCC-CC.

---

PE-234

ALPPS versus Two-Stage Hepatectomy (TSH): Indications, Safety, Efficacy

Andrey KAPRIN1, Dmitry SIDOROV1, Mikhail LOZHKIN1, Aisha ISAEVA1

1Abdominal Surgery, Moscow Oncological Research Institute n.a.P.
ALPPS Procedure in 20 Patients with Primary and Metastatic Malignancies: Single Centre Experience

Andrey KAPRIN², Dmitry SIDOROV³, Mikhail LOZHKIN¹, Aisha ISAEVA¹

¹Abdominal Surgery, Moscow Oncological Research Institute n.a. P. Hertsen, Russia

Aims: The main goal was to assess safety and outcomes of ALPPS procedure and find the optimal compromise between dropout and mortality risk, using our initial single-center experience.

Methods: 20 patients who have underwent ALPPS resection at the abdominal surgery department Moscow Oncological Research Institute n.a. P. Hertsen from January 2012 to June 2016 were retrospectively analyzed. Multivariate logistic regression analysis was performed to identify independent risk factors for severe complications, mortality and volume growth of the FLR.

Results: Mean age was 59±1±6,3 (49 -72) years. Indications for surgical resection were CRLM in 80% cases and HCC in 20% cases. One patient had salvage ALPPS after failed PVL. Patients were operated for 2.8±1.6 metastases, the largest was 64.6±18.8 mm(40-104). The increase in FLR between the two procedures was 95.3±53.6% (range: 13-164%, P < 0.001). The average time between steps of the procedure was 9.4±1.4 days. Severe complications including mortalities (Clavien-Dindo≥IIIb) occurred in 6,7 and 9,1% of patients after ALPPS-1 and 2 respectively. Follow-up median was 20 mo. Medium overall survival rate was 26,1 [22,5-29,6] mo. Medium disease-free survival 24,1 [19,6-28,5]mo. Primary liver cancer, age, histologic changes of liver parenchyma, led to morbidity and mortality rate.

Conclusions: ALPPS should be reserved to a small proportion of patients, the young ones with very small future liver remnant, with the low rate of liver function reserve or experiencing inadequate hypertrophy after portal vein occlusion. For these patients ALPPS could still offer a benefit, being the only chance of resectability.

Surgical Tactics for Colorectal Cancer with Synchronous Liver Metastases

Muraliev Eral, Mamashev Nurlan, Bebezov Bakhadyr, Surov Edir, Marshankulov Rezuan

Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

Aims: Comparative assessment of the immediate results of simultaneous removal of the primary colorectal tumor with liver resection and two-step operations.

Methods: The results of treatment of 36 patients from 2010 to 2018 were analyzed. 15 simultaneous and 21 consecutive operations were performed for synchronous colorectal metastases in the liver. Of these, extensive liver resections were performed in 41.7% and 58.3% of cases, respectively. Clinical, intraoperative, postoperative data were analyzed to assess the immediate results of the treatment.

Results: Simultaneous operations did not increase intraoperative blood loss (756 ± 76 against 835 ± 83 ml, P = 0.4), the number of postoperative complications (6.6% against 3.8%) and mortality (0% against 2.9% (1 patient)) in comparison with sequential operations. During operations on the colon and rectum, the number of postoperative complications and mortality did not differ (P = 0.61 and P = 0.48, respectively). Comparative assessment of postoperative complications and mortality after extensive synchronous and sequential operations also revealed no differences (P = 0.93 and P = 0.96, respectively). All patients received adjuvant chemotherapy according to the XELOX, FOLF-OX scheme.

Conclusions: If simultaneous intrahepatic metastases of colorectal cancer are detected and there are no marked associated diseases, it is advisable to perform simultaneous operations,
Immediate Results of Surgical Treatment Hepatocellular Cancer

Keywords: Liver metastasis, Colorectal cancer, Liver resection, Simultaneous operation

Methods: The results of treatment of 25 patients with hepatic HCC from 2010 to 2018 are analyzed. There were 14 men (56.0%), women-11 (44.0%). The average age of patients was 61 ± 9 years. In 9 patients, the formation is localized in the left lobe, in 13 in the right lobe and 3 patients with bilobar liver damage.

Results: The following types of liver resection were performed: RHHE – 13, LHHE - 9, LLE - 1, exploratory laparotomy - 2. Blood loss averaged 798 ± 256 ml., minimum 200 ml. According to the international classification of TNM, patients were distributed as follows: T2N0M0 (stage I) - 19, T3N0M0 (stage II) - 6, T4N1M0 (stage IV) - 1 patients. There were the following types of complications in the postoperative period: hepatic failure in 6th, received conservative therapy; in 2 patients, the formation of a biloma in the abdominal cavity, followed by drainage under local anesthesia, received conservative treatment. One patient has a biliary fistula, closed on the 14th day after the operation. Postoperative mortality was not observed.

Conclusions: The presence of cirrhosis and hepatitis in patients with hepatic HCC worsens the immediate and long-term results of treatment, but is not a contraindication to surgical treatment. Surgical treatment of HCC requires an accurate preoperative assessment of the functional reserve of the liver.

Keywords: Hepatocellular cancer, Liver resection, Surgical treatment, Immediate results

The Current Status of Selecting Treatment Modalities for Naive Hepatocellular Carcinoma Patients over 70 Years Old: Single-Center Experience

Aims: To evaluate the immediate results of surgical treatment of HCC.

Methods: The results of treatment of 25 patients with hepatic HCC from 2010 to 2018 are analyzed. There were 14 men (56.0%), women-11 (44.0%). The average age of patients was 61 ± 9 years. In 9 patients, the formation is localized in the left lobe, in 13 in the right lobe and 3 patients with bilobar liver damage.

Results: The following types of liver resection were performed: RHHE – 13, LHHE - 9, LLE - 1, exploratory laparotomy - 2. Blood loss averaged 798 ± 256 ml., minimum 200 ml. According to the international classification of TNM, patients were distributed as follows: T2N0M0 (stage I) - 19, T3N0M0 (stage II) - 6, T4N1M0 (stage IV) - 1 patients. There were the following types of complications in the postoperative period: hepatic failure in 6th, received conservative therapy; in 2 patients, the formation of a biloma in the abdominal cavity, followed by drainage under local anesthesia, received conservative treatment. One patient has a biliary fistula, closed on the 14th day after the operation. Postoperative mortality was not observed.

Conclusions: The presence of cirrhosis and hepatitis in patients with hepatic HCC worsens the immediate and long-term results of treatment, but is not a contraindication to surgical treatment. Surgical treatment of HCC requires an accurate preoperative assessment of the functional reserve of the liver.

Keywords: Hepatocellular cancer, Liver resection, Surgical treatment, Immediate results

A Current Status of Therapeutic Choice and Feasibility for Hepatocellular Carcinoma Patients over 70 Years Old

Aims: Hepatocellular carcinoma (HCC) is the third most common cancer in the digestive system based on survey of domestic cancer incidence, and the ratio of elderly aged 65 or older is expected to rise steadily, leading to a higher incidence of total hepatocellular carcinoma. Benefit of treatment should be greater than the reduction of survival period or maladjustment due to treatment. Based on these perspectives, we investigated how the detailed treatment of hepatocellular carcinoma in elderly patients and overall survival of each treatment modalities.

Methods: From January 2003 to December 2005 and January 2008 to December 2014, the National Cancer Center (NCC) and Korean Liver Cancer Study group (KLC5G) collected 3,006 options for hepatocellular carcinoma(HCC) patients who were over 70 years old. This study evaluated the current status of treatment modalities for naive elderly HCC patients in single-center to determine optimal management strategy.

Results: Among these patients, 39.3% of them were Hepatitis B carrier and 75% of them had been previously diagnosed as liver cirrhosis. 65 of 280 patients(23.2%) underwent surgical resection who mostly considered as single lesion (95.4%), and all 65 patients obtained R0 resection. For the patients aged 70-75 years old, 26.9% of them underwent surgical resection, and 48.7% of them received transarterial therapy. For the patients over 80 years old, 6.7% of them underwent surgical resection, and 82.2% of them received transarterial therapy. There were statistically significant differences in selection of treatment between two groups. The overall survival and disease-free survival analysis showed a statistically significant superiority of surgical resection compared with transarterial therapy. In the propensity score matching analysis of the surgical and transarterial therapy group, there was no significant difference between the two groups in overall survival and disease-free survival.

Conclusions: Although transarterial therapy is most common treatment of choice in elderly naive HCC patients, adequate surgical resection is another important therapeutic option to consider in achieving survival benefit in treating HCC.
Results: In Period 2003-2005, there were 578 patients and in period 2008-2014, 2428 patients were analyzed. Transarterial therapy (period 2003-2005: 49.1%, period 2008-2014: 44.4%) was the most commonly used treatment modality. Among them, Transarterial chemoembolization (TACE) with gelatin sponge occupied largest proportion (96.1%, 65.6%). In overall survival analysis, surgical resection showed statistically significant superiority than other treatment modalities ($P < 0.001$), followed by local ablation therapy and transarterial therapy in both periods. Other modalities showed no statistical differences including no treatment. Among transarterial and chemotherapy, there are no statistically significant differences between transarterial therapy modalities except sorafenib. However, there were no statistically significant differences in propensity score matching for surgical resection, local ablation therapy, and transarterial therapy for relatively early stage lesions. In subgroup analysis, there was statistically significant difference between the surgical resection, local ablation therapy, transarterial therapy and the rest of other treatment modalities in the 70-75 year period. However, there was no significant difference between surgical resection, local ablation therapy, transarterial therapy in the ages of 75-80 years and over 80 years period.

Conclusions: Transarterial therapy was the most commonly used treatment modality in HCC patients over 70 years old, however surgical resection showed statistically significant superior overall survival rate than other modalities.

Keywords: Hepatocellular carcinoma, Surgical resection, Elderly, Transarterial therapy
The Meaning of Enhanced Liver Fibrosis (ELF) Score as a Predictive Factor for HCC Patient after Liver Resection

Alshandeer Marei Hussein M1,2, Dai Hoon Han1, Gi Hong Choi1, Jin Sub Choi2

1Department of Surgery, Yonsei University College of Medicine, Seoul, Korea; 2Department of Surgery, King Khalid University, Abha, Saudi Arabia

Aims: The enhanced liver fibrosis (ELF) score is an extracellular matrix marker set consisting of tissue inhibitor of metalloproteinases 1 (TIMP-1), amino-terminal propeptide of type III procollagen (PIIINP) and hyaluronic acid (HA) having good correlations with fibrosis stages in chronic liver disease. Moreover, elevated ELF score has been suggested as a poor prognostic factor for cholangiocarcinoma probably related to tumor’s desmoplastic nature. Thus, this study aimed to figure out the predictive value of ELF score for the hepatocellular carcinoma (HCC) patients having liver resection.

Methods: From April 2015 to December 2018, preoperative ELF score was collected for 62 patients with HCC having curative liver resection. The patients were grouped according to ELF score as 10 and perioperative outcome was compared. Perioperative prognostic factors were also analyzed for disease-free survival after liver resection.

Results: Patients group over 10 of ELF score had significantly higher liver stiffness by transient elastography (8.26 ± 3.28 Vs 17.60 ± 14.52 Kpa, P = 0.004), lower platelet count (190.91 ± 51.10 Vs 149.53 ± 70.56 x 10³/mm³, P = 0.01) lower serum albumin level (4.47 ± 0.35 Vs 4.06 ± 0.37 g/dL, P < 0.001), and higher AST level (30.20 ± 9.80 Vs 45.22 ± 20.97, P = 0.002). Liver stiffness over 14 kPa and ELF over 10 was significant prognostic factors for disease-free survival (P = 0.042 and 0.030, respectively). ELF over 10 was the significant prognostic factors on multivariate analysis (relative risk with 95% CI= 2.795 (0.989 – 7.903), P = 0.053).

Conclusions: Higher ELF score may be correlated with poor liver condition correlating liver fibrosis. Moreover, ELF score was the only significant prognostic factor for disease-free survival for the patient having HCC after liver resection.

Keywords: ELF, HCC, Liver resection, Predictive factor

Long-Term Post-Resection Prognosis of Primary Neuroendocrine Tumors of the Liver

Jay Jung1, Shin Hwang2, Seung-Mo Hong2, Ki-Hun Kim1, Chul-Soo Ahn1, Deok-Bog Moon1, Tae-Yong Ha1, Gi-Won Song2

1Department of Surgery and 2Department of Pathology, Asan Medical Center University of Ulsan College of Medicine, Seoul, Korea

Aims: Primary hepatic neuroendocrine tumor (PHNET) is a very rare neoplasm, requiring strict exclusion of metastasis from possible extrahepatic primary sites for its diagnosis.

Methods: We reviewed our clinical experience of 13 patients with hepatic primary NET who underwent hepatic resection from January 1997 to December 2015.

Results: The mean age of 13 patients was 51.1±12.8 years, with 8 males and 5 females. The most common clinical manifestation was vague nonspecific abdominal pain (n = 9). Of them, 7 patients underwent preoperative liver biopsy, which was correctly diagnosed as neuroendocrine tumor (NET) in 4. Ten patients R0 resection and 3 underwent R1 resection. Diagnosis of hepatic primary NET was confirmed immunohistochemically and by absence of extrahepatic primary sites. All tumors were single lesions, with size of mean 9.6±7.6 cm and median 4.3 cm. All showed positive staining for synaptophysin and chromogranin. During a mean follow-up of 95.1±86.6 months, 7 patients died from tumor recurrence, whereas the other 6 remain alive to date, making the 5-year tumor recurrence rate 56.0% and the 5-year patient survival rate 61.5%. When confining to R0 resection, 5-year recurrence and survival rates were 42.9% and 70.0%, respectively. Univariate analysis showed that Ki-67 proliferative index was the only risk factor for tumor recurrence.

Conclusions: PHNET is a very rare tumor with no specific clinical features. Final diagnosis of PHNET depends mainly on pathology and immunohistochemistry and exclusion of metastasis from other sites. Active surgical treatment is effective for PHNET because of acceptably favorable post-resection outcomes.

Keywords: Neuroendocrine tumor, Metastasis, Resection, Diagnosis

Development and Validation of Novel Scoring System for the Prediction of Disease Recurrence Following Resection of Colorectal Liver Metastasis

Wan-Joon KIM1, Tae-Wan LIM1, Sang-Hee KANG2, Pyoung-Jae PARK1, Sae-Byeol CHO1, Sun-II LEE3, Byung-Wook MIN2, Wan-Bae KIM1

1Division of Hepatobiliary Pancreas Surgery, Department of Surgery, Korea University Guro Hospital, Republic of Korea; 2Division of Colorectal Surgery, Department of Surgery, Korea University Guro Hospital, Republic of Korea; 3Division of Transplantation Vascular Surgery, Department of Surgery, Korea University Guro Hospital, Republic of Korea

Aims: The aim of this study was to identify predictive factors for the recurrence of colorectal cancer liver metastasis (CRLM) and then to develop a corresponding novel scoring system that should improve the sensitivity of predicting recurrence in patients with CRLM.

Methods: A total of 295 consecutive CRLM patients were enrolled in our institution between January 2002 and December 2015. Multivariate analyses were performed to identify the variables associated with disease recurrence and established the
novel scoring system based on it.

**Results:** The scoring system considered seven variables: synchronicity, CA19-9 level, number of liver metastasis, largest size of liver metastasis, resection margin of hepatic lesion, neutrophil-to-lymphocyte ratio and prognostic nutritional index. The area under the curve of ROC was 0.824 (95% confidence interval 0.767–0.882); the sensitivity of our scoring system was 87.9%, specificity was 66.7%, positive predictive value was 20.6%, and negative predictive value was 20.9%.

**Conclusions:** For patients with CRLM undergoing curative hepatic resection, our novel scoring system would improve the sensitivity for prediction of disease recurrence in Case of CRLM patients.

---

**PE-244**

Surgical Strategies of Huge Hepatocellular Carcinoma with Main Portal Vein Thrombosis: A Case Report

Cheon Soo PARK

Surgery, Eunpyeong St. Mary’s Hospital, College of Medicine, The Catholic University, Republic of Korea

**Aims:** Huge hepatocellular carcinoma (HHCC) is commonly considered tumor diameter over 10 cm. The prognosis of HHCC or HCC with PVTT was poor, many investigator performed non-surgical treatment. But some study reported that aggressive operation for HHCC with PVTT brought good results and prognosis compared to non-surgical interventions.

**Methods:** 46 years old, HBV carrier man was referred to our hospital for hepatic mass. In laboratory test, platelet counts: 80,000, PT: 1.17 INR, total bilirubin: 1.61mg/dl, GOT/GPT: 32/12, Cr: 0.49, albumin: 3.9g/dl, AFP: 76,430, PIVKA-II: 1478.78. In radiologic examinations, HHCC (11 cm) abutting middle hepatic vein (HV) was located in right hepatic lobe and combined with PVTT from right PV to main PV.

**Results:** We performed right hepatectomy and PV thrombectomy. Surgical procedures were summarized as follows; (1) cholecystectomy, (2) right, left and main PV and right hepatic artery (HA) were respectively isolated and hung with vessel loops after hepatic hilar dissection; (3) left and main PV were clamped by vascular clamps for protection thrombosed propagation; (4) right PV was transversely opened, and then PV thrombectomy was performed; (5) right PV and HA was ligated; (6) right liver was mobilized and right HV was isolated and ligated; (7) after blocking off hepatic inflow and outflow, right hepatectomy was performed by CUSA system.

**Conclusions:** In conclusion, surgical strategies of HHCC with main PVTT is that we initially perform PV thrombectomy while preserving hepatic side PV is clamping, and then ligate removed side HA, PV and HV for protection of tumor propagation during hepatic manipulation and resection.
Results: Total 66 patients underwent pure minimally invasive approach for liver resection and primary cancer operation. On the other hand, 325 patients was performed open liver resection. Between two group, length of stay (LOS, 14.7 days vs 9.7 days) and imaging liver metastasis lesion numbers (3.9 vs 1.5) and final pathologic liver metastasis number (3.8 vs 1.4), tumor size (2.8 cm vs 1.9 cm) were statistically higher in open group. In survival analysis, minimally approach for liver resection group was more favorable than open resection group in overall survival (mean 87.9 vs 110.9 months, P = 0.011) and disease free survival (mean 40.6 months vs 59.3 months, P = 0.033). After propensity score matching, LOS of still longer in open resection group in statistically significance. In survival analysis, there were no differences between two groups.

Conclusions: Synchronous minimally invasive liver resection for colorectal cancer liver metastasis is safe and feasible with benefit of short LOS. In terms of oncologic outcome, minimally invasive liver resection was not inferior to open liver resection. In selected patients, minimally invasive approach for liver metastasis resection synchronously should be considered.

Hypothermic Perfusion Hepatectomy for Unresectable Liver Cancer: A Single-Center Experience
Youngin YOON, Sung-Gyu LEE
Division of Hepatobiliary Surgery and Liver Transplantation, Asan Medical Center, Republic of Korea

Aim: Despite technical advancements in liver surgery, resection of liver tumors that involve the hepatic veins adjacent to the vena cava or hepatic hilum remains technically challenging. We present our surgical techniques and the long-term outcome of 5 patients with conventionally unresectable tumors.

Methods: Between September 1999 and March 2016, we encountered 5 patients with conventionally unresectable tumors that were successfully treated by "ex-situ liver resection" and "in-situ & ante-situm hypothermic liver perfusion" under total vascular exclusion and venovenous bypass.

Results: These approaches allowed complete tumor removal with vascular reconstruction under a bloodless operation field, while minimizing hepatic ischemic injury and preserving liver function. No perioperative mortalities occurred and postoperative complications were minimal. The postoperative survival periods were limited due to the advanced malignancies in our patients, but the survival benefit was encouraging. The median postoperative survival time was 29.1 months, with the longest survival period being nearly 10 years. Furthermore, these approaches improved the quality of life and provided our patients with an opportunity for additional treatment.

Conclusions: Hypothermic perfusion hepatectomy is a realistic option for achieving surgical cure or significantly improved survival and quality of life in patients with tumors deemed unresectable using conventional normothermic hepatectomy. These approaches can overcome the limitations of the liver’s restricted normothermic ischemia tolerance or inaccessible tumor locations.
pattern and the prognosis after hepatectomy.

Methods: 55 patients who underwent hepatectomy (Open 47 and Laparoscopic 8) for HCC > 5 cm without major vascular invasion from 2008 to 2018 at single institute were retrospectively analyzed. We divided two groups such as 5 cm < HCC < 10 cm or huge HCC ≥10 cm (hHCC).

Results: The level of alpha-feto protein and PIVKA with 5 cm < HCC < 10 cm (n = 44) (1369ng/ml and 3278mAU/ml) were lower than those of patients with hHCC (n = 11) (19128ng/ml and 3761mAU/ml). Pathologically, hHCC showed more frequent than 5 cm < HCC <10 cm cm with microvessel and intrahepatic invasion (100 and 55% versus 71.8 and 25%). The overall survival and DFS (disease free survival) of patients with hHCC (38 and 20.2 months) were significantly worse than those of patients with 5 cm<hHCC <10 cm (40.25 and 22.8 months). The intra/extra hepatic recurrence rate showed 36% (16), 2% (1) with 5 cm < HCC < 10 cm and 27% (3), 27% (3) with hHCC. Both group has an independent risk factor for extra-hepatic recurrence (Hazard ratio 7.86, P < 0.005). The DFS of patients with extra-hepatic recurrence was worse than patients with intra-hepatic recurrence. (13.3 and 14.6 months).

Conclusions: In our study, the extra-hepatic recurrence is an independent risk factor in HCC greater than 5 cm in diameter. Especially, hHCC has higher rate of extra-hepatic recurrence and lower DFS.

**PE-250**

Preoperative Glasgow Prognostic Score (GPS) as a Predictor of Poor Prognosis in Synchronous Colorectal Cancer Liver Metastasis

Soon Ha KWON, Sang Ho BAE

Department of Surgery, Soonchunhyang University Cheonan Hospital, Republic of Korea

Aims: Recently, the Glasgow prognostic score (GPS) and the modified GPS (mGPS), an inflammatory response marker, have been reported to be associated with the prognosis in patients with various type of cancer. We investigated the value of the GPS and mGPS for the predictor of prognosis in patients with synchronous liver-limited colorectal metastases (sCRLM).

Methods: Eighty-three patients who histologically diagnosed as sCRLM were selected. Their laboratory and clinical data were collected retrospectively. We calculated the GPS and mGPS. Univariate and multivariate analysis were performed to examine the score on overall survival and disease free survival.

Results: Length of hospital stay was significantly correlated with high mGPS (P = 0.038). The multivariate analysis identified the GPS as independent prognostic factors for OS and DFS in all patients (P = 0.021, P < 0.001). Patients with high mGPS had a significantly longer OS and DFS (P = 0.048, P < 0.001).

Conclusions: In conclusion, elevated preoperative GPS and mGPS is correlated with both survival and disease free survival in patients who have been diagnosed with resectable sCRLM.

**PE-251**

Computed Tomograph Imaging Features and Early Response of Hepatocellular Carcinoma Treated by Transarterial Chemoembolization with Drug Eluting Beads

Dong Duc Hoang

Thai Nguyen University of Medicine And Pharmacy, Vietnam

Aims: To describe imaging features and evaluate tumor response to first session of transarterial chemoembolization (TACE) with drug-eluting beads (DEB) in patients with hepatocellular carcinoma.

Methods: In this prospective study, 78 HCC patients were treated with one session TACE using Doxorubicin-eluting Bead. CT was performed in all patients before treatment and from 1 to 3 months after the procedure. Imaging response was evaluated according to the modified Response Evaluation Criteria in Solid Tumours (mRECIST).

Results: Records of 78 patients were reviewed. Mean age was 60.5 ± 10.1. Male was 89.7%, female was 10.3%. Child-Pugh severity rate: Child A 94.9%, Child B 5.1%. BCLC score: stage B 88.5%, stage C 11.5%. Most tumors located in the right lobe 79.5%. The number of tumor: single 37.2%, multiple 62.8%. Size of tumor rate < 5 cm: 14.1%, 5-10 cm: 55.1%, >10 cm: 30.8%. In hepatic arterial phase, there was the most enhancement with mean 84.4 ± 32.8 (HU). 11.5% patients had branch portal vein thrombosis. After one session of treatment with TACE, the mean size of tumor decreased from 8.8 ± 3.6 cm to 7.2 ± 3.8 cm, P = 0.001. The rate of complete response was observed in 25.6%, partial response 47.4%, stable disease 20.5% and progressive disease 6.4%.

Conclusions: Computed tomography imaging is helpful method for guiding the selection of an optimal treatment strategy and assessing the tumor response to treatment in patients with HCC.

Keywords: Transarterial chemoembolization, Computed tomograph, Hepatocellular carcinoma

**PE-252**

Clinical Outcomes after Risk-Adapted Proton Beam Therapy Using Three Dose-Fractionation Regimens for Hepatocellular Carcinoma

Tae Hyun Kim1,2, Joong-Won Park1, Bo Hyun Kim, Hyunjung Kim3, Sung Ho Moon1, Sang Soo Kim1, Sang Myung Woo1, Young-Hwan Koh1, Woo Jin Lee1, Dae Yong Kim1, Chang-Min Kim1

1Center for Liver Cancer, Research Institute and Hospital, National Cancer Center, Goyang, Korea; 2Center for Proton Therapy, Research Institute and Hospital, National Cancer Center, Goyang, Korea

Aims: The aim of this study was to evaluate the long-term efficacy and safety of risk-adapted PBT in patients with hepatocellular carcinoma (HCC).

www.theliverweek.org 511
Methods: Inclusion criteria for the present study were: i) HCC was diagnosed by pathologic confirmation or radiologic findings according to the guidelines of the Korean Liver Cancer Study Group and the National Cancer Center; ii) HCC lesions were unsuitable, ineffective, or refused for any other loco-regional treatments; iii) patients were treated with risk-adapted PBT using three dose-fractionation regimens depending on the proximity of the GI organs; iv) there was no uncontrolled intrahepatic disease outside of the targeted lesion; v) liver function of Child-Pugh class A or B7 was present; and vi) no extrahepatic metastasis. Between June 2012 and April 2017, 243 patients who met all of the inclusion criteria were analyzed in present study. Three dose-fractionation regimens were used according to the proximity of the gastrointestinal (GI) organs: (1) regimen A, the prescribed doses to planning target volume (PTV)1 and PTV2 were 50 GyE (EQD2, 62.5 GyE,0) and 30 GyE (EQD2, 32.5 GyE,0) in 10 fractions, 5 fractions a week, respectively, for the patients with GTV < 1 cm from the GI organs; (2) regimen B, the prescribed doses to PTV1 and PTV2 were 60 GyE (EQD2, 80 GyE,0) and 30 GyE in 10 fractions, respectively, for the patients with GTV within 1.9 cm from the GI organs; and (3) regimen C, the prescribed dose to PTV1, identical to PTV2, was 66 GyE (EQD2, 91.3 GyE,0) in 10 fractions for the patients with GTV > 2 cm from the GI organs.

Results: In all patients, the 5-year local recurrence-free survival (LRFS) and overall survival (OS) rates were 87.5% and 48.1%, respectively, with grade ≥ 3 toxicity of 0.4%. In regimens A, B, and C, the 5-year LRFS and OS rates were 62.4%, 94.7%, and 92.4% (P < 0.001), and 16.7%, 39.2%, and 67.9% (P < 0.001), respectively. The 5-year OS rates of the patients with uMCC stages I, II, and III, and IVA and BCLC stages A, B, and C were 69.2%, 65.4%, 43.8%, and 26.6% (P < 0.001), respectively and 65.1%, 40%, and 32.2% (P < 0.001), respectively. In a multivariate analysis, the Child-Pugh classification, alpha-fetoprotein level, mUICC stage, dose-fractionation regimens, and primary tumor response were independent prognostic factors associated with OS.

Conclusions: Risk-adapted PBT using three dose-fractionation regimens could achieve promising long-term tumor control across all stages of HCC.

Keywords: Hepatocellular carcinoma, Proton beam therapy, Overall survival, Local recurrence-free survival

PE-253

Clinical Outcomes of Stereotactic Body Radiation Therapy for Single Viable Hepatocellular Carcinoma at the Site of Incomplete Transarterial Chemoembolization

Jinhong Jung1, Hee Hyun Park2, So Yeon Kim3, Young-Suk Lim, Han Chu Lee4, Jin-hong Park5, Jong Hoon Kim4, Sang Min Yoon4

Departments of 'Radiation Oncology, 'Radiology, and 'Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Aims: Transarterial chemoembolization (TACE) in hepatocellular carcinoma (HCC) patients may show unsatisfactory local control, with “incomplete TACE” cases having viable HCCs after multiple consecutive TACE. Moreover, no study to date has provided clear recommendation on effective local treatment option for residual viable HCC at the site of incomplete TACE. Therefore, we evaluated the clinical outcomes of patients who received stereotactic body radiation therapy (SBRT) for single viable HCC at incomplete TACE sites.

Methods: A total of 313 patients were treated with SBRT for single viable HCC after incomplete TACE between March 2012 and July 2017 at Asan Medical Center (Seoul, Korea). Incomplete TACE was defined as evidence of viable HCC at the site of TACE on follow-up imaging following one or more consecutive TACE procedures.

Results: The median follow-up period was 32.9 months (interquartile range [IQR], 23.6–41.4) and the median tumor size was 2.0 cm (IQR, 1.5–2.5). Almost all patients had ECOG performance status of 0 (93.3%). The median radiation dose was 45 Gy (36–60) with a median fraction size of 15 Gy (12–20). The local control rate at 3 years was 91.5%. The overall survival, out-of-field intrahepatic recurrence-free survival, and distant metastasis-free survival rates at 3 years were 72.5%, 35.8%, and 82.7%, respectively. Elevations in the level of transaminases or bilirubin of CTCAE grade ≥ 2, which may be related to SBRT without progression of intrahepatic HCC, were observed in 8 patients (2.5%). Worsening of Child-Pugh score ≥ 2 was observed in 6 patients (1.9%). No patients experienced late gastrointestinal bleeding within the radiation field.

Conclusions: SBRT showed excellent clinical outcomes in terms of local control, survival, and adverse events when used as an ablative treatment modality for residual single viable HCC at the site of incomplete TACE.

Keywords: Hepatocellular carcinoma, Incomplete transarterial chemoembolization, Stereotactic body radiation therapy

PE-254

Yttrium-90 Radioembolization Might Have Better Efficacy in Progression-Free Survival and Disease Control Rate in Patients with Hepatocellular Carcinoma Compared with Conventional Chemoembolization: A Retrospective Cohort Study

Minseok Albert Kim1, Heejoon Jang1, Sun Woong Kim1, Cheol-Hyung Lee2, Yun Bin Lee1, Eun Ju Choi1, Jeong-Hoon Lee1, Su Jong Yu1, Jung-Hwan Yoon1, Hyo-Cheol Kim3, Jin Wook Chung2, Yoon Jun Kim1

1Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; 2Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Aims: Locoregional therapies, such as yttrium-90 (Y-90) radio-
embolization (RE) and conventional chemoembolization (CE) can effectively control localized hepatocellular carcinoma (HCC) in patients who are not amenable to curative resection. However, it has not yet been fully established which modality is more effective. The aim of this study was to compare effectiveness of RE and CE in the treatment of HCC.

Methods: A total of 135 patients who were initially treated with RE (n = 45) or CE (n = 90, age and sex matched) between March 2012 and May 2017 were reviewed retrospectively. Primary endpoints were overall survival and progression-free survival, and secondary endpoints were clinical response, the rate of down-staged HCC, and the rate of curative surgery.

Results: Of 135 patients, median age was 59 and median follow-up period was 19.1 months. There was no difference in baseline stage of HCC between treatment groups. During follow-up period, eighty-four patients (62.2%) experienced progression. There was no significant difference in overall survival between both groups after treatment ($P = 0.22$ by log-rank test). However, progression-free survival was higher in RE group than CE group (median, RE, 24.9 months; CE, 29.4 months; $P = 0.037$ by log-rank test) and RE group showed better disease control rate than CE group (55.6%, RE; 28.9%, CE; $P = 0.003$). In multivariable cox regression analysis, RE was in independent factor for progression (adjusted HR 0.43, 95% CI=0.22–0.84, $P = 0.013$). RE showed remarkably lower toxicities of all grades than CE group. Among 119 patients beyond Milan criteria, the proportion of patients who were down-staged tumor within Milan criteria were higher in the RE group than the CE group (60.5%, RE; 24.7%, CE; $P = 0.025$).

Conclusions: Radioembolization might provide better progression-free survival and might be more effective in disease control of unresectable HCC than chemoembolization. Furthermore, there is a high chance of undergoing curative surgery by down-staging and low toxicities.

Keywords: Hepatocellular carcinoma, Radioembolization, Chemoembolization, Down-staging

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (135)</th>
<th>RE (45)</th>
<th>CE (90)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>59 (35–81)</td>
<td>60 (35–81)</td>
<td>58 (35–84)</td>
<td>0.025</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>117 (86.7%)</td>
<td>17 (82.2%)</td>
<td>80 (88.9%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Etiology</td>
<td>0.83</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV</td>
<td>85 (63.0%)</td>
<td>18 (82.2%)</td>
<td>67 (74.4%)</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>10 (7.4%)</td>
<td>4 (6.7%)</td>
<td>6 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>11 (8.2%)</td>
<td>6 (13.3%)</td>
<td>5 (5.6%)</td>
<td></td>
</tr>
<tr>
<td>NASH</td>
<td>2 (1.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV + Alcohol</td>
<td>11 (8.2%)</td>
<td>6 (13.3%)</td>
<td>5 (5.6%)</td>
<td></td>
</tr>
<tr>
<td>HCV + Alcohol</td>
<td>1 (0.7%)</td>
<td></td>
<td>1 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>HBV + HCV + Alcohol</td>
<td>2 (1.5%)</td>
<td></td>
<td>1 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11 (8.6%)</td>
<td>9 (20.0%)</td>
<td>2 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Child-Pugh score</td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>121 (90.6%)</td>
<td>40 (88.9%)</td>
<td>81 (90.0%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>14 (10.4%)</td>
<td>5 (11.1%)</td>
<td>9 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>111 (82.3%)</td>
<td>38 (84.4%)</td>
<td>73 (81.1%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Tumor extent</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UICC</td>
<td>75 (55.9%)</td>
<td>18 (82.2%)</td>
<td>57 (63.3%)</td>
<td></td>
</tr>
<tr>
<td>Child-Pugh score</td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child-Pugh score</td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage ≥ 2 Scan*</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>121 (90.6%)</td>
<td>40 (88.9%)</td>
<td>81 (90.0%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>14 (10.4%)</td>
<td>5 (11.1%)</td>
<td>9 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>TMM stage</td>
<td>0.49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>15 (11.1%)</td>
<td>1 (2.2%)</td>
<td>14 (15.6%)</td>
<td></td>
</tr>
<tr>
<td>III and III</td>
<td>35 (25.9%)</td>
<td>13 (28.9%)</td>
<td>22 (24.4%)</td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>46 (34.1%)</td>
<td>14 (31.3%)</td>
<td>32 (35.6%)</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>6 (4.4%)</td>
<td>3 (4.4%)</td>
<td>3 (4.4%)</td>
<td></td>
</tr>
<tr>
<td>IVB</td>
<td>2 (1.5%)</td>
<td>1 (2.2%)</td>
<td>1 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>BCLC stage</td>
<td>0.07</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 (0.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>30 (22.2%)</td>
<td>15 (33.3%)</td>
<td>15 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>50 (37.0%)</td>
<td>15 (33.3%)</td>
<td>35 (38.9%)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>54 (40.0%)</td>
<td>15 (33.3%)</td>
<td>39 (43.3%)</td>
<td></td>
</tr>
<tr>
<td>Ochsner stage</td>
<td>0.48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>110 (81.5%)</td>
<td>75 (83.3%)</td>
<td>35 (38.9%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>13 (9.7%)</td>
<td>13 (14.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3 (2.1%)</td>
<td>2 (2.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APP ≥ 200 mg/dL</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RE</td>
<td>115 (86.1%)</td>
<td>80 (88.9%)</td>
<td>35 (38.9%)</td>
<td></td>
</tr>
</tbody>
</table>

*Size of primary index tumor

Table 2. Multivariable cox regression for progression-free survival

<table>
<thead>
<tr>
<th></th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60</td>
<td>0.67</td>
<td>0.43–1.04</td>
</tr>
<tr>
<td>Male</td>
<td>0.61</td>
<td>0.30–1.13</td>
</tr>
<tr>
<td>ECOD 0 or 1</td>
<td>0.63</td>
<td>0.36–1.09</td>
</tr>
<tr>
<td>Portal vein</td>
<td>1.91</td>
<td>1.23–2.96</td>
</tr>
<tr>
<td>Invasive</td>
<td>0.98</td>
<td>0.54–1.90</td>
</tr>
<tr>
<td>5.90 RE</td>
<td>0.54</td>
<td>0.31–0.94</td>
</tr>
<tr>
<td>5.90 RE</td>
<td>0.50</td>
<td>0.28–0.88</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, ECOG, and portal vein invasion

Table 4. Cautious resection or liver transplantation rate

<table>
<thead>
<tr>
<th></th>
<th>RE</th>
<th>CE</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rejection</td>
<td>3/45 (6.6%)</td>
<td>4/35 (11.4%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>1/45 (2.2%)</td>
<td>1/35 (2.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Downstaging within Milan criteria</td>
<td>23/33 (69.7%)</td>
<td>20/31 (64.5%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusions: Radioembolization might provide better progression-free survival and might be more effective in disease control of unresectable HCC than chemoembolization. Furthermore, there is a high chance of undergoing curative surgery by down-staging and low toxicities.

Keywords: Hepatocellular carcinoma, Radioembolization, Chemoembolization, Down-staging

Safety of Transarterial Chemoembolization in Patients with Recurrent Hepatocellular Carcinoma after Liver Transplantation
Hepatocellular Carcinoma

Keywords:

Results:

Methods:

Beom Kim, Joong-Won Park

Heejoon Jang

Myungsu Lee

Goyang, Republic of Korea

Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Republic of Korea

Aims: Transarterial chemoembolization (TACE) is a widely accepted therapeutic modality for multinodular hepatocellular carcinoma (HCC). TACE is generally considered a safe procedure even after surgical resection, but the safety data of TACE after transplantation is still lacking. The aim of this study is to investigate the safety of TACE for recurrent HCC after liver transplantation.

Methods: Medical records of 38 patients who had received living donor liver transplantation and then underwent TACE for recurrent HCC January 2001 to December 2018 were retrospectively reviewed.

Results: A total of 112 TACE procedures were performed for 38 patients, and complications were occurred in 25 patients (65%) with the incidence of 42% (48/113) per TACE procedures. Out of 112 TACE procedures performed, most frequently encountered complications were as follows: postembolization syndrome (n = 19, 17%), biloma (n = 10, 8.9%), liver abscess (n = 7, 6.2%), intrahepatic duct dilatation (n = 6, 5.4%), bacteremia (n = 2, 1.8%), hepatic artery stenosis (n = 1, 0.9%), biliary stricture (n = 1, 0.9%), and hematomata (n = 1, 0.9%). The median interval between TACE and the diagnosis of complications was 3 days (interquartile range 0–81). Most cases were managed conservatively. However, endoscopic stenting was required for intrahepatic duct obstruction (n = 2), biloma (n = 1) and liver abscess (n = 2) required endoscopic stenting or percutaneous drainage. No one died of complications. Of 24 patients who had postoperative biliary complications after transplantation, 18 patients (75%) had TACE-related complications with incidence of 42.6% (29/68) per TACE procedure, while out of the remaining 14 patients who had no postoperative complications, 7 (50%) had TACE-related complications with incidence of 28.8% (13/45) per procedure.

Conclusions: TACE is still regarded a safe procedure; however, biliary or infectious complications seem more frequently occurred in recurrent HCC following living donor liver transplantation.

Keywords: Transarterial chemoembolization (TACE), Recurrence, Hepatocellular carcinoma, Complications

PE-256

An Earlier Follow-Up Imaging Was Not Associated with Better Overall Survival after Transarterial Chemoembolization for Intermediate- or Advanced-Stage Hepatocellular Carcinoma

Heejoon Jang1, Jeong-Hoon Lee1, Minseok Albert Kim1, Sun Woong Kim1, Cheol-Hyung Lee1, Yun Bin Lee1, Eun Ju Cho1, Myungsu Lee1, Su Jong Yu1, Hyo-Cheol Kim1, Yoon Jun Kim1, Jin Wook Chung1, Jung-Hwan Yoon1

1Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea; 2Department of Radiology, Seoul National University College of Medicine, Seoul, Korea

Aims: The optimal interval of follow-up imaging after transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC) has not been well established. This study aimed to evaluate whether earlier follow-up imaging is associated with better overall survival (OS) among patients who underwent on-demand TACE.

Methods: This retrospective study included 519 patients who underwent superselective TACE as an initial treatment for intermediate- or advanced-stage HCC at Seoul National University Hospital between 2013 and 2015. The included patients were categorized into two groups by the interval of follow-up dynamic imaging: within 30 days (the early follow-up group, n = 133) or between 30 and days (the late follow-up group, n = 386) after TACE. The primary endpoint was OS.

Results: During follow-up (median = 26.8 months), 308 patients (59.3%) died. There was no difference in baseline age, sex, Child-Pugh score, and Barcelona-Clinic Liver Cancer (BCLC) stages between two groups. However, the mean baseline alpha-fetoprotein (AFP) level was significantly higher in the early follow-up group (25,147 ± 16,058 ng/mL; P = 0.03). The OS was comparable between two groups (early vs. late follow-up: hazard ratio [HR]=1.003, 95% confidence interval [CI]=0.775–1.299; log-rank P = 0.98). The median OS of both early and late follow-up groups were 35.3 months (Figure 1). In a multivariable analysis, follow-up imaging interval was not independently associated with earlier death (adjusted HR=1.079, 95% CI=0.832–1.399; P = 0.57) after adjustment for Child-Pugh score, BCLC stage, and AFP. There was no significant difference in OS between the two groups, when sensitivity analyses were performed according to baseline AFP levels (<400; 400–4,000; and >4,000 ng/mL) with HRs ranging from 0.807 to 1.337 (all P > 0.2, Figures 2A–C).

Conclusions: There was no significant association between follow-up imaging interval (<30 days vs. >30 days) after TACE and OS in a large-volume center with highly experienced interventional radiologists.

Keywords: Hepatocellular carcinoma, TACE, CT, Follow-up, Overall survival
Survival Outcomes of TACE in Treatment-Naïve and Recurrent HCC after Curative Resection: A Propensity Score-Matched Analysis

David Sooik Kim 1, Tae Seop Lim 1,2, Mi Young Jeon 1,2, Beom Kyung Kim 1,2, Jun Yong Park 1,2, Do Young Kim 1,2, Sang Hoon Ahn 1,2, Kwang-Hyub Han 1,2, Oidov Baatarkhuu 1,2, and Seung Up Kim 1,2

1Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, South Korea; 2Department of Infectious Diseases, Mongolian National University of Medical Sciences, South Korea

Aims: Transarterial chemoembolization (TACE) improves the survival of patients with hepatocellular carcinoma (HCC); however, TACE treatment outcomes of patients with treatment-naïve HCC (TN-HCC) and those with recurrent HCC after curative resection (R-HCC) have not yet been compared.

Methods: We recruited 448 patients with TN-HCC and 275 patients with R-HCC treated with TACE as first-line anti-cancer treatment.

Results: At first TACE, patients with TN-HCC showed a significantly lower proportion of male gender (74.9% vs. 84.3%), higher proportion of liver cirrhosis (61.9% vs. 49.3%), higher aspartate aminotransferase (median 48 vs. 31 IU/L), alanine aminotransferase (median 38 vs. 26 IU/L), alpha-fetoprotein (AFP) (median 96.6 vs. 7.7 ng/mL), and total bilirubin (mean 1.0 vs. 0.8 mg/dL) levels, longer prothrombin time (median 1.05 vs. 1.01 international normalized ratio), higher tumor number (mean 2.1 vs. 1.7), larger tumor size (median 3.1 vs. 1.6 cm), and lower proportion of Barcelona Clinic Liver Cancer stage 0-A (55.6% vs. 71.9%) than patients with R-HCC (all P < 0.05). Multivariate analysis showed that TACE for TN-HCC (vs. R-HCC) was an independent predictor of mortality (hazard ratio, 1.328; P = 0.024) with AFP level and tumor number (all P < 0.05). However, treatment outcomes between TN-HCC and R-HCC became statistically similar after propensity score-matched (PSM) analysis using liver cirrhosis, tumor size, and multiple tumors (P < 0.05).

Conclusions: Based on the similar TACE treatment outcomes observed with the PSM analysis, the current TACE treatment guideline for patients with TN-HCC might similarly be applied for patients with R-HCC.

Keywords: Hepatocellular carcinoma, Curative resection, Trans-arterial chemoembolization, Recurrence

Establishment and Validation of a Risk Prediction Model in Patients with Hepatocellular Carcinoma Treated with Trans-Arterial Radioembolization

Jae Seung Lee1, Han Ah Lee2, Mi Young Jeon1,2, Tae Seop Lim1,2, Beom Kyung Kim1,2, Jun Yong Park1,2, Do Young Kim1,2, Sang Hoon Ahn1,2, Soon Ho Um1, Kwang-Hyub Han1,2, Yeon Seok Seo2, and Seung Up Kim1,2

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea; 3Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 4Yonsei Liver Center, Severance Hospital, Seoul, Korea

Aims: Few studies have reported the treatment outcomes of trans-arterial radioembolization (TARE) using yttrium-90 (90Y) for hepatocellular carcinoma (HCC). We established and validated a new risk prediction model for patients with HCC treated with TARE.

Methods: Between 2010 and 2017, 113 and 35 patients with intrahepatic HCC treated with TARE were selected for the training and validation cohorts, respectively. The modified response evaluation criteria in solid tumors (mRECIST) were used for response evaluation.

Results: In the training cohort, the median age was 64.1 years (92 male and 19 female) and the mean survival after TARE was 50.3 months. The cumulative survival rates at six and 12 months were 92.0 and 84.0%, respectively. A new risk prediction model for patients with HCC treated with TARE (Y-scoring system) was established from the training cohort using five independent baseline variables (serum albumin <3.5 g/dL, hazard ratio [HR]=5.446; alpha-fetoprotein >200 ng/mL [HR=5.071]; tumor number ≥3 [HR=2.933]; portal vein thrombosis [HR=4.915]; and hepatic vein invasion [HR=8.500]) and two on-treatment variables (no des-gamma-carboxy prothrombin response [HR=15.346] and progressive disease at three months [HR=4.154]) for mortality (all P < 0.05). The predictive accuracy of the Y-scoring system was acceptable to predict six- (area under the curve [AUC]=0.886) and 12-month mortality (AUC=0.886) (all P < 0.05). The predictive accuracy of the model was similarly maintained in the validation cohort (AUC 0.737-0.901 at six to 12 months).

Conclusions: Our new risk prediction model can be used to stratify different prognoses in patients with HCC treated with TARE. Validation studies are required.

Keywords: Hepatocellular carcinoma, Transarterial radioembolization, Risk prediction, Survival
Predictors of Radiological Complete Response in Patients with Intrahepatic Hepatocellular Carcinoma Treated with Transarterial Radioembolization

Yoon Ah Kim1, Jae Seung Lee1, Beom Kyung Kim1,2, Jun Yong Park2,3, Do Young Kim1,3, Sang Hoon Ahn1,3, Kwang-Hyub Han1,3, and Seung Up Kim1,3

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; 2Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea; 3Yonsei Liver Center, Severance Hospital, Seoul, Korea

Aims: Transarterial radioembolization (TARE) has shown promising results for treating hepatocellular carcinoma (HCC). We identified the independent predictors of radiological complete response (rCR) in patients with intrahepatic HCC treated with TARE.

Methods: Patients with intrahepatic HCC treated with TARE between 2011 and 2017 were recruited. The rCR was defined according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Cox-regression analysis was used to find independent predictors of rCR.

Results: The median age of the study population (83 males and 19 females) was 64.3 years. The mean survival after TARE was 55.5 months and 21 (20.6%) patients were dead during the study period. The rCR was achieved in 14 (13.7%) patients who had significantly higher serum albumin level (median 4.1 vs. 3.9 g/dL), lower total bilirubin level (median 0.6 vs. 0.7 mg/dL), lower aspartate aminotransferase level (median 30.0 vs. 43.0 IU/L), lower alkaline phosphatase level (median 79.0 vs. 103.0 IU/L), lower alpha-fetoprotein level (median 12.7 vs. 39.9 ng/mL), lower des-gamma-carboxyprothrombin level (median 43.0 IU/L), lower alkaline phosphatase level (median 575.5 vs. 2772.0 mAU/mL), lower MELD score (median 6.0 vs. 7.0), and smaller maximal tumor diameter (median 6.3 vs. 9.0 cm) than those of patients without rCR (all P < 0.005). Multivariate Cox-regression analysis showed that lower MELD score (hazard ratio [HR]=0.436, P = 0.015) and maximal tumor size <9 cm (HR=11.180, P = 0.020) independently predicted the increased probability of radiological CR after TARE.

Conclusions: Low MELD score and smaller maximal tumor size were independently associated with the increased probability of rCR after TARE in patients with intrahepatic HCC.

Digital Subtraction Angiography Outcome during DC Bead Transarterial Chemoembolization for Hepatocellular Carcinoma

Tran Ngoc Thuy
Thai Nguyen Medical College, Vietnam

Aims: To describe short-term outcomes after drug-eluting bead (DEB) transarterial chemoembolization in hepatocellular carcinoma (HCC).

Methods: Patients with unresectable HCC were retrospectively assigned to this study. Angiographic operators determined which feeding arteries were potentially supplying the target tumor. TACE was performed and the dosage of Doxorubicin-eluting Bead was judged by tumor size and achievement of stagnant arterial flow.

Results: A total of 118 patients, male 89.8%, female 10.2%, (mean age 60.7 ± 9.8) had a total of 176 tumor feeding arteries. The origin sites of the artery were the following: the right hepatic artery (n = 35), the left hepatic artery (n = 19), the anterior sectional artery (n = 30), the posterior sectional artery (n = 36), the segment artery (n = 41), the left gastric artery (n = 1), the gastroduodenal artery (n = 3) and the right inferior phrenic artery (n = 12). The degree of tumor feeding arteries: slight 1.7%, moderate 44.1%, serious 54.2%. The right branch portal vein thrombosis 5.9%, the left branch portal vein thrombosis 0.8%, 93.3% patients had no thrombosis. The hepatic arterioporal shunts 11.9%. After TACE, the achievement of stagnant arterial flow: complete occlusion 61.1%, near complete occlusion 34.7%, non occlusion 4.2%.

Conclusions: Digital subtraction angiography can demonstrate the type, the site and the degree of tumor feeding arteries completely and directly, thus having important value in treating HCC.

Keywords: Digital subtraction angiography, Transarterial chemoembolization, Hepatocellular carcinoma

Curative Treatment after Transarterial Radioembolization is Associated with Better Survival Outcomes in Patients with Hepatocellular Carcinoma

Yoon Ah Kim1,4, Han Ah Lee1, Jae Seung Lee1, Mi Young Jeon1, Beom Kyung Kim1,4, Young Kul Jung1, Jun Yong Park1,4, Ji Hoon Kim1, Yeon Seok Seo1, Do Young Kim1,4, Hyung Joon Yim1, Sang Hoon Ahn1,4, Jong Eun Yeon1, Kwan Soo Byun1, Soon Ho Um1, Kwang-Hyub Han1,3, and Seung Up Kim1,3

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; 2Institute of Gastroenterology, Yonsei University; 3Yonsei Liver Center, Severance Hospital, Seoul, Korea

Aims: To compare the survival outcomes of patients with hepatocellular carcinoma undergoing curative treatment after TARE with those of patients undergoing nontreatment.

Methods: We performed a retrospective analysis of all patients with HCC who underwent TARE at our institution between 2003 and 2017. The survival outcomes of the patients who underwent curative treatment were compared with those of the patients who underwent nontreatment.

Results: A total of 118 patients, male 89.8%, female 10.2%, (mean age 60.7 ± 9.8) had a total of 176 tumor feeding arteries. The origin sites of the artery were the following: the right hepatic artery (n = 35), the left hepatic artery (n = 19), the anterior sectional artery (n = 30), the posterior sectional artery (n = 36), the segment artery (n = 41), the left gastric artery (n = 1), the gastroduodenal artery (n = 3) and the right inferior phrenic artery (n = 12). The degree of tumor feeding arteries: slight 1.7%, moderate 44.1%, serious 54.2%. The right branch portal vein thrombosis 5.9%, the left branch portal vein thrombosis 0.8%, 93.3% patients had no thrombosis. The hepatic arterioporal shunts 11.9%. After TACE, the achievement of stagnant arterial flow: complete occlusion 61.1%, near complete occlusion 34.7%, non occlusion 4.2%.

Conclusions: Digital subtraction angiography can demonstrate the type, the site and the degree of tumor feeding arteries completely and directly, thus having important value in treating HCC.

Keywords: Digital subtraction angiography, Transarterial chemoembolization, Hepatocellular carcinoma

*Yoon Ah Kim and Han Ah Lee equally contributed to this work.
Background/Aims: Transarterial radioembolization (TARE) has been used to treat hepatocellular carcinoma (HCC). We identified the independent predictors of achieving subsequent curative treatments after TARE for patients with intrahepatic HCC. Also, we investigated whether the achievement of curative treatments after TARE is associated with better survival outcomes.

Methods: A total of 143 patients with intrahepatic HCC treated with TARE between 2011 and 2017 were recruited. Subsequent curative treatment was applied according to the physician’s decision.

Results: The median age of the study population (115 males and 28 females) was 65.0 years. Twenty seven (18.9%) patients received curative treatments (resection in 16, transplantation in 9, and ablation in 2) after TARE, who were likely to be younger (< 65 years) (77.8% vs. 44.0%) and less likely to have hypertension (40.7% vs. 62.9%) than those who did not receive curative treatments (all P < 0.05). On multivariate analysis, younger age (< 65 years) (hazard ratio [HR] = 9.295, 95% confidence interval [CI] = 2.859-30.221, P = 0.001) and AFP ≤ 200 ng/mL (HR=4.246, CI 1.294-13.935, P = 0.017) were independent predictors of receiving curative treatment after TARE. On multivariate analysis, curative treatment was selected as an independent predictor of mortality (HR=0.089, CI 0.011-0.721, P = 0.023), together with tumor burden > 50% (HR=5.690), portal vein thrombosis (HR=5.635) and progressive disease by mRECIST criteria at 3 months after TARE (all P < 0.05). The cumulative survival rate of patients who achieved curative treatment after TARE was significantly higher than that of patients who did not (P<0.001 by log-rank test).

Conclusions: Younger age and AFP ≤ 200 ng/mL independently predicted the increased probability of receiving curative treatment after TARE. The achievement of curative treatment after TARE is independently associated with better overall survival in patients with unresectable HCC. Tumor burden > 50%, presence of portal vein thrombosis, and progressive disease by mRECIST criteria at 3 months after TARE are independently associated with the increased risk of mortality in patients with unresectable HCC.

Keywords: Transarterial radioembolization, Hepatocellular carcinoma, TARE, HCC

Table. Independent predictors of achieving curative treatment after TARE.

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>Hazard ratio</td>
</tr>
<tr>
<td>Demographic variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt; 65 years</td>
<td>0.003</td>
<td>9.295</td>
</tr>
<tr>
<td>AFP ≤ 200 ng/mL</td>
<td>0.008</td>
<td>4.246</td>
</tr>
<tr>
<td>Multiple tumors</td>
<td>0.071</td>
<td>0.380</td>
</tr>
<tr>
<td>BCLC stage 3</td>
<td>0.087</td>
<td>0.484</td>
</tr>
<tr>
<td>Progressive disease by mRECIST criteria at 3 months</td>
<td>0.076</td>
<td>0.166</td>
</tr>
</tbody>
</table>

Variables are expressed as median (interquartile range) or n (%). CI, confidence interval; TARE, trans-arterial radioembolization; AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; mRECIST, modified Response Evaluation Criteria in Solid Tumors.

Conclusion: Younger age and AFP ≤ 200 ng/mL independently predicted the increased probability of receiving curative treatment after TARE. The achievement of curative treatment after TARE is independently associated with better overall survival in patients with unresectable HCC. Tumor burden > 50%, presence of portal vein thrombosis, and progressive disease by mRECIST criteria at 3 months after TARE are independently associated with the increased risk of mortality in patients with unresectable HCC.

Keywords: Transarterial radioembolization, Hepatocellular carcinoma, TARE, HCC

Role and Limitation of Hepatic Arterial Infusion Chemotherapy

Beom-Hui LEE, Dong-Shik LEE, Chan-Woo CHO, Sung-Su YUN
Department of Surgery, College of Medicine, Yeungnam University, Republic of Korea

Aims: The patients with advanced hepatocellular carcinoma (HCC) have a poor oncologic outcome. In this study, we evaluated role and limitation of Hepatic Arterial Infusion Chemotherapy (HAIC) in patients with advanced HCC and the efficacy of liver resection after downstaging following HAIC.

Methods: This retrospective study included 103 inoperable HCC patients with Child-Pugh class A were treated with HAIC between April 2003 to March 2015. The early response and overall response were evaluated by Modified Response Evaluation Criteria In Solid Tumors (mRECIST) and the alpha-fetoprotein (AFP) ratio. Liver resection was performed to patients who were considered to obtain a tumor-free resection.

Results: The early response was better than overall response. Response rate and disease control rate were 37 (36.3%) vs 20 (19.6%) and 83 (81.4%) vs 45 (44.1%), respectively. The median survival time (MST) in all patients was 13 months. The MST was significant different according to early response to HAIC (disease control and AFP ratio ≤ 1, 16 months; disease control and AFP ratio >1, 13 months; disease progression and AFP ratio ≤ 1, 7 months; disease progression and AFP ratio >1, 5 months; P = 0.000). 12 patients (11.7%) underwent liver resection following HAIC and the median survival was 37 months. Liver resection was only independent prognostic factor that associated with overall survival in multivariate analysis (P = 0.002).

Conclusions: HAIC could be another alternative to treat patients with advanced HCC who have preserved hepatic functional reserve. Evaluating the response to HAIC and the feasibility of operation early would provide good long-term outcomes.

Laparoscopic Right Hepatectomy Is Feasible and Safe in Solitary Hepatocellular Carcinoma

Hoang Duct Nam1, Jong Man Kim2, Gyu-Seong Choi3, Jae-Won Joh2
1Department of Surgery, Vinmec International Hospital, Hanoi, Vietnam; 2Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Background: Laparoscopic liver resection has been reported as a
safe and effective approach for the management of hepatocellular carcinoma (HCC). However, its perioperative and oncological outcomes have not been evaluated in right hepatectomy (RH) patients. Aim of present study is to compare the outcomes between laparoscopic RH (LRH) and open RH (ORH) in HCC patients.

**Methods:** From January 2013 to August 2017, 345 patients with HCC underwent RH. Patients with portal vein tumor thrombosis, history of preoperative locoregional therapies, multiple tumors, bile duct tumor thrombosis, the history of abdominal operation, and serosal involvement were excluded. 189 patients were selected because of Child-Pugh class A and solitary HCC.

**Results:** The numbers of ORH and LRH groups were 134 and 55 patients. Among LRH group, four patients (7.3%) converted open conversion due to bleeding (n = 3) and close to the tumor (n = 1). Median tumor size of ORH and LRH was 4.0 cm and 3.5 cm, respectively (P = 0.086). Preoperative factors, preoperative AFP levels, and pathologic factors were not different between the two groups. Operation time in ORH group was shorter than in the LRH group (243 min vs. 271 min; P = 0.032), but amounts of blood loss in the ORH group was more than in the LRH (300 ml vs. 200 ml; P < 0.001). Two patients in the ORH group received red blood cells transfusion, but none in the LRH group were not transfused. Ten patients in the ORH group developed postoperative complications (Clavien grade I and II), but three patients in the LRH group had postoperative complications (Clavien grade I and II). Median hospitalization in the ORH group was longer than in the LRH group (10 days vs. 7 days; P < 0.001). Disease-free survival (DFS) rates and patient survival (PS) rates at 1-, 2-, and 3-year were 92.1%, 89.2%, 87.4% and 95.3%, 92.4%, 90.2% in the ORH group and 100%, 94.1%, 94.1% and 100%, 100%, 100% in the LRH group, respectively. The DFS and PS in the LRH group were better than in the ORH group, but the difference did not reach significant levels.

**Conclusions:** LRH is feasible and safe for solitary HCC patients in experienced center. However, the oncologic outcome of LRH should be needed in further investigations.

---

**PE-264**

**Predicting the Choice of Operative Treatment for Common Bile Duct Diseases Complicated by Obstructive Jaundice**

Valeriy Vladimirovich Boyko1, Yurii Vladimirovich Avdosev2, Anastasia Lvovna Sochnieva3, Maria Segeevna Mazorchuk3

1Kharkiv National Medical University, Department of Surgery #№1; 2Zaytsev Institute of General and Emergency Surgery NAMS of Ukraine; 3Kharkiv National University of Radio Electronics

**Aims:** The choice of operative treatment for benign and malignant common bile duct diseases remains an unsolved issue. The aim of the study is to create a mathematical predictive model of choosing the operative treatment in patients with common bile duct diseases complicated by obstructive jaundice.

**Methods:** Based on the statistical processing of data for 118 patients who underwent surgical treatment, a mathematical model was developed for predicting the choice of biliary decompression in patients with common bile duct diseases complicated by obstructive jaundice. The patients had the following diseases: cholelithiasis in 21 (17.8%), common bile duct strictures in 6 (5.1%), biliodigestive anastomosis strictures in 7 (5.9%), and cholangiocarcinomas of different localization in 84 (71.2%) patients. The following operative interventions were performed: percutaneous transhepatic biliary drainage (PTBD) in 88 (74.6%) cases, endoscopic in 19 (16.1%) cases, biliodigestive anastomosis or external common bile duct drainage in 4 (3.4%) cases and radical surgery without prior biliary decompression in 7 (5.9%) cases. The predictive model was developed based on the results of retrospective analysis (92 patients) and applied in patients from the prospective part of the study (26 patients).

**Results:** The most significant disease complication risk factors included: correct diagnosis on admission, biliary blockade level, obstructive jaundice duration, clinical diagnosis at the pre-hospital stage, Gologorsky’s operation risk, presence of cholangitis, total serum bilirubin at baseline, and findings of ultrasound, fibrogastroduodenoscopy (EGD) and spiral CT. Based on the statistical data discriminant coefficients were calculated using discriminant analysis for each type of operative treatment. The designed predictive model was assessed for predictive value. For this purpose, types of interventions were selected based on initial data and factorial parameter statistics in patients from the retrospective study sample. In 89.1% of cases, the biliary decompression type was predicted correctly. The biliary decompression type in patients from the prospective part of the study was predicted correctly in 88% of cases.

**Conclusions:** The designed predictive model ensures a high probability and precision of choosing the operative treatment type as well as an individual approach to the pathogenetic choice.

**Keywords:** Choice of operative treatment, Common bile duct diseases, Obstructive jaundice, Prediction

---

**PE-265**

**The Value of Serum Levels of Procalcitonin for Predicting the Severity of Acute Pancreatitis in Patients According to the 2012 Revised Atlanta Classification**

LE THI THU HIEN1, LE QUOC TUAN2

1Thai Nguyen University of Medicine and Pharmacy, Vietnam; 2Thanh Ba Hospital, Vietnam

**Aims:** Acute pancreatitis (AP) has always been a clinical challenge. Timely assessment of severity in patients with AP is of prime importance in guiding an optimal management for these patients. Various biomarker, computerized tomography and certain scoring systems are used for assessing the severity of this disease. To evaluate serum procalcitonin (PCT), a marker of
systemic inflammation, as an effective single biomarker in determining the severity of AP.

**Methods:** A prospective observational study of 69 patients presenting with AP in 103 Cam Khe Clinic from May 2018 to February 2019 were included in the study. Blood samples were collected for the estimation of PCT on day of admission. Chemiluminescent immunoassay (Elecsy Brahms PCT Roche Diagnostic) was used for measuring serum PCT concentration. The Revised Atlanta classification was used as the gold standard to stratify severity of AP. The predictive accuracy of PCT was measured as the area under the receiver operating characteristic curve (AUC).

**Results:** Female accounted for 55.2%. Mean age was 48 years (from 35 to 68). Severe AP with organ failure, moderate AP and mild AP accounted for 12.6%, 15.4% and 72% respectively. Causes of AP such as gall stone: 46.8%, alcoholic: 20.6%.

Mean ± SD value of serum PCT for mild, moderate and severe AP on day of admission were 0.5 ± 1.23 ng/ml, 1.58 ± 1.36 ng/ml and 3.2 ± 4.3 ng/ml respectively. The cut off value of serum PCT was 0.5 ng/ml between mild and moderate AP (AUC = 0.81, 95% CI = 0.683 - 0.853, sensitivity: 71%, specificity: 86.5%). The cut off value of serum PCT was 0.61 ng/ml between moderate and severe AP (AUC = 0.76, 95% CI = 0.628 - 0.91, sensitivity: 79.3%, specificity: 62.1%).

**Conclusions:** Procalcitonin is a practical, simple parameter that can be used in order to diagnose severe acute pancreatitis earlier and to monitor the clinical prognosis of the disease.

**Keywords:** Acute pancreatitis, Procalcitonin, Prognosis, Severity

**PE-266**

**Statins Use Is Associated with Reduced Risk of Cholangiocarcinoma: A Systematic Review and Meta-Analysis**

Gaurav Nepal
Maharajgunj Medical Campus, Tribhuvan University Institute of Medicine, Kathmandu, Nepal

**Aims:** Statins are widely used for primary and secondary prevention of cardiovascular disease. Preclinical studies have shown that statins have anticancer properties. Epidemiological studies have shown that the use of statins is associated with reduced risk of various cancers and cancer related morbidity/mortality. We conducted a meta-analysis of all available studies to investigate the association between the use of statins and the risk of developing cholangiocarcinoma (CCA), which, to our knowledge, is the first meta-analysis on this matter.

**Methods:** A comprehensive literature search for articles and abstracts published from January 2000 to December 2018 was carried out. Studies that had strictly reported Odds Ratio (OR), Relative Risk (RR), or Hazard Ratio (HR), with 95% confidence interval (CI) were included in the study. Pooled adjusted ORs with corresponding 95% CIs were calculated using fixed effects model.

**Results:** Five observational studies were included in our analysis, with 8,450 CCA subjects and 978,008 healthy controls. Administration of statins significantly reduced the incidence of CCA (OR = 0.79, 95% CI: 0.73-0.86, P < 0.0001). No heterogeneity was found in the study (I² = 46%, P = 0.12). No evidence of publication bias was observed in this meta-analysis.

**Conclusions:** Our study shows statistically significant association between the use of statins and 0.79-fold decreased risk of CCA.

**Keywords:** Statins, Cholangiocarcinoma

**PE-267**

**Molecular Characteristics Associated with 18F-FDG Uptake in Intrahepatic Cholangiocarcinoma**

Keun Soo Ahn1, Koo Jeong Kang2, Yong Hoon Kim3, Tae-Seok Kim4, Kyoung Sook Won5

1Department of Surgery, Keimyung University Dongsan Medical Center; 2Department of Nuclear Medicine, Keimyung University Dongsan Medical Center, Korea

**Aims:** In intrahepatic cholangiocarcinoma (iCCA), genetic characteristics on 18F-FDG-PET scans are not yet clarified. If they are evaluated, we can predict molecular features based on the FDG uptake. We analyzed RNA sequencing in iCCA patients to evaluate gene expression signatures associated with FDG uptake patterns.

**Methods:** We performed RNA sequencing of 22 cases iCCA who underwent preoperative 18F-FDG- PET, and analyzed the clinical and molecular features according to the maximum standard uptake value(SUVmax). Genes and biological pathway which are associated with SUVmax were analyzed.

**Results:** Patients with SUVmax higher than 9.0(n = 9) had poorer disease-free survival than those with lower SUVmax(n = 13, P = 0.035). Genes related to glycolysis and gluconeogenesis, phosphorylation and cell cycle were significantly correlated with SUVmax (| r | ≥0.5). RRM2, which is related to the toxicity of Gemcitabin was positively correlated with SUVmax, and
SLC27A2 which is associated with Cisplatin response was negatively correlated with SUVmax. Cell cycle, hypoxia and metabolism-related pathways were enriched in high SUVmax patients.

**Conclusions:** The genomic features of gene expression and pathways can be predicted by FDG uptake features in iCCA. Patients with high FDG uptake have enriched cell cycle, metabolism and hypoxic pathways, which may lead to a more rational targeted treatment approach.

**Keywords:** Cholangiocarcinoma, FDG, Gene expression

---

**PE-268**

**Risk Factors Associated with Locoregional Failure and Estimation of Survival after Curative Resection for Patients with Distal Bile Duct Cancer**

Ik Jae Lee, Jun Won Kim, Jung Ho Im, Joon Seong Park, Dong Sup Yoon, Dong Ki Lee

Departments of Radiation Oncology, Gangnam Severance Hospital Yonsei University College of Medicine, Department of Radiation Oncology, CHA Bundang Medical Center CHA University School of Medicine, Department of Radiation Oncology, Yonsei Severance Hospital Yonsei University College of Medicine, Department of Internal Medicine, Gangnam Severance Hospital Yonsei University College of Medicine, Korea

**Aims:** Our aim was to identify the risk factors associated with locoregional recurrence in resected distal bile duct cancer (DBDC), and to determine the subgroup that may benefit from adjuvant radiotherapy.

**Methods:** Between 2001 and 2013, we retrospectively analyzed 93 patients with DBDC who had undergone curative resection. Patients who received adjuvant radiotherapy were excluded. The primary outcome was the 3-year LRFFS in patients undergoing surgical resection for distal bile duct cancer; the secondary outcomes were OS and patterns of failure.

**Results:** The 3-year locoregional failure-free survival (LRFFS) and overall survival (OS) rates for all patients were 50.7%, and 53.2%, respectively. On multivariate analysis, the preoperative carcinoembryonic antigen (CEA) level, resection margin, histologic grade, T stage, and N stage were significant prognostic factors for LRFFS. Locoregional recurrence was observed in more than 78% of the patients who underwent R1 resection and were node-positive, and the 3-year LRFFS rate was 19.3%. The 3-year LRFFS rate was 46.9% in the patients who underwent R0 resection and was node-negative with more than 2 risk factors for LRFFS. Patients with more than 2 risk factors showed a 7-fold higher risk of death, compared with patients with 1 or no risk factor. The important risk factors of locoregional failure in patients with DBDC who underwent resection were R1 resection and positive lymph nodes.

**Conclusions:** Adjuvant radiotherapy should be considered for these patients to improve oncologic outcomes. Patients undergoing selective R0 resection and those with node-negative status and multiple locoregional failure risk factors may benefit from adjuvant radiotherapy.

**Keywords:** Distal bile duct cancer, Locoregional failure, Curative resection

---

**PE-269**

**Beneficial Effects of Cassia Angustifolia (Senna Leaves) Treatment Improves Constipation, Liver Functions and Defense of Red Blood Cells in Type 2 Diabetic Patients**

Sumit Rajput, Sagar Verma

School of Biotechnology, Guru Gobind Singh Indraprastha University, India

**Aims:** Diabetes has been reported with constipation leading to the development of diabetic complications in spite of controlling the blood glucose levels by antidiabetic drugs. Our objective was to investigate effects of Cassia angustifolia (Senna leaves) extract on constipation, liver dysfunctions and defense of red blood cells in type 2 diabetic patients.

**Methods:** A total number of 100 subjects were selected with the age ranging from 45 to 60 years. Among them, 50 diagnosed type 2 diabetes individuals were included in the Group A and 50 apparently healthy individuals were selected as Group B for comparison. Cassia angustifolia (Senna leaves extract) was prepared in hot water and orally administered to type 2 diabetic patients with constipation. This treatment was thrice a week in 1st month, twice in a week in corresponding 2nd and 3rd months and once in a week from 4th to 6th months. The defensive enzyme, the glutathione peroxidase, sodium dismutase and catalase were measured in the red blood cells along with the levels of reduced glutathione. The liver function test was performed by measuring hepatic enzymes aminotransferases (Aspartate amino transferase (ASAT) activity, alanine amino transferase (ALAT)) and lipid profile levels.

**Results:** The present study showed that higher levels of serum hepatic enzymes in diabetic patients. The diabetic patients were found to be high blood glucose levels and altered lipid profile with vulnerable to skin infection particularly in the pelvic regions, backside, legs, etc. which were reversed to normal after six months of Senna leaves treatments. The neurological disorder like sustaining pain in legs was also recovered with the treatment. The stools quality also changed to normal. The glutathione peroxidase decreased in red blood cells of diabetics by 20-30%, normalized after six months of treatment with Senna leaves extract. The reduced glutathione found to be decreased in diabetics by 15-20%, normalised. There was also normalize enzymes activity of aminotransferases with treatment to diabetic patients.

**Conclusions:** Senna leaves extract treatment to diabetic patients not only normalize the defense of red blood cells but also corrects skin infection, liver disorder, neurological disorder and physiological disorder.
Comparison of Surgical Outcomes of Robotic and Laparoscopic Pancreatectoduodenectomy in Patient with a Soft Pancreas: Multi-Institutional Study

Sung Hoon Choi1, Jae Hoon Lee2, Chang Moo Kang2,4
1Division of Hepatobiliary and Pancreas, Department of Surgery, CHA Bundang Medical Center, CHA University, Seongnam, Korea; 2Division of Hepatobiliary and Pancreas, Department of Surgery, Ansan Medical Center Ulsan University, Seoul, Korea; 3Division of Hepatobiliary and Pancreas, Department of Surgery, Severance hospital, Yonsei University-Seoul, Korea; 4Pancreateobiliary cancer clinic, Yonsei cancer center, Severance Hospital, Seoul, Korea

Aims: A soft pancreas remains a potent risk factor of postoperative pancreatic fistula following pancreatectoduodenectomy (PD). Recently, minimally invasive PDs have been gradually expanding its application. This study aims to evaluate the effect of anastomotic technique of robotic versus laparoscopic pancreatectoduodenostomy (PJ) on postoperative pancreatic fistula formation among patients with soft pancreas in multi-institutional database.

Methods: From January 2014 to January 2019, 147 patients with soft pancreas and small pancreatic duct less than 3 mm diameter, who underwent minimally invasive PD for periampullary pathologies, were identified. Surgical outcomes of 97 patients who underwent laparoscopic PJ and 50 patients who underwent robotic PJ were compared.

Results: General demographics were comparable between laparoscopic and robotic group, except patients with higher ASA score were more included in laparoscopic group. Majority of indications were common bile duct cancer and ampullary cancer in both laparoscopic and robotic group (61.8% vs. 60%, P = 0.166). All patients underwent duct-to-mucosa anastomosis for pancreatectoduodenostomy. Mean pancreatic duct size was also comparable (1.98±0.69 vs. 2.08±0.96, P = 0.475) Mean operative time and estimated blood loss were similar. Total postoperative pancreatic fistula rate (57.7% vs. 46.0%) and Clinically significant fistula rates higher than grade B (11.3% vs. 14.0%) were not statistically different (P = 0.279). Delayed gastric emptying was more often in laparoscopic group (7.2% vs. 0%, P = 0.239) without statistical significance. Total postoperative complications (30.9% vs. 38.0%) and severe complications higher than grade III (4.1% vs. 18.0%) were more frequent in robotic group (P = 0.024). Length of hospital stay was comparable.

Conclusions: Our study showed similar postoperative pancreatic fistula rate in both surgical modality. However, robotic approach demonstrated higher postoperative complication rate.

Keywords: Robot, Laparoscopy, Pancreatectoduodenostomy, Soft pancreas

Mucinous Cholangiocarcinoma with Hemobilia: A Case Report

Hanlim Choi1,2, Jae-Woon Choi1,2, Dong Hee Ryu1,2
1Department of Surgery, Chungbuk National University; 2Department of Surgery, Chungbuk National University College of Medicine, Korea

Aims: Pure mucinous cholangiocarcinoma is a very rare variant of intrahepatic cholangiocarcinoma.

Methods: An 83-year-old female was presented to our hospital with an epigastric pain. She had no liver disease. Contrast-enhanced abdominal computed tomography showed a dilatation of left hepatic duct containing both irregularly nodular enhancing components and hematomas. Endoscopic retrograde cholangiogram revealed a hemobilia of common bile duct. We initially diagnosed as an intraductal papillary neoplasm of the bile duct with hemobilia. Both left hemihepatectomy including middle hepatic vein and caudate resection was performed.

Results: Pathologic examination reported mucinous adenocarcinoma with directly invades into hepatic parenchyma and beyond the wall of bile duct. She was discharged without complication on postoperative day 9 and had no recurrence for 6 months.

Conclusions: Herein, we described a rare case of mucinous cholangiocarcinoma with hemobilia.

Keywords: Mucinous, Cholangiocarcinoma, Hemobilia

Gallbladder Paraganglioma with Hemorrhage: A Case Report

Sanghwa Song1, Chulkyoon Cho2
1General Surgery, Chonnam National University Hospital, China; 2HPBS, Chonnam National University Hospital, Republic of Korea

Aims: Gallbladder paraganglioma is a very rare tumor and only a few cases have been reported so far. Most of these tumors are asymptomatic and confirmed incidentally after operation. The clinical significance of gallbladder paraganglioma is differential diagnosis with gallbladder cancer or other gallbladder tumor.

Methods: A 48-year-old woman presenting with intermittent abdominal pain. The laboratory tests were all within normal range including tumor marker. MRI showed 8 cm sized mass lesion in gallbladder body and fundus with low signal intensity in T2-weighted images considered as hemorrhage. We planned a laparoscopic cholecystectomy under the impression of gallbladder tumor with hemorrhage.

Results: We performed laparoscopic cholecystectomy successfully. In the gallbladder lumen, several black stones less than 1 cm in diameter and large hematomas were observed. And about 1 cm sized polypoid lesion was detected in the fundus. In microscopic examination of polypoid lesion showed cuboidal cells including granular cytoplasm surrounded by a fibrous septum containing blood vessels. The chief cell was nested in the inside and the spindle shape sustentacular cells surrounded by the
Zellballen cellular arrangement. Synaptophysin, CD56, chromogranin staining were strongly positive for chief cells. In the histopathologic examinations, the diagnosis was gallbladder paraganglioma with hemorrhage.

Conclusions: Gallbladder paraganglioma is extremely rare tumor and usually diagnosed incidentally after operation. We need to aware of this disease entity for differentiation of this tumor with other gallbladder tumors.

**PE-274**

Differentiation of the Gallbladder Adenomyomatosis from Early-Stage Gallbladder Cancer before Surgery

Yong Chan SHIN, Jisum MOON

Surgery, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Republic of Korea

Aims: This study compared perioperative and clinical outcomes in patients undergoing laparoscopic cholecystectomy for gallbladder adenomyomatosis (GBA) or early-stage gallbladder cancer (GBC).

Methods: Among the patients who underwent laparoscopic cholecystectomy from January 2011 to December 2017 in our institution, 194 patients histopathologically diagnosed with GBA and 30 patients with GBC were enrolled in this study. Their perioperative and clinical outcomes were compared.

Results: There were no significant differences in sex (1.0:0.8 vs. 1.0:0.7, male:female, P = 0.734), BMI (23.9 ± 3.4 vs. 24.0 ± 3.8 kg/m², P = 0.916), or preoperative liver function tests between the GBA and GBC groups. The GBC group was significantly older (50.5 ± 14.1 vs. 65.9 ± 10.6 years, P < 0.001) and had higher ASA grade (40.3 vs. 63.4, grade II or III (%), P = 0.043) than the GBA group. Although there was no significant difference in preoperative diagnostic methods (P = 0.442), the GBC group showed significantly higher rate of misdiagnosis on preoperative imaging work-up, compared with postoperative histopathologic findings (30.9% vs. 53.3%, P = 0.011). Patients with gallstones in the GBA group were significantly more than those in the GBC group (68.6% vs. 40.0%, P = 0.004).

Conclusions: This study revealed the difficulty of accurate diagnosis of early-stage GBC. If an older patient who was hospitalized for biliary colic does not have any gallstones but thickened gallbladder wall with inflammation on preoperative diagnostic exam, the possibility of early-stage GBC as well as benign diseases such as acute / chronic cholecystitis and GBA should be considered.

**PE-275**

Management of Xanthogranulomatous Cholecystitis Combined With Common Bile Duct Adenoma Mimicking Biliary Malignancy of Old Age Patient: A Case Report

Junghyun PARK, Jin Hyung PARK

HBP Surgery, General Surgery, St. Paul Hospital, The Catholic University of Korea, Republic of Korea

Aims: Xanthogranulomatous cholecystitis is an unusual variant of chronic cholecystitis with infiltrative inflammatory condition. and it is not easy to distinguish this disease entity from gallbladder malignancy on radiologic findings. Therefore, there are a lot of concerns about determination of treatment methods preoperatively. We present a case report of an unusual case of Xanthogranulomatous cholecystitis accompanied by bile duct tumor of old age with multiple comorbidity.

Methods: The patient was a 81-year-old male and he was underwent general weakness with nausea and vomiting for several days. There was right upper quadrant tenderness without fever on physical examination. There was multiple comorbidity include diabetes melitus, hypertension, reflux esophagitis and hiatal hernia on past history. Serum laboratory findings showed mild anemia, creatinine 1.42 mg/dl, alkaline phosphatase 590 IU/L, r-GTP 89IU/L and normal liver enzyme. Serum total bilirubin level was 0.4mg/dl. CA 19-9 was 714.90U/mL. Abdomen CT showed gangrenous cholecystitis with a small stone in cystic duct and perforation of GB wall with pericholecystic abscess and edematous hepatoduodenal ligament. PET CT showed
Laparoscopic Resection of Schwannoma in the Pancreas
Yu Ni LEE, Woo Young KIM
Department of General Surgery, Presbyterian Medical Center, Republic of Korea

Aims: Pancreatic schwannomas are very rare neoplasm that arise from Schwann cells. They can be misdiagnosed as another pancreatic tumor. Although they are rare, they must be considered during the differential diagnoses of cystic pancreatic masses. We experienced a pancreatic schwannoma case.

Methods: A 60-year-old female with back pain was transferred to our hospital. CT showed a homogenous low density mass containing solid and cystic portion with a smooth margin with a clear border of 3.5 x 4 cm size in the pancreas body.

Results: Laparoscopic pancreatic tumor resection was performed. The tumor was histologically diagnosed as schwannoma. Immunohistochemically, the tumor was positive for S-100 protein and negative for C-kit, CD-34, smooth muscle actin.

Conclusions: Pancreatic schwannoma can be adequately treated with laparoscopic enucleation when suspected during exploration.

Synchronous Ampullary Neuroendocrine Tumor and Extra-Gastrointestinal Stromal Tumor in Association with Neurofibromatosis Type 1: A Case Report
Eunkyu PARK
Department of Surgery, Div. of HBP, Chonnam National University Hospital, Republic of Korea

Aims: The coexistence of synchronous gastrointestinal stromal tumor (GIST) and neuroendocrine tumor (NET) in a patient with neurofibromatosis type 1 (NF1) is extremely rare, and furthermore report of combined extra-gastrointestinal stromal tumor (E-GIST) and NET in NF-1 patient was not described yet, in the literature. Here, we report two discrete synchronous neoplasms in a patient with NF-1.

Methods: A 80-year-old lady presented with general weakness and dizziness. She had a medical history of perforated acute cholecystitis and peritonitis managed with percutaneous cholecystostomy, 2 years ago. Physical examination revealed icterus skin color and multiple neurofibromas all over the body. Before her visiting our hospital, abdomen CT scan was done at local clinic and CT showed dilated both intra- and extrahepatic bile ducts and hypervascular mass around 2nd portion of duodenum. Laboratory test revealed no specific abnormal findings. Endoscopy was performed and it showed an ampullary mass lesion with ulceration which was biopsied but other mass around duodenal 2nd portion wasn’t discovered. Histopathologic result was reported neuroendocrine tumor of ampulla of Vater with histologic grade 1.

Results: The patient underwent open laparotomy, cholecystectomy and transduodenal ampullectomy with retroperitoneal mass excision placed at the retroperitoneum, behind posterior wall of duodenum in view of CT findings. On microscopic section and immunohistochemistry, ampullary mass reported NET, grade 1 as same as previous endoscopic biopsy and retroperitoneal mass, behind the duodenal 2nd portion was turned out GIST, very low risk.

Conclusions: Herein, we report a extremely rare case of synchronous E-GIST and NET with a history of neurofibromatosis type 1.
high frequency of complication (78.6% vs 61.7%) even though there was no statistically significance (P = 0.083). Disease free survival and overall survival were not significantly different between two groups (P = 0.939 and P = 0.575, respectively).

Conclusions: NACCRT does not affect long-term survival. However, NACCRT could contribute to allow tumor downstaging and has potential to increase resection rate and curability in patients with locally advanced PHCC. High mortality and complication rates should not be overlooked. Optimal treatment protocol should be developed in a well-designed prospective study.

**PE-279**

**Surgical Outcomes of Bismuth Type IV Perihilar Cholangiocarcinoma**

Incheon KANG, Gi Hong CHOI
Division of HPB Surgery, Department of Surgery, Yonsei University College of Medicine, Republic of Korea

**Aims:** Perihilar cholangiocarcinoma (PHCC) Bismuth type IV tumors is generally regarded as unresectable owing to tumor location where extends into secondary biliary radicals on both side of the liver. With optimized preoperative management and advancement of surgical techniques, aggressive surgical resection has been applied in patients with Bismuth type IV, but still challenging. In this study, we introduced our experience on surgical resection in patients with Bismuth type IV.

**Methods:** Between January 2000 and December 2018, 325 consecutive patients with perihilar cholangiocarcinoma underwent surgical resection at Severance Hospital, Korea. Among them, 81 patients (24.9%) present Bismuth type IV PHCC. Short term and long-term surgical outcomes were analyzed between Bismuth type IV and other types.

**Results:** Of the 81 patients with type IV PHCA, right sided hepatectomy was the most common procedure (44 patients) (right hepatectomy, left hepatectomy, right trisectionectomy, central bisectionectomy). R0 resection rate was 59 patients (72%). Complications of Clavien-Dindo grade III or more occurred in 43 patients (53.0%) and 11 (13.6%) died from 90 days hospital mortality. Total Complication rate was significantly higher in type IV than other type of tumors. (63.8% vs 46%, P = 0.006). Disease free survival and overall survival were not significantly different between type IV PHCC and other type. (P = 0.592 and P = 0.328, respectively) In multivariate analysis, R0 resection was only significant prognostic factor for long-term survival. (P = 0.001).

**Conclusions:** Although resection for type IV PHCC is technically challenging with high complication rate, aggressive tumor resection to achieve R0 resection should be considered as a first treatment to provide long-term survival.

**PE-280**

**Minimally Invasive Interventions in Patients with Mechanical Jaundice**

Altai Meirambek, B. Kuanyshbayev
Regional Medical Center, Kyzylorda City, Kazakhstan

**Aims:** The results of 23 patients with mechanical jaundice syndrome who underwent percutaneous cholangiostomy were analyzed.

**Methods:** In the Department of surgery of the regional medical center of Kyzylorda in 2017, 23 patients received with mechanical jaundice syndrome had percutaneous cholangiostomy. Of these, cancer of the pancreatic head – 11 (47,8%), cancer of the large duodenal papilla of the duodenum in 5 (21,7%), choledocholithiasis – 4 (17,3%), cancer Klatskin – 3 (13.0 per cent). The age of patients from 55 years to 76 years. Of these, 9 men (39.1%), 14 women (60.8%). The level of total bilirubin ≥ 380,0 mmol/L.

**Results:** After complete examination of patients, performed preventive antibiotic therapy. Under angiographic installation in the operating unit, under local anesthesia, a puncture was performed inside the hepatic bile ducts under ultrasound control in Doppler mode. Further aspirates stagnant bile, a Guidewire is 0.38. According to the method of the Seldinger bile ducts biroute to 10 Fr. Then, under the control of intraoperative cholangiographies sets hydrophilic Pigtail catheter 8 Fr. Further drainage is fixed on the skin. In the early postoperative period, the cholangiostomy tube is washed with 5 ml 0.9% sodium chloride solution several times a day. In office patients receive analgesics, medications, infusion terapia, according to testimony carried zamorojenoi infusion of fresh plasma, plasmapheresis fractional. 15-25 days after surgery the level of total bilirubin is reduced to 40,0-60,0 mmol/L. Then it is possible to conduct radical surgery. The average duration of treatment was 11.5 days. There was no mortality.

**Conclusions:** Percutaneous cholangiostomy under ultrasound control is a promising direction of biliary decompression

**Keywords:** Minimally invasive, Interventions, Mechanical, Jaundice

**PE-281**

**Minimally Invasive Endoscopic Technologies in Complex Treatment of Patients with Obstructive Jaundice Syndrome**

Aitbayeva Aliya, Zhakhyev Bazylbek
Department of Surgical Diseases №2, West Kazakhstan Marat Ospanov State Medical University, Kazakhstan

**Aims:** The aim of the study was to assess the possibility of endoscopic methods of decompression of the biliary system in optimizing the treatment of patients with obstructive jaundice.

**Methods:** The analysis of the results of treatment of 587 pa-
Patients with obstructive jaundice of various etiologies for the period from 2010 to 2017 was conducted at the clinic of West Kazakhstan Marat Ospanov state medical university. Obstructive jaundice of benign genesis in 541 (92.2%), malignant genesis in 46 (7.8%) patients. Endoscopic retrograde cholangiopancreatography (ERCP) was performed, resulting in 369 (62.8%) cases of choledocholithiasis (including after cholecystectomy - in 202), stenosis of the major duodenal papilla - in 140 (23.9%), terminal choledochal stricture - in 59 (10.1%), a tumor of the pancreatic head - in 12 (2.0%), Klatkin’s tumor - in 3 (0.5%) and a stricture of the hepaticocholedochus after laparoscopic cholecystectomy - in 4 (0.7%). Concomitant diseases were observed in 72.1%.

**Results:** In order to decompress the bile ducts, endoscopic papillosphincterotomy (EPST) was performed in 187 (31.8%) patients, EPST with choledocholithoextraction - 320 (54.5%) patients, 23 of them underwent mechanical lithotripsy with subsequent extraction of concretions, EPST and endoprosthetics - in 75 (12.7%), and nasobiliary drainage - in 5 (0.8%). In 4 patients litoextraction after EPST was not successful. Frequency of complications was 13.6% (80 cases), in the structure: acute pancreatitis - in 65 (11%); duodenal bleeding in 12 (2%); in 3 patients perforation of the back wall of the intestine was registered (in 1 (0.2%) case death was registered).

**Conclusions:** Minimal invasive endoscopic decompression interventions are effective for biliary obstruction, allowing for routine surgical interventions in the most favorable conditions, and can serve as an alternative to surgical treatment in elderly patients with severe concomitant pathology.

**Keywords:** Biliary system, Cholecolithiasis, Obstructive jaundice, Endoscopic interventions

---

**PE-282**

**The Efficacy of Single-Stage Endoscopic Treatment of Complicated Forms of Cholelithiasis**

Utenui Nurbulat, Aitbayeva Aliya

Department of Surgical Diseases №2, West Kazakhstan Marat Ospanov State Medical University, Kazakhstan

**Aims:** The aim of our study was to evaluate the efficacy and safety of a single-stage endoscopic treatment of cholelithiasis complicated by choledocholithiasis and mild severity of obstructive jaundice.

**Methods:** A prospective cohort study of patients diagnosed of cholelithiasis complicated by choledocholithiasis and mild severity of obstructive jaundice were treated with the single-stage treatment a single-stage treatment - laparoscopic cholecystectomy and intraoperative endoscopic retrograde cholangiopancreatography, endoscopic papillosphincterotomy with endoscopic mechanical lithoextraction of calculi and laparoscopic cholecystectomy, laparoscopic choledocholithotomy, drainage of the common bile duct in hospital surgery clinic of West Kazakhstan Marat Ospanov state medical university for the period from 2014 to 2018. The primary outcomes were complications, hospital stay, operative time and timing of cholestasis resolution.

**Results:** The study included 35 patients. All patients underwent laparoscopic cholecystectomy. Intraoperative endoscopic retrograde cholangiopancreatography, endoscopic papillosphincterotomy with endoscopic mechanical lithoextraction of calculi performed in 24 (68.6%), 11 (31.4%) - laparoscopic cholecystectomy, laparoscopic choledocholithotomy, drainage of the common bile duct. Normalization of biochemical parameters characterizing cholestasis (bilirubin, alkaline phosphatase) and cytolysis (AsAT and AIAT) within 3 days after single-stage treatment was observed in 31 patients (88%). Mean operative time was 102.6 ± 34.2 minutes. Mean hospitalization stay was 6.8 ± 1.5 days. Complications directly related to the operation were found in 2 patients (5.7%): acute pancreatitis was observed, accompanied by increased levels of blood amylase and leukocytosis. Comprehensive conservative therapy in these patients had a positive clinical result. Deaths were not recorded.

**Conclusions:** This study demonstrated that single-stage endoscopic treatment may be effective and safe for cholelithiasis complicated by choledocholithiasis and mild severity of obstructive jaundice.

**Keywords:** Single-stage, Endoscopic treatment, Cholelithiasis, Obstructive jaundice

---

**PE-283**

**Rare Experience of Complication of a Spilled Gallstone after Laparoscopic Cholecystectomy: Case-Report**

Eun-Kyoung Jwa, Dong-Lak Choi

Department of Surgery, Daegu Catholic University College of Medicine, Daegu, Republic of Korea

**Aims:** Laparoscopic cholecystectomy is the gold standard for gallstone disease and worldwide procedure. The spillage of gallstones, rarely makes late complication but may cause major complications.

**Methods:** Retrospective review of medical records was performed for the patient who had suffered from a spilled stone.

**Results:** A 46-year-old man came to my center for right flank pain. He checked abdominal Computed tomography (CT) in local clinic, the clinic doctor accessed to liver abscess and referred to my center. First my clinic hepatologist check abdomen sonography for the abscess aspiration. The radiologist found a big stone in abscess poket. He did laparoscopic cholecystectomy 2 years ago. The cause of his abdominal pain was fluid collection around stone. I decided to operate for remove the stone. We did laparoscopic exploration, removed abscess and found a big gallstone (18 mm). The patient was discharged on the 3rd post-operative day. We followed up abdominal CT on 24th post-operative days and Perihepatic fluid collection was decreased and the patient is free from abdominal pain.

**Conclusions:** When we do laparoscopic cholecystectomy, we...
must try to avoid gallbladder perforation and try to minimize spillage of gallstones.

**PE-284**

Iatrogenic Bile Duct Injury Associated with Anomalies of Isolated Right Anterior Segmental Hepatic Duct Injury Following Laparoscopic Cholecystectomy: A Rare Case Report

Hyukjai Jang, Cheon Soo Park
Department of Surgery, University of Ulsan, Gangneung Asan Hospital

**Aims:** Bile duct injuries remain one of the most devastating complications of both open and laparoscopic cholecystectomy. Bile duct injury with LC has often been attributed to surgical inexperience, but it is also clear that aberrant bile ducts are present in a significant number of patients who sustain biliary injuries during these procedures.

**Methods:** We presented a patient with iatrogenic bile duct injury associated with anomalies of isolated right anterior segmental hepatic duct injury following laparoscopic cholecystectomy.

**Results:** (CASE REPORT) The anomaly of the right anterior hepatic duct was unexpectedly identified in an old woman following laparoscopic cholecystectomy. Anomalies of bile duct located in the right anterior hepatic duct to cystic duct. This duct was 3mm sized and clipped. Patient had a bile duct injury and subsequent bile leak. Treatments included endoscopic retrograde cholangiopancreatography (ERCP), and percutaneous drainage for 2 months. The patient was treated successfully by nonsurgical procedures after 2 months.

**Conclusions:** This unusual anatomical variation of the biliary tract is mainly discovered during the operation. Thus, surgical injury of these ducts is inevitable and it provokes the severe complication of bile leak. Anomaly of bile ducts are associated with a high risk of surgical bile duct injury. Meticulous operative technique combined with surgeons’ awareness concerning this peculiar anatomical aberration leads to a safe laparoscopic cholecystectomy. Successful management requires adequate identification of the lesion, and multidisciplinary treatment is necessary. Some of patients could be treated successfully by nonsurgical procedures.

**PE-285**

PD-L1 Expression in Extrahepatic Biliary Tract Cancers: A Comparative Study Using 22C3, SP263 and E1L3N Anti-PD-L1 Antibodies

Soomin Ahn, Yangkyu Lee, Ji-Won Kim1, Jong-chan Lee1, Jin-Hyeok Hwang1, Yoo-Seok Yoon1, Jai Young Cho1, Ho-Seong Han1, YoungRok Choi1, Haeryoung Kim2
Department of Pathology, Seoul National University Bundang Hospital, 1Department of Internal Medicine, Seoul National University Bundang Hospital, 2Department of Surgery, Seoul National University Bundang Hospital, 3Department of Pathology, Seoul National University Hospital, Korea

**Aims:** Treatment with monoclonal antibody to programmed cell death protein 1 (PD-1) has showed promising results in patients with programmed cell death ligand-1 (PD-L1)-positive advanced biliary tract cancer. In an ongoing clinical trial of pembrolizumab on biliary tract cancer, 22C3 assay is being used for PD-L1 evaluation. The frequency of PD-L1 positivity varies in bile duct cancers, which may be due in part to the assay used.

**Methods:** We evaluated PD-L1 expression in 183 extrahepatic bile duct cancers, including 89 perihilar and 94 distal bile duct cancers, using 22C3, SP263 and E1L3N antibodies.

**Results:** Using 22C3 antibody, tumoral PD-L1 was expressed in 16.9% at a 1% threshold. Using the SP263 and E1L3N, the tumoral PD-L1 positivity was 26% and 7.1%, respectively. In evaluation of whole tissue sections, 59.6% of PD-L1 positive cases exhibited low percentage (<10%) of positive tumor cells. Tumoral PD-L1 positivity was associated with histologic differentiation (P = 0.017) and mucin phenotype (P = 0.041). Although there was no statistically significant association between clinical outcome and tumoral PD-L1 expression at 1% cut-off, PD-L1 expression ≥10% was associated with worse overall survivals and disease-free survivals (SP263 OS: P = 0.012, DFS: P = 0.042).

**Conclusions:** By 22C3 assay, tumoral PD-L1 was expressed in 16.9% at a 1% threshold. The SP263 assay showed the highest PD-L1 positivity both on tumor cells and immune cells, followed by 22C3 and E1L3N assay. High PD-L1 expression (≥10%) was associated with poor prognosis in extrahepatic bile duct cancer patients.

**Keywords:** Cholangiocarcinoma, Bile duct cancer, PD-L1, Immunohistochemistry

**PE-286**

ELCC

Zhanadil Almyrzauly, Galymzhan Aubakirov, 1Zhazylbek Abdin, 1Bazylbek Zhakiev
Aktobe Medical Center, Aktobe, Kazakhstan, 1West-Kazakhstan Medical University, Aktobe, Kazakhstan

**Aims:** Gallbladder stones – is one of the worldwide disease, which occurs in 10% of the population in the world. And 97-98% of cholecystectomies perfume by the laparoscopic method. According to many reports after laparoscopic cholecystectomy (LCE) complications observed at 1% to 8.5%. The aim is to evaluate the complications of laparoscopic cholecystectomy in our centre.

**Methods:** 1628 LCE operations were analyzed, which performed in period 2010-2018. Among them 1016 patients (62,4%) had GS with acute cholecystitis, 612 (37,6%) – chronic cholecystitis. Woman – 75,8% (n = 1234), man – 24,2% (n = 394), average age was 49,5±6,6 year.

**Results:** Intraoperative and early postoperative complications
The Value of Lymphadenectomy in Surgical Resection of Perihilar Cholangiocarcinoma
Lei LIANG¹, Ming-Da WANG¹, Hao XING¹, Chao LI¹, Jun HAN¹, Han ZHANG¹, Wan Yee LAU², Timothy M. PAWLIK², Feng SHEN³, Tian YANG¹
¹Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, the Second Military Medical University, Shanghai, China; ²Department of Surgery, Ohio State University, Wexner Medical Center, Columbus, OH, USA; ³Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T., China

Aims: Surgical resection is the only potentially curative treatment for patients with resectable perihilar cholangiocarcinoma (PHC). There is still no consensus on the value of lymphadenectomy despite evidence indicating lymph node (LN) status is an important prognostic indicator for postoperative long-term survival. We sought to perform a meta-analysis to summarize the current evidence on the value of lymphadenectomy among patients undergoing surgery for PHC.

Methods: The PubMed, Embase, Medline and Cochrane Library were systematically searched for studies published before October 2018 that reported on lymphadenectomy at the time of surgery for PHC after curative surgery.

Results: 7,748 patients from 28 studies were included in the meta-analysis. No survival benefit was identified with increased number of LN resected (all P > 0.05). Meanwhile, overall LN status was an important prognostic factor. Patients with lymph node metastasis had a pooled estimate hazard ratio of death that was over two-fold higher than patients without lymph node metastasis (HR: 2.07, 95% CI 1.65–2.59, P < 0.001). The examination of 5 LNs on histology was associated with better staging of lymph node status and stratification of patients into positive or negative LN groups.

Conclusions: While the extent of LN dissection was not associated with a survival benefit, examination of more than 5 LNs may better stage patients into positive or negative LN groups with a lower risk of nodal understaging.

Who Can Benefit from Adjuvant Transcatheter Arterial Chemoembolization after Surgical Resection of Hepatocellular Carcinoma?
Lei LIANG, Jiong-Jie YU, Hai-Ying SUN, Ming-Da WANG, Chao LI, Hao XING, Jun HAN, Xin-Fei XU, Timothy M. PAWLIK, Wan Yee LAU, Feng SHEN, Tian YANG
¹Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, the Second Military Medical University; ²Department of Surgery, Ohio State University, Wexner Medical Center, Columbus, OH, USA; ³Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T., China

Aims: Although adjuvant transcatheter arterial chemoembolization (TACE) has been used to prevent postoperative recurrence after hepatocellular carcinoma (HCC) resection, the survival benefits of adjuvant TACE remain controversial. To evaluate the effectiveness of adjuvant TACE for HCC, as well as identify patient populations that might benefit from adjuvant TACE.

Methods: The PubMed, Embase, Medline and Cochrane library were systematically searched for studies published before October 2018 that compared adjuvant TACE versus surgery alone for HCC. The primary endpoints were overall survival (OS) and disease-free survival (DFS). Patients with large HCC (≥ 5 cm), multinodular HCC, microvascular invasion (MVI), or portal vein tumor thrombosis (PVTT) were analyzed in subset analyses.

Results: Twenty-five studies with 6,977 patients were included in the analytic cohort. The pooled analysis demonstrated that adjuvant TACE was associated with a better OS and DFS [HR: 0.67 and 0.67, both P < 0.01]. In subgroup analyses, pooled results revealed that adjuvant TACE was associated with an improved OS and DFS in patients with multinodular HCC (HR: 0.79 and 0.31, both P < 0.01), MVI (HR: 0.62 and 0.67, both P < 0.01), or PVTT (HR: 0.49 and 0.58, both P < 0.01), but not among patients with large HCC (≥ 5 cm) (HR: 0.82 and 0.97, both P > 0.20).

Conclusions: Postoperative adjuvant TACE may be effective to improve OS and RFS in selected patients with multinodular HCC, or HCC with MVI or PVTT. Future randomized controlled trials are needed to better define the benefit of adjuvant TACE.
**PE-289**

**Exosomal miRNA-106b from Cancer-Associated Fibroblast Promotes Gemcitabine Resistance in Pancreatic Cancer**

Yuan FANG, Wentao ZHOU, Yefei RONG, Dansong WANG, Tian-tao KUANG, Wenchuan WU, Xuefeng XI, Wenhui LOU

Department of Pancreatic Surgery, Zhongshan Hospital, Fudan University

**Aims:** Gemcitabine (Gem)-based chemotherapy is commonly used to treat pancreatic ductal adenocarcinoma (PDAC). However, intrinsic and acquired resistance to Gem therapies remains a challenge for PDAC patients. Cancer-associated fibroblasts (CAFs), comprising the majority of the tumor bulk, play vital roles in regulating tumor progression and drug resistance by transferring exosomes (Exo) to cancer cells.

**Methods:** We investigated the potential role of CAFs in the resistance of pancreatic cancer cells to Gem and revealed its underlying mechanism.

**Results:** We found that CAFs were innately resistant to Gem. The conditioned medium (CM) and exosomes derived from CAFs contributed to Gem resistance of pancreatic cancer cells, and Gem treatment further enhanced the effect of CAFs or CAFs-Exo on pancreatic cancer cells survival. We identified that miR-106b level was upregulated in CAFs and CAFs-Exo following Gem treatment. And miR-106b was directly transferred from CAFs to the pancreatic cancer cells by the mediation of exosomes. Furthermore, pretreatment of CAFs with miR-106b inhibitor suppressed miR-106b expression in CAFs-Exo, and resulted in a decreased resistance of pancreatic cancer cells to Gem. Finally we identified that miR-106b promoted Gem resistance of cancer cells by directly targeting TP53INP1.

**Conclusions:** CAFs-mediated Gem resistance in PDAC is partially related to overexpression of miR-106b in CAFs-Exo and that inhibiting the transfer of CAFs-derived miR-106b might be a potential treatment to alleviate Gem resistance.

---

**PE-291**

**Metformin Inhibited Pancreatic Cancer Growth by Upregulating miR-143/145 Cluster and Suppressing MAPK Signaling Pathway**

Yaolin XU, Zizhen WU, Peng YUAN, Mofang LIU, Wenhui LOU

1General Surgery Department, Zhongshan Hospital Fudan University, 2Shanghai Key Laboratory of Molecular Andrology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, China

**Aims:** Accumulating evidence suggests that metformin treatment is associated with decreased risk and better survival outcome of pancreatic cancer (PC) in patients with diabetes. Besides, our previous study revealed that miR-143 was as essential regulator of cancer glycolysis and miR-143/145 cluster was reported as a tumor suppressor in a range of cancer. The aim of present study was to investigate whether miR-143/145 cluster was associated with antitumor effect of metformin in PC and its potential mechanism.

**Methods:** We analyzed miRNA sequencing dataset of PC from NCBI (GSE37406) to identify miRNA that were differently expressed between metformin treatment and control group. MiR-143/145 expression level were determined by qRT-PCR, and expression level of target protein were detected by western blot. Potential target genes of miR-143/145 were identified by bioinformatic analyses and confirmed by luciferase reporter assays. Furthermore, biological consequences of miR-143/145 alternation and metformin treatment were examined by cell...
proliferation, invasion, and apoptosis assays in vitro and by patient derived xenograft models in vivo.

**Results:** MiR-143/145 was upregulated in metformin-treated PC. Overexpression of miR-143/145 inhibited proliferation and induce apoptosis of PC in vitro. Metformin inhibited tumor growth while downregulation of mir-143/145 cluster downstream of metformin treatment abrogated its antitumor effect both in vitro and vivo. Furthermore, miR-143/145 cluster directly targeted 3'-UTR of MAPK and AKT and repressed their expression. Low MAPK and AKT expression level correlated with better prognosis in PC.

**Conclusions:** Our data demonstrated the pivotal role of metformin/miR-143/145 cluster/MAPK axis and suggested miR-143/145 cluster as a candidate therapeutic target in PC.

---

**PE-292**

**Acute Pancreatitis Induced by Etoposide-Lobaplatin Combination Chemotherapy Used for the Treatment of Lung Cancer**

**Xiao-Yu GUO, Gang WANG**

Department of Pancreatic and Biliary Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang Province, China

**Aims:** Drug-induced pancreatitis (DIP) is a rare type of pancreatitis that is not usually observed in the clinical practice. It is generally difficult to distinguish from acute pancreatitis (AP) induced by other causes.

**Methods:** Here, we report a 62-year-old Chinese female patient with “small cell lung cancer” as the initial presentation. Because the patient could not bear the surgical treatment, the chemotherapy composed of lobaplatin and etoposide was performed. Three days later, the patient displayed sudden abdominal pain, distension, nausea, and vomiting without obvious inducements. Laboratory tests showed that the levels of serum and urine amylase were enhanced; abdominal computed tomography (CT) result showed the enlargement of the pancreas, peripancreatic effusion, and a rough edge, which suggested the diagnosis of AP. The patient had no history of biliary tract disease, alcoholism, binge overeating, hyperlipidemia, and hereditary pancreatitis. The patient was diagnosed with DIP and the chemotherapy was stopped at once. Then we performed fluid resuscitation, pain alleviation, prophylactic antibiotics, and nutritional support, etc on the patient. Later, the patient’s clinical symptoms were obviously relieved, and she recovered successfully.

**Results:** The chemotherapy was continued, but later, the patient showed abdominal pain, distension, nausea, and vomiting again. The levels of serum amylase and urine amylase were enhanced again. Further imaging examination strongly indicated the recurrence of AP.

**Conclusions:** We should raise awareness of the clinicians regarding DIP, thereby enabling its timely diagnosis and accurate treatment, as well as promoting the rational and safe use of drugs.

---

**PE-293**

**Exosomes and Pancreatic Diseases: Status, Challenges, and Hopes**

**Xiao-Yu GUO, Gang WANG**

Department of Pancreatic and Biliary Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang Province, China

**Aims:** Pancreatic disease is a complicated and dangerous clinical condition involving the disruption of exocrine or endocrine function, including pathologies such as acute pancreatitis (AP), chronic pancreatitis (CP), and pancreatic cancer (PC). PC has one of the highest mortality rates, due to insufficient diagnosis in early stages.

**Methods:** There remains a lack of efficient treatment options for disease etiology in AP or CP. Thus, the identification of new therapeutic targets and reliable biomarkers is required. As essential couriers in intercellular communication, exosomes have recently been confirmed to play an important role in pancreatic disease, but the specific mechanisms at play are still unknown.

**Results:** In this review, we discuss current research progress on exosomes, particularly with respect to their role as intracellular couriers, biomarkers, and therapeutic vectors for pancreatic diseases.

**Conclusions:** We summarize the current knowledge of exosomes in pancreatic disease, with respect to diagnosis, molecule mechanism, and treatment, proposing new ideas for the study of pancreatic disease.

---

**PE-294**

**Immunogenicity of Neoplastic Cells in PDA (Review)**

**Dariga SYRLYBAY, Wenhui LOU**

Pancreatic Surgery, Zhongshan Hospital, Fudan University

**Aims:** Immune-based therapies that enhance the ability of cytotoxic T cell to target tumor cells showed a moderate promise to several solid tumors. However, the neoplastic cells in pancreatic cancers are refractory to all immune-based therapies or the combination of immune-based therapies with chemotherapies including PD-L, IDO target therapies. Multiple mechanisms cause the insensitivity of neoplastic cells to immune-based therapies including low immunogenicity of pancreatic cancer neoplastic cells.

**Methods:** The recent study in Japan has revealed the tumor-infiltrating CD4+ and CD8+ T-cells as independent prognosticators useful for evaluating the immune microenvironment of PDC. Using immunohistochemistry, the examination and analysis of tumor-infiltrating cells pan-macrophages, M1, CD163+ or CD204+ M2 macrophages (M2), CD66b+ neutrophils, CD4+
T cells, CD8+ T cells, regulatory T cells in 212 cases of PDC, it is anticipated that tumor-infiltrating immune/inflammatory cells would be useful hallmarks for evaluating and monitoring the characteristics of a tumor immune microenvironment.

Results: Several studies showed that immunotherapy point agents showed a promising therapeutic effect to inhibit murine pancreatic cancer development by enhancing the immunogenicity of pancreatic tumor cells. Recognizing the neoplastic cells by cytotoxic T cells is the first step in exerting cytotoxic effects of tumor killing T cells.

Conclusions: Collectively, the precise strategy of PDA treatment remained unclear but based on recent studies and trials, the most promising target to suppress cancer cells is immunotherapy. The dual mechanism of both increasing CD4+ and CD8+ T-cells along with deactivating the tumor microenvironment, as well as drug combination therapy might significantly improve the response to chemotherapy and overall survival.

Pancreatic Stellate Cells Promote Epithelial-Mesenchymal Transition of Cancer Cells by Notch-3 Promoter Demethylation

Feng CAO, Fei LI
Department of General Surgery, Xuanwu Hospital, Capital Medical University, China

Aims: Pancreatic stellate cell (PSC) promoted epithelial-mesenchymal transition (EMT). However, the potential mechanism had not been fully elucidated. The aim of this study was to explore the effect of Notch-3 on EMT of PANC-1 cells induced by PSC.

Methods: We explore the effect of PSC on PANC-1 cell EMT. The potential signal pathway involved in EMT is determined by adding different inhibitors. The role of Notch-3 in EMT process is verified through Notch-3 siRNA transfection. Bisulphite sequencing PCR and chromatin immunoprecipitation are performed to explore the methylation status of Notch-3 promoter. To confirm the relationship between EMT, Notch-3 status and patient survival, Kaplan-Meier analysis is performed.

Results: After co-culture with PSC, the ability of migration is significantly enhanced, and the PSC can also induce EMT phenomenon of PANC-1. Meanwhile, the Notch-3 expression is also promoted. The effect blocked by Notch signal pathway inhibitor(L1790) and Notch-3 siRNA revealed the critical role of Notch-3 in EMT process. The methylation status of three CpG islands located in promoter region of Notch-3 has been uninfluenced after co-culture with PSC. However, immunoprecipitation reveals a significant increase in hmcC for Notch-3 promoter. Our study also demonstrate that Notch-3 level is positively correlated with Vimentin and negatively with E-cadherin expression in pancreatic cancer patients. Overexpression of Notch-3 also predicts the poor prognosis of pancreatic cancer.

Conclusions: PSC induces Notch-3 expression by demethylation and promote EMT phenotype of PANC-1 cell. EMT and Notch-3 are the poor prognostic factors in pancreatic cancer patients. Notch-3 might be a potential target for treatment of pancreatic cancer.

Smad4 Inhibits Cell Migration via Suppression of KPNA4 and MMP26 in Human Pancreatic Cancer Cells

Mingzhe LI, Huahu GUO, Zhengkui ZHANG, Yazhou WANG, Xiaodong TIAN, Yinmo YANG
General Surgery, Peking University First Hospital, China

Aims: Smad4 was known as a tumour-suppressor gene that frequently mutates in pancreatic cancer. Previous studies indicated that Smad4 is the central component of the bone morphogenetic protein (BMP) signaling pathway, forming a complex with p-smad1/5/9 and regulating the target genes in the nucleus. It is attractive to explore the potential genes regulated by the complex and uncover the molecular mechanism of Smad4 in pancreatic cancer cells.

Methods: The enrichment of BMP signaling pathways in three GEO databases was analyzed by GSEA software. Immunohistochemistry was used to detect the expression of Smad4 in pancreatic cancer and adjacent tissues. ChiP-sequence analysis explored the target genes regulated by Smad4/p-smad1/5/9 complex. The cell migration and invasion ability were assessed by Transwell assays. The nude mouse lung metastasis model was used to detect the invasive ability of pancreatic cancer cell lines in vivo.

Results: The BMP signaling pathway is hyperactivated in pancreatic cancer, and its key molecule Smad4 is highly expressed in 80 pancreatic tissue specimen and is related with prognosis. Ectopic expressed Smad4 in Smad4-deficient BxPC-3 significantly inhibited cell migration and invasion. Downregulated Smad4 in Mia-PaCa-2 dramatically promoted cell migration and invasion, and we demonstrated that p-Smad1/5/9-Smad4 complex can regulate the expression of KPNA4 and MMP26, and hence regulate the migration and invasion ability of pancreatic cancer cells.

Conclusions: The present findings indicate that Smad4 may suppress the expression of KPNA4 and MMP26 mediated by p-smad1/5/9 and inhibit the tumor characteristics of pancreatic cancer cells.
patients who underwent LPD with SSPDSPJ at our hospital were included. Patients and their families were informed of this procedure before operation. Clinical data including estimated blood loss, operative time, pancreaticojejunostomy (PJ) time and postoperative data such as hemorrhage, pancreatic fistula, bile leakage, delayed gastric empty were collected prospectively. The definition and grade of complications were recorded according to the ISGIPS definition.

**Results:** Eighty patients were included and no patients was converted to open surgery. The median operation time was 260 minutes (range from 200 minutes to 560 minutes). The median pancreatic-jejunum reconstruction time was 26 minutes (range from 18 minutes to 40 minutes). The median estimated blood loss was 160 ml (range from 30 to 800 ml). 10 patients (12.5%) underwent blood transfusion during operation. Thirty-one patients had firm pancreas and 49 patients had soft pancreas. The median diameter of pancreatic duct was 3 mm (range from 1 to 8 mm). Eight patients (10.0%) suffered from grade B pancreatic fistula, no patient with grade C fistula. Four patients (5%) suffered from bile leakage and 5 patients (6.3%) suffered from delayed gastric empty. Three patients (3.8%) had postoperative hemorrhage. No 30-day mortality occurred.

**Conclusions:** SSPDSPJ is a safe technique. Besides, it is simple, efficient, reproducible and easy to grasp that can shorten the learning curve time.

**PE-298**

**Lipopolysaccharide Increase PD-L1 Expression in Pancreatic Tumor via TLR4/MyD88/NF-κB Pathway**

Hanlin YIN, Guochao ZHAO, Ning PU, Wenchuan WU

Department of General Surgery, Zhongshan Hospital, Fudan University, China

**Aims:** The programmed death ligand 1(PD-L1) is essential for tumor cells to keep immune escape and related to poor prognosis. Previous studies have identified that bacteria lipopolysaccharide (LPS) can affect the expression of PD-L1 on immune cell, but its effect on the tumor cell hasn’t been investigated. This study is aimed at whether lipopolysaccharide (LPS) can induce PD-L1 on pancreatic tumor.

**Methods:** The effect of LPS on the two pancreatic tumor cell lines (Panc1 and Bxpc-3) was analyzed in vitro. The level of PD-L1 and its relevant pathway were verified by real time PCR and western blot.

**Results:** The expression of PD-L1, Toll-like receptor 4(TLR4) and MyD88 was upgraded after LPS stimulation in a concentration-dependent way and the nuclear factor-κB (NF-κB) pathway is also activated. TLR4-sh plasmid and MyD88-sh plasmid was transfected into cell lines respectively. Correspondingly, PD-L1 expression was obviously downgraded comparing with their control groups. Meanwhile, the effect of LPS was neutralized when cells were pre-treated with NF-κB pathway specific inhibitor PDTC and Bay-11-7082. Furthermore, we observed that p65 could bind to the PD-L1 promoter by Chip assay.

**Conclusions:** Overall, our study has shown that LPS can induce PD-L1 expression in pancreatic tumor via TLR4/MyD88/NF-κB pathway. Intervening LPS in vivo might be another way to reduce PD-L1-mediated immune escape.

**PE-299**

**Circulating Tumor Cells with Epithelial-Mesenchymal Transition Features Predict Metastatic Outcome in Pancreatic Cancer**

Xudong ZHAO1, Xi Dong2, Yongsu MA1, Xiaodong TIAN1, Xiaohang ZHAO1, Yinmo YANG2

1Department of surgery, Peking University First Hospital, 2State Key Laboratory of Molecular Oncology, National Cancer Center, Chinese Academy of Medical Sciences & Peking Union Medical College, China

**Aims:** To clarify the metastatic potential of CTCs with mesenchymal phenotype (mCTCs) characteristic in pancreatic cancer (PC).

**Methods:** Among both localized (n = 21) and metastatic (n = 14) patient populations, blood samples (7.5 ml each) were drawn from peripheral vein. Of them, portal and peripheral blood samples were simultaneously collected intra-operatively in 19 patients following surgical dissection prior to tumor removal. All samples were analyzed for CTCs with immunomagnetic negative enrichment together with 4-channel immunofluorescence against Cytokeratin, Vimentin, DAPI and CD45.

**Results:** CTCs were detected in 91.4% (32/35) and 100.0% (14/14) of patients with AJCC stage I-III and stage IV tumors, respectively. 21 localized patients had a mean count of (148.9±159.9) CTCs/7.5 mL in peripheral blood, compared with a mean count of (279.5±297.5) CTCs/7.5 mL in 14 metastatic patients (P = 0.127). Meanwhile, the mCTCs percentage tended to be higher in metastatic group, implying that mCTCs may be a risk factor for metastatic disease. Among 19 patients received operations, there was a mean count of (148.1±152.8) CTCs/7.5 mL in peripheral blood vs. (252.0±220.9) CTCs/7.5 mL in portal vein (P = 0.170). However, the mCTCs percentage of portal vein was significantly different from that of peripheral vein (P = 0.048), meaning an obvious spatial heterogeneity in epithelial and mesenchymal composition during circulation. The clinical significance of distant composition warrants further exploration.

**Conclusions:** CTCs with mesenchymal phenotype may in part represent tumor clones with high metastatic potential, suggesting that this special subtype CTC-positivity identifies patients with occult systemic disease and neoadjuvant therapy may improve the prognosis.

**PE-300**

**Serum Lipid Levels and the Risk of Gallbladder Stones: A Population-Based Study in China**

Jiwen WANG1, Sheng SHEN1, Bo WANG2, Xiaoqian NI1, Han LIU1, Xiaoling NI1, Rong YU1, Tao SUO1, Houbao LIU1

1Department of General Surgery, Zhongshan Hospital, Fudan University, China
Methods: From January 2014 to January 2015, participants (N = 216,161) were recruited by Meinian Onehealth Healthcare (Group) Co., Ltd. They received a physical examination, and GSD was determined by ultrasound. The prevalence of GSD was 8.1%. Risks of GSD were similar between males and females in all age groups. Risk factors for gallstones include body mass index, waist circumference, waist-to-hip ratio, and physical activity, as well as biological factors such as age, sex, and elevated blood lipid levels. Serum lipid levels of GSD were statistically different from controls in total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and apolipoprotein B (APOB). Furthermore, TC > 5.00 mmol/L, TG > 1.39 mmol/L, HDL < 1.19 mmol/L, LDL > 3.04 mmol/L, and APOB > 0.97 mmol/L were risk factors for gallstones.

Conclusions: Serum lipid levels are associated with GSD. TC, TG, LDL, and APOB are risk factors, while HDL is a protective factor.

PE-301
Any Time Laparoscopic Cholecystectomy in Moderate to Severe Acute Cholecystitis without Septic Shock: A Prospective Cohort Study
Bhavin Vasavada, Hardik Patel
Hepatobiliary and Liver Transplant, Shalby Hospitals, India

Aims: In laparoscopic cholecystectomy in acute cholecystitis most authors recommend surgery within first 72 hours. We offer laparoscopic cholecystectomies in every patient of acute cholecystitis regardless of timing of presentation.

Methods: We prospectively analyzed outcomes of our protocol of any time acute cholecystitis. We perform laparoscopic cholecystectomies within first 24 hour of presentation regardless of time of symptoms. All the data were prospectively analyzed.

Results: We performed 110 laparoscopic cholecystectomies between April 2016 to January 2019. We prefer single dose pre operative antibiotic (third generation cephalosporin) in all laparoscopic cholecystectomies and no post operative antibiotics. Total 74 patients were having grade 2 or grade 3 cholecystitis. 64 patient were having grade 2 and 9 patients were having grade 3 cholecystitis. One patient was having grade 3 cholecystitis and was having septic shock so he was managed with percutaneous cholecystostomy and according to survival sepsis protocol and lap choly was done after 72 hours and hence excluded from study. Out of 73 patient included in study 2 patient were converted to open, in two patient we performed lap subtotal cholecystectomy due to difficult calot triangle. Out of these only 1 patient developed port site infection and two patient developed bilioma which was managed by percutaneous drainage.

Conclusions: Post operative antibiotics are unnecessary in grade-2, grade-3 acute cholecystitis without septic shock.

PE-303
Preprocurement Pancreas Allocation Suitability Score Does Not Correlate with Long-Term Pancreas Graft Survival
Belzat ELDESOV1, Aidos BISSENBAY2
1General Surgery, National Science Center of Oncology and Transplantology, 2General Surgery, National Research Center for Maternal and Child Health, Kazakhstan

Aims: Single dose antibiotic is recommended for laparoscopic cholecystectomy, for symptomatic gall stones. However very few studies are there for subgroup grade-2 and grade-3 cholecystitis according tokyo guidelines 2018.

Methods: We prospectively analyzed outcomes of our protocol of no post operative antibiotics in grade-2 and grade 3 (moderate to severe) acute cholecystitis according to tokyo guidelines. We perform laparoscopic cholecystectomies within first 24 hour of presentation to us without considering time since attack if patient is not in septic shock where we follow survival sepsis guidelines and also perform percutaneous cholecystostomy.

Results: We performed 101 laparoscopic cholecystectomies between April 2016 to January 2019. We prefer single dose pre operative antibiotic (third generation cephalosporin) in all laparoscopic cholecystectomies and no post operative antibiotics. Total 74 patients were having grade 2 or grade 3 cholecystitis. 64 patient were having grade 2 and 9 patients were having grade 3 cholecystitis. One patient was having grade 3 cholecystitis and was having septic shock so he was managed with per cutaneous cholecystostomy and according to survival sepsis protocol and lap choly was done after 72 hours and hence excluded from study. Out of 73 patient included in study 2 patient were converted to open, in two patient we performed lap subtotal cholecystectomy due to difficult calot triangle. Out of these only 1 patient developed port site infection and two patient developed bilioma which was managed by percutaneous drainage.

Conclusions: Any time laparoscopic cholecystectomy should be the rule in experienced centre.
Aims: Within recent years, more marginal donors have been offered to Eurotransplant. To help identify suitable pancreas donors, the Eurotransplant Pancreas Advisory Committee introduced a donor score system (P-PASS). Little is known about the influence of P-PASS on long-term pancreas graft survival.

Methods: From June 2004 to September 2018, we performed 405 pancreas transplantations. In a retrospective study we analyzed P-PASS in 318 cases. Pancreas grafts from donors with P-PASS < 17 (n = 146) analyzed for graft and patient survival as well as for surgical complications were compared with donors of a PASS > or = 17 (n = 172). The mean follow-up was 7.2 +/- 4.3 years.

Results: Recipient characteristics were comparable in both groups. Mean P-PASS was 16.7 +/- 2.7 for both groups: 14.3 +/- 1.5 for P-PASS < 17 and 18.8 +/- 1.6 for P-PASS > or = 17. Pancreas graft survival rates for 1, 5, and 10 years were 85%, 77%, and 73% among P-PASS < 17 and 81%, 73%, and 64% among P-PASS > or = 17 groups (P = .12). The relaparotomy rate was significant higher (38.7% vs 28.7%) and duration of hospital treatment longer (40.2 vs 32 days) in the P-PASS > or = 17 group (P < .05).

Conclusions: The data demonstrated that utilization of pancreas grafts from donors with a P-PASS > or = 17 resulted in good overall outcomes and could expand the organ donor pool. Complications requiring relaparotomy were more frequent among patients after transplantation from donors with higher P-PASS.

Microvessel Density and Impact of Angiogenesis on Survival of Resected Pancreatic Cancer Patients: A Systematic Review and Meta-Analysis

Yerlan BAKHTORAZOV1, Bekzat ELDESOV2

1General Surgery, National Science Center for Oncology and Transplantology, 2General Surgery, National Science Center for Oncology and Transplantology, Kazakhstan

Aims: Angiogenesis plays a major role in tumor progression and metastasis; however, its role in pancreatic cancer (PC) remains unclear. The aim of the study was to explore the cumulative evidence concerning the impact of microvessel density (MVD), an estimator of angiogenesis, on resected PC patients.

Methods: A systematic review of literature and a meta-analysis of relevant reports were performed. Overall survival and disease-free survival were scrutinized.

Results: One thousand five hundred patients were analyzed. Overall survival (hazard ratio, 2.0; 95% confidence interval, 1.57-2.54; P < 0.001) and disease-free survival (hazard ratio, 1.99; 95% confidence interval, 1.24-3.2; P = 0.004) were in favor of the low-MVD group. Use of CD105 antibody and of a computerized image analysis system was found to significantly reduce the heterogeneity. Disease staging, tumor location, and grading showed significant effect on survival.

Conclusions: High-MVD expression was strongly associated with poorer survival and recurrence among resected PC patients, demonstrating a negative prognostic value. Use of CD105 antibody and of a computerized image analysis system is recommended in future studies because they reduce heterogeneity of results. The potential role of MVD as a marker to select PC patients who would benefit from antiangiogenetic treatment should be further explored in clinical trials.

Potential Value of Serum Total IgE for Differentiation between Autoimmune Pancreatitis and Pancreatic Cancer

Daulet AZIM, Nursultan KYDYR

Gastronenterology. City Hospital № 1 in Astana, Kazakhstan

Aims: Autoimmune pancreatitis (AIP) is associated with a marked elevation of serum total IgG4. Although there is evidence of autoimmunity in AIP, there are also signs of an allergic nature of its pathogenesis.

Methods: Therefore, we determined both IgE and IgG4 in 13 patients with AIP, in 12 patients with pancreatic carcinoma and in 14 patients with atopic allergy. The relationship between IgE and IgG4 was determined by automated nephelometry and total IgE by automated enzyme fluorimunoassay. Both total IgE and total IgG4 levels in patients with AIP were significantly higher than those in patients with pancreatic carcinoma (P = 0.0004 and P = 0.015, respectively). There was a significant correlation between the total IgE and total IgG4 levels in patients with AIP and patients with atopic allergy (r(s) = 0.82, P = 0.0006 and r(s) = 0.88, P < 0.0001, respectively).

Results: The IgE/ IgG4 ratio in sera from patients with atopic allergy was significantly different (P = 0.0012) from this ratio in sera from patients with AIP.

Conclusions: These results suggest that analysis of total IgE in serum might be useful in the differentiation between autoimmune pancreatitis and pancreatic carcinoma.
Hepaticojejunostomy (HJ): How We Do It?

Bo Bo HTAY, Myo Myat THU, Aye Min SAN, Myat Su Mon SOE
Department of Surgery, Institute of Medicine (1), Yangon General Hospital, Myanmar

Aims: Hepaticojejunostomy (HJ) is one of the common surgical procedures in hepatobiliary and pancreatic (HBP) surgery to treat both benign and malignant diseases. There were few studies in which an attempt has been made to describe the detailed procedure of HJ.

Methods: The total of 128 operations were performed. Most of the patients had recurrent pyogenic cholangitis (RPC) and had undergone Roux-en-Y HJ with permanent access. Anastomosis was done with both extrahepatic and intrahepatic bile duct. Construction of HJ was performed by detailed step-by-step method. PDS or Vicryl suture was used. The size of suture depends on the opening of the anastomosis. The anastomosis was made using interrupted stitches for the anterior layer and continuous fashion posteriorly. For special consideration, mucosal stitches and vertical incision to CHD were performed for smaller anastomosis, and in multiple bile duct openings, neighboring bile ducts were transformed into a common channel by inserting stitches between them.

Results: There were three mortalities in the study. All cases were associated with major bile leak. Two patients had RPC with cholangitic abscess. The other patient had periampullary CA who had undergone Whipple’s operation. Six patients had minor bile leak that recovered with conservative treatment.

Conclusions: In this paper, the proposed method for HJ is a reliable and feasible technique. It can be applied in a variety of diseases. The method is not a recommendation or procedural modification but a useful surgical option which follow the standard principles of anastomosis.

Liver Transplantation

PE-308
Program of Transplant Organization to Coordinate the Development of Organ Donation in Kazakhstan
Azat Chinaliyyev, Serik Zharikov
Republican Center for the Coordination of Transplant and High-Tech Medical Services, Kazakhstan

Aims: The aim of this study was to evaluate the progress of organ transplantation procedure.

Methods: In recent years organ transplantation has become a well-established procedure for management of renal, liver, cardiac, and respiratory failure. In spite of that, a shortage of organs still remains a serious problem for the full development of these therapeutic approaches in Kazakhstan. The first kidney transplantation was performed in Kazakhstan in 1979, approximately 40 years ago. The operation itself was technically successful, but the lack of immunosuppression caused graft rejection, and the patient died after a few days.

Results: Due to government policy, an organized organ transplant program started more than 4 years ago and the program was supported by the Ministry of Health. During this period a well-designed program of transplant organization has been established. In Kazakhstan, each potential donor hospital has a transplant coordinator who is responsible for the whole process of organ procurement. Eleven transplant centers work currently in Kazakhstan, and 557 transplantations have been performed up to the middle of the year 2015. We found that renal, liver and cardiac transplants increased since coordination program started.

Conclusions: We conclude that this program was successful in Kazakhstan and organ donation, procurement, and transplantation would become commonplace events to solve the problem of the organ donor shortage.

Keywords: Transplantation, Liver, Coordination, Development

Frequency and Main Risk Factors of Ventral Site Hernia Development in Patients Liver Transplantation
Alibek Serkulov, Berdibek Yelchibayev
JSC National Scientific Medical Center, Kazakhstan

Aims: The main purpose of this study was to perform a retrospective analysis for risk factors of ventral site hernia (VSH) in a
group of patients after living-donor liver transplantation with abdominal midline incisions.

**Methods:** Data collection involved the review of age, body mass index (BMI), smoking, and the presence of additional medical disorders, operative complications, postoperative care, surgical infections (SI), chemotherapy, and duration of follow-up. Appropriate statistical tests were used.

**Results:** Thirty-five patients were operated with midline incisions. 5 patients had VSH with a rate of 25% incidence. In our study, the main risk factors as age, BMI, operative complications, SI, chemotherapy, and duration of follow-up were statistically significant.

**Conclusions:** The presence of independent risk factors should be taken over by an oncologist in order to prevent the formation of VSH in a long-term follow-up. In the following studies it remains to provide evidence that, in the presence of several risk factors, the use of individual treatments (using meshes, etc.) is necessary.

**Keywords:** Liver, Transplantation, Hernia, Ventral, Operation

**PE-310**

**Portal Vein Thrombosis in Patients with End-Stage Liver Disease on the Waiting List**

Seidakhmetova Nazerke, Rysmakhanov Myltykbay

Aqtobe Medical Center, Kazakhstan

**Aims:** Among the patients with end-stage liver diseases on the waiting list, the portal vein thrombosis (PVT) complicates the liver transplant operation and theoretically disturbs survival. The aim of this research is to find the consequence of PVT on the survival benefit of liver transplantation.

**Methods:** From January 2015 to February 2018 patients with end-stage liver diseases were treated electively by liver transplant operation Aqtobe Medical Center. Data collection involved the review of age, body mass index (BMI), smoking, and the presence of additional medical disorders, operative complications, postoperative care, surgical infections (SI) and duration of follow-up. Appropriate statistical tests were used. Also by sequential stratification, we estimated the liver transplant survival benefit by MELD score and PVT status.

**Results:** The occurrence of described PVT among liver transplant recipients was not a predictor of waiting list mortality but was a forecaster of posttransplant mortality. With all of this, transplant advantage was not significantly different for patients with PVT vs. without PVT.

**Conclusions:** PVT does not disturb waiting list mortality, but it is related to meaningfully advanced posttransplant mortality. Transplant surgeons should sensibly reflect the risks of liver transplantation in clinically stable patients who have PVT.

**Keywords:** Waiting list, Liver, Portal vein, Thrombosis, End-stage, Transplantation

**PE-311**

**Influence of Adult Living Donor Liver Transplantation on the Waiting List in Kazakhstan**

Aigerim Mashyrap, Zharikov Serik

Republic Coordination Center for Transplantation and Hi-Tech Services, Kazakhstan

**Aims:** Living donor liver transplantation (LDLT) has become improved access to a lifesaving transplant for patients with end-stage liver disease especially in zones where waiting time mortality is high and availability of deceased donor organs is shortened. Due to the collaborative program with Seoul National University Hospital and several hospitals in Kazakhstan, this treatment option becomes available for our citizens.

**Methods:** This collaboration shows that there are noteworthy risks to the donor, including the risk of death and considerable morbidity, that must be occupied into interpretation before transplant programs board in LDLT. Significant developments in outcomes have been seen over the past years that have now been reported in several centers of our country.

**Results:** In spite of this, living donor liver transplant remains standing. It is well known that centers with more experience have improved outcomes. Upcoming investigation requirements to address best donor assessment, as well as identify the most appropriate LDLT donors and recipients.

**Conclusions:** With all these future studies should help quantify donor risk and recipient outcome, and confidently permit progress and development of the procedure.

**Keywords:** Living donor, Waiting list, Liver, Transplantation

**PE-312**

**Pure Laparoscopic Versus Open Right Hepatectomy in Live Liver Donors: A Propensity Score Matched Analysis**

Lee, Nam-Joon Yi, Kwang-Woong Lee

Department of Surgery, Seoul National University College of Medicine, Korea

**Aims:** Pure laparoscopic donor right hepatectomy (PLDRH) has been reported as a safe and feasible approach. However, its outcomes have not yet been evaluated in a large comparative study. The aim of this study is to describe our experience with PLDRH and to compare its outcomes with those of open right hepatectomy in live liver donors using propensity score matching.

**Methods:** The medical records of live liver donors between January 2010 and September 2018 at Seoul National University Hospital were retrospectively reviewed. Donors who underwent hepatectomy other than conventional open right hepatectomy or PLDRH were excluded. Propensity score matching study was conducted. Subsequently, 198 donors were included in each group.

**Results:** The total operation time (270.8 vs. 289.9; P < 0.001), time to remove the liver (166.2 vs. 211.4; P < 0.001), and...
warm ischemic time (3.7 vs. 12.3; \( P < 0.001 \)) were longer in the PLDRH group. The percentage of getting multiple bile duct openings was higher in the PLDRH group (44.9% vs. 56.1%; \( P = 0.027 \)). \( \Delta \)hemoglobin (Hb)%, calculated as \( \Delta \)Hb% = [(preoperative Hb – postoperative Hb)/preoperative Hb] x 100, was lower (21.3% vs 16.6%; \( P < 0.001 \)) and Aspartate aminotransferase (AST)%, calculated as \( \Delta \)AST% =[(postoperative AST – preoperative AST)/preoperative AST] x 100 (783.8% vs. 1136.9%; \( P < 0.001 \)), and Alanine aminotransferase (ALT)%, calculated as \( \Delta \)ALT%=[(postoperative ALT – preoperative ALT)/preoperative ALT] x 100 (912.7% vs. 1358.1; \( P < 0.001 \)), were higher in the PLDRH group. The length of postoperative hospital stay was significantly shorter in the PLDRH group (8.6 days vs. 7.5 days; \( P < 0.001 \)). However, the rate of complications was similar in both groups (10.6% vs. 6.1%; \( P = 0.102 \)).

Conclusions: PLDRH is safe and feasible when performed at an experienced LDLT center.

Keywords: Laparoscopic, Right hepatectomy, Donor hepatectomy

---

**PE-314**

Risk Factor of Delayed Hepaticojejunostomy Site Stricture in Pylorus Preserving Pancreaticoduodenectomy and Its Predicting Nomogram

Seoung Yoon RHO, Ho Kyoung HWANG, Woo Jung LEE, Chang Moo KANG

Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: Incidence of anastomotic stricture after hepaticojejunostomy (HJ) in pylorus-preserving pancreaticoduodenectomy is about 4-10% in benign disease, less common in malignancy such as pancreatic ductal adenocarcinoma. It is one of representative long-term complication, still it is not much investigated, such as risk factor for occurrence.

Methods: From Jan 2012 to May 2018, we investigated patients underwent hepaticojejunostomy during pancreaticoduodenectomy by single surgeon in Severance hospital. Patients who occurred HJ stricture confirmed by imaging studies, after 90 postoperative days, during follow-up period.

Results: Total 283 patients were included, and HJ stricture is confirmed in 27 patients (10.5%). Mean Body mass index in HJ stricture patients was slightly lower than NO HJ stricture patients (22.37 vs 23.41, \( P = 0.071 \)) with no statistical significances. However, proportion of postoperative bile leak is significantly higher in HJ stricture group (n = 4, 14.81%) than NO HJ stricture group (n = 9, 3.52%) (\( P = 0.026 \)). In multivariate COX regression, female (HR 0.39, 95% CI 0.16-0.96, \( P = 0.039 \)), bile duct size (HR 1.35, 95% CI 1.08-1.68, \( P = 0.007 \)), postoperative bile leak (HR 3.82, 95% CI 1.25-11.7, \( P = 0.019 \)) were most independent risk factor for HJ stricture. Based on this parameters, 3 year HJ stricture free probability was able to assumed with Harrell’s concordance index of 0.7131 (95% CI 0.58-0.82).

Conclusions: Delayed occurrence of HJ stricture after pancreaticoduodenectomy is able to be predicted with powerful risk factors such as female, bile duct size, postoperative bile leak event. With this prediction nomogram, external validation in large cohort and various surgeon is mandatory in near future.

---

**PE-315**

A Case of Migration of Cyanoacrylate into Portal Vein after Living Donor Liver Transplantation

Hee Yeon Kim1, Chang Wook Kim1, Soo Ho Lee2, Yoo Dong Won3, Su Lim Lee4

1Division of Hepatology, Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, College of Medicine, Catholic University of Korea, Seoul, Korea; 2Department of Surgery, Uijeongbu St. Mary’s Hospital, College of Medicine, Catholic University of Korea, Seoul, Korea; 3Department of Radiology, Uijeongbu St. Mary’s Hospital, College of Medicine, Catholic University of Korea, Seoul, Korea

Aims: Gastroesophageal varices bleeding is a major complica-
tion and carries a high mortality in patients with liver cirrhosis. Endoscopic injection of N-butyl-2-cyanoacrylate mixed with lipiodol has been used for hemostasis of bleeding gastric varices. We present a case of migration of injected cyanoacrylate to portal vein after living donor liver transplantation (LDLT).

Methods: A 53-year-old man presented with fever and abdominal pain 3 weeks after LDLT. He had received LDLT due to recurrent bleeding of esophageal and cardiac varices. Tissue adhesive (lipiodol and cyanoacrylate) was injected to cardiac varices 2 months before LDLT. Abdominal CT scan before LDLT showed high attenuation material (lipiodol/cyanoacrylate adhesive) in coronary veins with no evidence of portal vein thrombosis. However, CT scan 3 weeks after LDLT revealed high attenuation material in main portal vein. Fever and thrombocytopenia persisted. Liver enzymes were mildly elevated.

Results: Transsplenic portal vein stent was placed due to protrusion of tissue adhesive into main portal vein after obliteration of gastroesophageal varices. After portal vein stent placement, fever and thrombocytopenia has been improved and portal vein flow was intact.

Conclusions: Treatment of gastroesophageal varices using tissue adhesive is relatively safe. However, migration of injected cyanoacrylate to portal vein should be remembered as a complication caused by tissue adhesive even after LDLT.

Keywords: Living donor liver transplantation, Cyanoacrylate, Portal vein

---

**PE-316**

**Outcome of Living Donor Liver Transplantation for Secondary Biliary Cirrhosis in Adult: Single Center Experience**

Youngin YOON, Sung-Gyu LEE
Division of Hepatobiliary Surgery and Liver Transplantation, Asan Medical Center, Republic of Korea

Aims: Although liver transplantation is a definitive cure for secondary biliary cirrhosis (SBC), there is limited data about results of living donor liver transplantation (LDLT) in adults.

Methods: This retrospective study assessed data from 29 SBC patients who had LDLT between December 1994 and July 2018.

Results: The study cohort comprised of 10 males and 19 females, aged 50.0 ± 8.6 years. Except for 3 patients, the rest were diagnosed with secondary biliary cirrhosis from hepatolithiasis, and 25 out of 29 (86.2%) had a history of receiving the hepatobiliary surgery. Model for end-stage liver disease (MELD) score was 18.8 ± 9.4. The major complication rate was 62.1%, and the most common complication was bleeding. The ICU and hospital stay were 24.4 ± 13.8 and 40.9 ± 24.8 days. Four patients died in first month after LDLT; two died of rupture of hepatic artery rupture, one died of intra-cranial hemorrhage, and the other one died of sepsis.

Conclusions: LDLT for patients with SBC is very difficult, and there’s a big danger of massive bleeding. Even though operation time is long and there’s a lot of bleeding, thorough planning and a meticulous surgical technique that does not cause complications can reduce the mortality rate in LDLT for patients with SBC.

---

**PE-317**

**Liver Transplantation for Patient with Emergency Indication**

Sh. Jakanov, E. Kulteshova
Department of Surgery, Astana City Hospital, Kazakhstan

Aims: Decompensate liver cirrhosis is often accompanied by hepatorenal syndrome (HRS) with mortality up to 80%. The aim is improving the results of critical cases of decompensate liver cirrhosis in terminal phase.

Methods: Patient S., 32 years old, female, enrolled with decompensated Primary Liver Cirrhosis, Child-Pugh class C, portal hypertension, esophageal varices II degree, ascites and hydrothorax, secondary coagulopathy and hepatic encephalopathy – III. MELD was 38. In inpatient ward his condition become worse as marked dyspnea, itching, ascites, oliguria. The total bilirubin increased to critical levels (571 mc mol/L), hepatocellular, kidney (Cre 220 mc mol/L) and respiratory failure progression and growing of asctes tense. MARS-therapy was ineffective. Despite significant coagulopathy, the continuous renal replacement procedure was performed safely and without incident. Cadaveric donor liver transplantation was indicated and performed by standard method.

Results: In postoperative period intensive care and triple immunosuppression therapy (calcineurin inhibitor started on the 4th day, because of HRS) were done. In our patient, our treatment strategy resulted in resolution of ascites and edema, and improvement of renal function and hemodynamics. Patient discharged after 42 days after transplantation operation.

Conclusions: Thus, in this emergency case just organized and undertaken by highly qualified emergency medical care to a patient in a terminal state would save lives.

Keywords: Liver, Transplantation, Emergency indication, Hepatorenal syndrome

---

**PE-318**

**Machine-Learning Models to Predict Tacrolimus Dosage in Liver Transplant Recipients**

Jeong-Moo LEE1, Hyung-Chul LEE2, Kyung-Suk SUH1, Suk Kyun HONG1, Jae-Hyung CHO1, Nam-Joon YI1, Kwang-Woong LEE1

1Department of Surgery, Seoul National University Hospital, Republic of Korea, 2Department of Anesthesiology, Seoul National University Hospital, Republic of Korea

Aims: Tacrolimus is the most widely used immunosuppressive agents to prevent rejection after solid organ transplantation. However, the use of tacrolimus should be cautious due to its narrow therapeutic index Machine learning techniques could
De Novo Malignancy after Liver Transplantation: A Single Center Experience

Jeong-Moo LEE, Kwang-Woong LEE, Suk Kyun HONG, Jae-Hyung CHO, Nam-Joon YI, Kyung-Suk SUH
Department of Surgery, Seoul National University Hospital, Republic of Korea

Aims: There are many report about solid organ transplantation recipients appear to have a higher risk of malignant tumor. It caused by suppressed immune system fail to surveillance malignant transformation. De novo malignancy after transplantation is the most common cause of late mortality. The aim of the study is to describe of experiences of de novo cancer of liver transplantation in South Korea.

Methods: We retrospectively reviewed the postoperative tacrolimus levels of patients who underwent liver transplantation at the Seoul National University Hospital from March 2016 to March 2018. We implemented an artificial intelligence model predicting future tacrolimus level by tacrolimus concentrations. We investigated hyperparameters (the number of layers in the network and the number of nodes in each layer) using a grid search and found the model with the lowest validation error.

Results: A machine learning model was derived using data from the 187 patients. As a result of testing the model with 18 patients, the predicted value of the model had an error of 1.5 ug/ml from the actual measured tacrolimus level. Simulating the model in random case with a calculated tacrolimus dose to ensure the next drug concentration to be within the therapeutic range, more than 95% of the final predicted tacrolimus level comes in the therapeutic window.

Conclusions: This is the first study to use machine learning models to predict optimal dosage after liver transplantation. Machine-learning model is useful to decide optimal dose of tacrolimus immediate postoperative period after liver transplantation.

The Impact of Extra-Anatomical Hepatic Artery Reconstruction during Living Donor Liver Transplantation on Biliary Complications and Graft and Patient Survival

Jinsoo RHU, Jong Man KIM, Gyu Seong CHOI, Jae-Won JOH
Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Aims: This study was designed to analyze the feasibility of extra-anatomical hepatic artery reconstruction in living donor liver transplantation.

Methods: Patients who underwent their first living donor liver transplantation at our center between January 2008 and December 2017 were reviewed. Hepatic artery reconstruction was classified as anatomical or extra-anatomical reconstruction. We compared the background characteristics and post-transplantation outcomes, including complications, biliary complications, graft survival, and overall survival. The potential risk factors for bile leakage was analyzed using multivariable logistic regression while risk factor for biliary stricture-free, graft, and overall survival were analyzed using multivariable Cox regression.

Results: Among 800 patients, 35 (4.4%) underwent extra-anatomical reconstruction while seven patients (7/35, 20.0%) experienced hepatic artery complications after the initial anatomical reconstruction and required extra-anatomical reconstruction during reoperation. Patients who underwent extra-anatomical reconstruction (n = 2/35, 5.7%) had a similar rate of hepatic artery complications compared to those who underwent anatomical reconstruction (n = 46/772, 5.9%, P = 0.699). Extra-anatomical reconstruction was a significant risk factor of bile leakage (OR = 4.167, CI 1.928-9.006, P < 0.001) along with multiple bile ducts (OR = 1.606, CI=1.022-2.526, P = 0.040), and hepaticojejunostomy. (OR = 4.108, CI=2.190-7.707, P < 0.001) However, extra-anatomical reconstruction had no statistical relationship to biliary stricture-free survival (HR=1.602, CI=0.982-2.613, P = 0.059), graft survival (HR=1.745, CI=0.741-4.109, P = 0.203), or overall survival (HR=1.405, CI=0.786-2.513, P = 0.251). Hepatic artery complications were associated with poor biliary stricture-free survival (HR=2.060, CI=1.329-3.193, P = 0.001), graft survival (HR=5.549, CI=2.883-10.681, P < 0.001), and overall survival (HR=1.958, CI=1.195-3.206, P = 0.008).

Conclusions: Extra-anatomical hepatic artery reconstruction during living donor liver transplantation was not a risk factor of biliary stricture, graft failure, or overall survival.
**PE-321**

**Living Donor Liver Transplantation Using Right Lobe Graft from a Donor with the Left-Sided Gallbladder Anomaly**

Sung Yeon HONG, Hee-Jung WANG, Bong-Wan KIM, MinA KIM, Xue-Yin SHEN
Department of Liver Transplantation and Hepatobiliary Surgery, Ajou University, School of Medicine, Republic of Korea

**Aims:** The occurrence of left-sided gallbladder in the absence of situs inversus is a rare congenital anomaly. It is characterized by a complex liver structural abnormalities. We, herein, describe the inclusion criteria for liver donation of the potential donors with left-side gallbladder anomaly and technical modifications in performing donor hepatectomy.

**Case:** A 34-year-old blood-type AB Rh+ son donated right lobe (1.27% graft volume to recipient weight ratio; GRWR) to his mother (blood type B Rh+) with B-viral hepatitis and hepatocellular carcinoma.

**Results:** The liver with left-sided GB anomaly should meet the following criteria for successful liver donation. First, the portal vein must be a bifurcation type. It must be a bifurcation type rather than a trifurcation type. Second, the P2 and P3 must have a common trunk. This is crucial for the remnant left lobe to retain normal portal inflow after right lobe donation. Third, the volumnetry of the right and left lobe should meet the usual donation criteria. That is, the GRWR of the right lobe, greater than or equal to 0.8, and remnant left liver volume over 35% of original donor liver.

**Conclusions:** We have shown that it is technically feasible to retrieve the right lobe liver grafts from living donor without complication. Although, the donor with this anomaly must meet above mentioned criteria for successful LDLT, and they must be meticulously evaluated in prior to the operation.

---

**PE-322**

**The Effect of Downstaging by Locoregional Treatments for Hepatocellular Carcinoma beyond Milan Criteria before Living Donor Liver Transplantation**

Byeong-Gon NA, Seong Hoon KIM, Eung Chang LEE, Sang Jae PARK
Center for Liver Cancer, National Cancer Center, Republic of Korea

**Aims:** This study aimed to assess the survival outcomes after living donor liver transplantation (LDLT) in patients beyond Milan criteria (MC) after downstaging (DS) to within MC by locoregional treatments (LRT) and to investigate the prognostic factors for HCC recurrence.

**Methods:** A total of 113 patients undergoing LRT before LDLT from Jan, 2010 to Dec. 2016 were enrolled. The initial tumor size and number, and alpha-fetoprotein (AFP) before LRT and at the immediate pretransplant periods were examined.

**Results:** The thirty-one patients beyond MC treated with LRTs resulted into DS group (n = 8) and non-downstaging (non-DS) group (n = 23). There were no significant differences related to the type and number of LRT. The 1-, 3-, and 5-year HCC recurrence-free survival (RFS) estimates of DS group were superior to those of non-DS group (100%, 100%, and 87.5% vs. 54.8%, 49.3%, and 37%, P = 0.028). In a regression model predicting DS, the HCC with the lower initial number (odds ratio [OR]: 0.54, P = 0.036) and initial log AFP (OR: 0.53, P = 0.048) before LRT tended to downstage. Multivariate predictors of posttransplant recurrence were initial tumor largest size (hazard ratio [HR]: 1.20, P = 0.025), initial tumor number (HR: 1.11, P = 0.101), and immediate pretransplant log AFP (HR: 2.38, P = 0.002).

**Conclusions:** The DS may lead to favorable RFS after LDLT. The lower initial tumor size and number before LRT, and initial and immediate pretransplant AFP can corroborate a better prediction of DS by LRT and RFS after LDLT.

---

**PE-323**

**Effect of Internal Stent Insertion in Duct-to-Duct Biliary Reconstruction to Reduce Bile Duct Complication in Living Donor Liver Transplantation**

Ho Jong Choi, Tae Yun LEE, Joseph AHN, Bong Jun KWAK, Gun Hyung NA, Tae Ho HONG, Young Kyong YOU
Department of Surgery, 1Seoul St. Mary’s Hospital, The Catholic University of Korea, 2Bucheon St. Mary’s hospital, The Catholic University of Korea

**Aims:** Biliary complication is still considered to be a technical “Achilles’ heel” of living donor liver transplantation (LDLT) due to the high incidence, requiring long-term interventional treatment, and potential risk for graft failure. The purpose of this study was to evaluate the effectiveness of internal stent for duct-to-duct anastomosis in LDLT.

**Methods:** From December 2016 to October 2018, LDLT was performed in 91 patients in our center. Duct-to-duct anastomosis was performed in all LDLT patients. Ninety-one patients were divided into non-stent group and stent group according to presence or absence of internal stent. Biliary complications were diagnosed as anastomosis leakage and anastomosis stenosis when interventional treatment was required.

**Results:** Biliary complications occurred in 20 (22.0%) patients and anastomosis site leakage occurred in 5 (5.5%) patients. Of the 91 patients, non-stent group was 48 (52.7%) patients and stent group was 43 (47.3%) patients. Anastomosis site leakage was higher in the non-stent group (n = 4, 8.3%) than in the stent group (n = 1, 2.3%), although there was no statistical difference (P = 0.21). Biliary complications were also higher in the non-stent group (n = 14, 29.2%) than in the stent group (n = 6, 14.0%), although there was no statistical difference (P = 0.08). In univariate analysis, the operation time was longer in the biliary complications group (P = 0.04).

**Conclusions:** Although there was no statistically significant
difference due to small case number, when internal stent was inserted, biliary complications including anastomosis leakage were reduced compared to no insertion. Further large-scale analyses of clinical data are required to support this study.

**PE-324**

**Experience of Hepatic Artery Anastomosis in Living Donor Liver Transplantation Using Surgical Loupe: In Small Volume Center**

Kwan woo KIM, Shung wha KANG
Surgery, Dong-A University Hospital, Republic of Korea

**Aims:** The hepatic artery (HA) reconstruction in living donor liver transplantation (LDLT) is a crucial step because of the smaller diameter of the artery and the increased risk of HA related complications. Also, any occurrence of the HA flow abnormalities in the immediate postoperative period may lead to fatal complications. Therefore, many centers use a micro-surgical technique for HA reconstruction. The aim of our study was to investigate the outcomes that HA reconstruction was performed under surgical loupe.

**Methods:** This study included 44 LDLTs with various end stage liver diseases at Dong-A University hospital Busan, Korea from January, 2014 to August, 2018. The medical records were retrospectively analyzed for the outcomes and HA related complications.

**Results:** HA reconstruction for the initial 13 LDLT surgeries was performed using a micro-surgical technique. From 14 LDLT case, HA reconstruction was performed in 31 recipients under surgical loupe with interrupted suture on posterior HA wall and running suture on anterior wall. We performed HA reconstruction in 30 adults, 1 pediatric patient (one year old) under surgical loupe, which included one dual graft LDLT. The most notable factor in surgical loupe group compared with micro-surgical group (33±5 minutes) was the quick HA anastomosis procedure with a mean time of 12±3 minutes. Fortunately, there were no HA related complications in both groups.

**Conclusions:** Although our case is not enough, we could consider that the HA reconstruction using surgical loupe even in smaller diameter hepatic arteries is a reliable technique and can easily be applied by an experienced surgeon.

**Keywords:** Hepatoblastoma, Liver transplantation, Laparoscopic resections, Hepatic tumor

**PE-326**

**Chronic Renal Dysfunction Following Liver Transplantation**

Nurlan Makhambetov, Samat Issakov
General Surgery, National Research Center for Maternal and Child Health, Kazakhstan

**Aims:** With most of the immunosuppressive protocols consisting of calcineurin inhibitors (CI), nephrotoxicity has become a major long-term complication often compromising outcome.

**Methods:** In a single-center retrospective study, we reviewed 173 liver transplantations to identify variables indicative for the occurrence of chronic renal dysfunction (CRD) (defined as > or = 1 episode of serum creatinine increase > or = 1.8 mg/dL, or > or = 2 wk). Chronic renal dysfunction was found in 20 (11.7%) of all transplants (12 (7%) early (after 3-12 months), 8 (4.7%) late-onset (> 12 months). Compared to 5-10-yr survival rates in non-CRD transplants (84/74%) survival was significantly decreased in early (66/46%), but unchanged in late-onset CRD (98/86%). Rates of alcoholic cirrhosis and prior renal dysfunction were significantly increased in patients with CRD. In a multivariate logistic regression analysis, only cyclosporine A (CyA) as immunosuppression remained an independent risk factor.

**Results:** No correlations to age, gender, rejection/retransplantation or diabetes were found. Surprisingly, renal function (creatinine) showed no difference between patients on CI monotherapy (FK/CyA) compared to those who had mycophenolate mofetil (MMF) added. In liver transplantation, early onset CRD

**Conclusions:** Though long term follow-up data is necessary for validation, we suggest that an individualized surgical strategy based on the accurate evaluation of the tumor extent might improve the clinical outcomes of patients with hepatoblastoma.

**Keywords:** Hepatoblastoma, Liver transplantation, Laparoscopic resections, Hepatic tumor
Sirolimus and Metformin Synergistically Inhibits Colon Cancer in Vitro and in Vivo

Nadiar Mussin1, Seung Cheol Oh2, Kwang-Woong Lee3, Min Young Park4, Sooin Seo5, Nam-Joon Yi6, Hyeyoung Kim7, Kyung Chul Yoon7, Sung-Woo Ahn7, Hyo-Sin Kim7, Suk Kyun Hong7, Dong Kyu Oh7, and Kyung-Suk Suh7

1Aktobe Medical Center, Kazakhstan, 2Seoul National University Hospital, Korea

Aims: Colon cancer has been reported as one of the frequent de novo cancer in Asia. However, there is no optimal treatment strategy for de novo colon cancer after LT. The effect of various immunosuppressants (IS) and metformin were estimated to provide the theoretical background of optimal therapeutic strategy for de novo colon cancer.

Methods: Three colon cancer cell lines (HT29, SW620, and HCT116) were used in an in vitro study. Furthermore, in an in vivo study, colon cancer models induced by subcutaneous injection of HT29 in BALB/c-nude mice. Then, the following treatments were done in both in vitro and in vivo studies, sirolimus (S), tacrolimus (T), cyclosporin A (CsA), metformin (M), metformin/sirolimus (MetS), metformin/tacrolimus (MetT), and metformin/cyclosporin A (Met CsA). Then, 3-(4-5-Dimethylthiazol-2-yl)-2 5-diphenyltetrazolium bromide (MTT) assay was performed for analysis of cell viability. Apoptosis components (EMT proteins, and mTOR pathway proteins were evaluated by Western blot analyses. Tumor volumes were measured for 4 weeks after inoculation.

Results: MTT-assay revealed significant cell viability inhibition in all three colon cancer cell lines in groups of S, M, and MetS. Of note, group MetS showed synergistic effect compare to M or S group in in vitro study. Western blot analysis showed significantly low levels of all investigated proteins in groups of S and MetS in both in vitro and in vivo experiment. Tumor growth was significantly inhibited only in the MetS group.

Conclusions: Combination of metformin and sirolimus had the most potent inhibition in the evaluated colon cancer cell lines in vitro and in vivo. This finding might have application for de novo colon cancer.

Keywords: Liver transplantation, immunosuppression, metformin, sirolimus
alveococcosis were performed at the Regional Medical Center in Kyzylorda from 2016 to 2018. 3 patients underwent related liver fragment transplantation (in all cases - the right lobe of the liver), 1 patient received a liver transplant from a post-mortem donor. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine. In 2 patients (72.7%) there was a parasitic invasion of the intestine.

Results: The operation duration was 430 (390–480) min, the volume of intraoperative blood loss was 1500 (1300–2200) ml, and the duration of cold ischemia was 30 (25–45) min. The overall incidence of postoperative complications reached 45.4%, the main ones were biliary complications. Hospital mortality was 4.5%. The postoperative period lasted 20 (15–23.5) bed-days. Remote survival was 100%. The maximum observation period was 58 months.

Conclusions: Liver transplantation with resection and grafting of the great vessels, including resection of the inferior vena cava and even the right atrium, can serve as the only radical method of treating unresectable alveococcosis of the liver, allowing for satisfactory immediate and long-term results of surgical treatment in seemingly “doomed” patients. These interventions should be performed exclusively in highly specialized centers with a developed program of surgical hepatology and liver transplantation.

Keywords: Liver, Transplantation, Alveokokkoz

PE-330
Renal Safety of Entecavir and Tenofovir with Hepatitis B Immunoglobulin in Liver Transplant Patients

Juhan Lee1, Deok Gie Kim1, Jee Youn Lee2, Seok Jeong Yang3, Dong Jin Joo1, Myoung Soo Kim1, Soon Il Kim1, and Jae Geun Lee1
1Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea; 2Department of Surgery, Gangbuk Samsung Hospital, Sungkyunkwan University College of Medicine, Seoul, Republic of Korea

Aims: Combination of potent nucleos(t)ide analogues (NAs) and hepatitis B immunoglobulin is recommended after liver transplantation for the prevention of hepatitis B virus (HBV) recurrence. Despite its proven efficacy, renal safety of NAs in liver transplant recipients has not been well defined. We aimed to assess the impact of entecavir and tenofovir on glomerular and tubular function.

Methods: We analyzed 201 liver transplant patients treated with entecavir (n = 122) or tenofovir (n = 79) with hepatitis B immunoglobulin between 2012 and 2016. Serum creatinine, phosphorus, and uric acid were measured, and estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. Proximal tubular dysfunction was defined as the combination of hypophosphatemia (< 2 mg/dL) and hypouricemia (< 2 mg/dL).

Results: Mean eGFR at start of NAs after liver transplant was 100.8 for entecavir, 102.7 mL/min/1.73 m² for tenofovir group (P = 0.554). Mean eGFR at the last on-treatment visit was 80.0 for entecavir and 82.5 mL/min/1.73 m² for tenofovir group (P = 0.491). During the 28 months of median follow-up, 30 patients experienced decrease of eGFR < 30 mL/min/1.73 m² (20 [16.4%] of entecavir and 10 [12.7%] of tenofovir group, P = 0.468). Serum phosphorus and uric acid in both groups were statistically not significant at start of NAs. A total of 37 patients developed renal tubular dysfunction (11 [9.0%] of entecavir and 26 [32.9%] of tenofovir group, P < 0.001). Tenofovir (HR, 5.24; 95% CI, 2.25–12.19; P < 0.001), decrease of eGFR < 30 mL/min/1.73 m² (HR, 4.44; 95% CI, 1.67–11.85; P = 0.003), and use of mTOR inhibitor (HR, 2.31; 95% CI, 1.04–5.11; P = 0.04) were independent risk factors for proximal tubular dysfunction.

Conclusions: The effect of tenofovir on glomerular function was comparable to that of entecavir in liver transplant patients. However, tenofovir increased the risk of proximal tubular dysfunction. Longitudinal studies are needed to assess the long-term outcomes.

Keywords: Hepatitis B virus, Tenofovir, Renal toxicity, Liver transplantation

Acquired Hyponatremia in Pediatric Living Donor Liver Transplantation

Akmaral Dossanova, Lazzat Dossanova

Republican Children’s Clinical Hospital “Alksai” KazBMU named after SD Asfendiyarov, Almaty, Kazakhstan

Aims: The aim of this study was to evaluate the incidence of acquired hyponatremia (AH) in our pediatric living donor liver transplantation (LDLT) patients, and to identify the potential predictive risk factors of the causes of AH.

Methods: The 25 pediatric LDLT patients were divided into 2 groups: serum sodium level at the end of the surgery lower than 130 mEq/L in G1 (n = 2) and higher than 130 mEq/L in G2 (n = 23). Patients’ data were analyzed by Mann-Whitney U test, univariate analysis, and multiple binary logistic regression model. The Hosmer-Lemeshow goodness-of-fit test was used to evaluate the logistic model formulated. P value <0.05 was regarded as statistically significant.

Results: In the multiple binary logistic regression model, the hypotonic solution administration rate (ml/kg/h) was the only independent predictor of AH with a P < 0.017. Receiver operating curve (ROC) analysis indicated that giving more than 3.5 ml/kg/h hypotonic solution infusion may cause AH. Preoperative hyponatremia did not increase the incidence of acquired hyponatremia.

Conclusions: Increasing the administration of hypotonic solution by 1 ml/kg/h in pediatric LDLT would increase the risk of developing AH by 1.272 times. The critical administration rate of hypotonic solution was 3.5 ml/kg/h.

Keywords: Hyponatremia, Pediatric living donor liver transplantation, Hypotonic solution, Arterial hypertension
**PE-332**

**Initial Experience of Laparoscopic Right Lobectomy after Portal Vein Embolization**

Hwui-Dong Cho, Ki-Hun Kim, Dong-Hwan Jung, Gil-Chun Park, Young-In Yoon, Shin Hwang, Chul-Soo Ahn, Deok-Bog Moon, Tae-Yong Ha, Gi-Won Song, Sung-Gyu Lee

Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, University of Ulsan and Asan Medical Center

**Aims:** Portal vein embolization is a technique used before hepatic resection to increase the size of remnant liver after surgery. This therapy redirects portal blood to segments of the future liver remnant, resulting in hypertrophy. The purpose of this study was to find out the safety and feasibility of laparoscopic right lobectomy after portal vein embolization.

**Methods:** All consecutive cases of laparoscopic right lobectomy after portal vein embolization between July 2014 and April 2018 in a tertiary referral hospital were enrolled in this retrospective cohort study. All surgical procedures were performed by one surgeon. There were 14 cases of laparoscopic right lobectomy after portal vein embolization. The group was analysed in terms of donor demographics, preoperative data, postoperative outcomes.

**Results:** The mean age of the donors was 51.3 ± 6.7 years, the gender ratio for men and women was 18:96. The mean operative time was 402.5 ± 78.8 minutes and mean postoperative hospital stay was 10.1 ± 1.7 days. The number of complications was 6 cases (5.3%) and among them, the Clavien-Dindo classification III or higher complication was 2 (1.8%). There were no mortality cases.

**Conclusions:** Minimal invasive living donor right hepatectomy was a safe and feasible procedure for donors. It showed an acceptable incidence of complications. The authors suggest that minimal invasive living donor right hepatectomy could be a reasonable operative option for donors in terms of cosmetic effect.

---

**PE-333**

**Analysis of Cancer Incidence after Liver Transplantation in Korea Using Big Data**

Han Joon KIM1, Yun Kyung JUNG1, Dongho CHO1, Boyoung PARK2, Junghyun YOON1, Kyeong Geun LEE1, Hwon Kyum PARK1

1Department of Surgery, Hanyang University College of Medicine, Republic of Korea, 2Department of Preventive Medicine, Hanyang University, College of Medicine, Republic of Korea, 3Graduate School of Public Health, Hanyang University, Republic of Korea

**Aims:** Solid organ transplantation is the lifesaving procedure for patients with end organ diseases. The occurrence of malignant diseases is common after organ transplants, which affect postoperative outcomes.

**Methods:** We used NIH database and HIRA database for analyzing 3D-laparoscopic hemihepatectomy from live donors for patients with terminal stage of liver diseases. The use of live donors to some extent allowed to solve the problem of shortage of the donor organs. In the world, most donors under traditional open hemihepatectomy. In recent years, more and more often, a part of the liver has been withdrawn from living donors with the use of laparoscopic techniques. In the CIS countries, this technology is only being introduced. The aim of this report is to provide the first experience in implementing 3D-laparoscopic hemihepatectomy from living donors for transplantation in Akhtobe Medical Center («AMC») and in the Republic of Kazakhstan

**Methods:** In AMC, 12 liver transplantations have been performed since 2016, 11 of which are from living donors, 1 - from cadaveric donor. All liver transplantation operations from live donors were conducted with the direct participation of specialists from the Seoul National University Hospital. Of 11

---

**PE-334**

**3D-Laparoscopic Living Donor Hepatectomy: First Experience in Kazakhstan**

K-W. Lee1, Lyailash Kydyrbayeva2, M.S. Rysmakhano2, A.A. Kaliev2, E.B. Sultangereyev2, A.A. Yelemessov2, Zh. Almyrzauly2, and N.M. Mussin2

1Department of Surgery of Seoul National University Hospital; 2Department of Surgery of Akhtobe Medical Center; 3West-Kazakhstan Medical University after M.Ospanov, Kazakhstan

**Aims:** To date, the liver transplantation is the only radical treatment for patients with terminal stage of liver diseases. The use of live donors to some extent allowed to solve the problem of shortage of the donor organs. In the world, most donors undergo traditional open hemihepatectomy. In recent years, more and more often, a part of the liver has been withdrawn from living donors with the use of laparoscopic techniques. In the CIS countries, this technology is only being introduced. The aim of this report is to provide the first experience in implementing 3D-laparoscopic hemihepatectomy from living donors for transplantation in Akhtobe Medical Center («AMC») and in the Republic of Kazakhstan.

**Methods:** In AMC, 12 liver transplantations have been performed since 2016, 11 of which are from living donors, 1 – from cadaveric donor. All liver transplantation operations from live donors were conducted with the direct participation of specialists from the Seoul National University Hospital. Of 11
Transforming Growth Factor β1 in Children of Early Age with Liver Transplantation

Yerbulan Serikbayev¹, Aiman Atakhozhaeva²

¹National Research Center for Maternal and Child Health, Kazakhstan, ²Green Clinic, Kazakhstan

Aims: Transforming growth factor β1 (TGF-β1) plays a key role in the development of the immune response, as well as in the process of liver regeneration. Measuring the level of TGF-β1 may have important clinical implications in liver transplantation, because cytokine concentration in the tissue and in blood plasma varies with different liver diseases. Aim. To analyze the dynamics of TGF-β1 levels in children-recipients with liver transplant from related donors, including from incompatible blood groups.

Methods: The study involved 12 children aged 3 to 72 months, with liver cirrhosis, developed as the result of congenital and hereditary diseases of the hepatobiliary system. All patients underwent transplantation of the left lateral liver sector from living related donors. The concentration of TGF-β1 was determined by enzyme immunoassay method in blood plasma samples.

Results: Average level of TGF-β1 in blood plasma of children with liver cirrhosis, developed as the result of congenital and hereditary diseases of the hepatobiliary system was 5.2 ± 5.5 ng/ml. A month after liver transplantation from a related donor level of TGF-β1 in blood plasma of recipients increased to 8.1 ± 9.6 ng/ml. One year after transplantation, the average level of TGF-β1 in the recipients of liver fragment was 7.7 ± 8.4 ng/ml. No association between TGF-β1 level in a month and a year after transplantation and the compatibility of the recipient with AB0 donor was found. A correlation between level of TGF-β1 prior to transplantation and the development of graft dysfunction was observed: in recipients with graft dysfunction cytokine level prior to surgery was lower than in other recipients.

Conclusions: Liver transplantation leads to a significant increase in the level of TGF-β1 in the blood plasma of children and that level is not different in recipients after transplantation of a liver fragment from AB0-compatible and AB0-incompatible donors.

Keywords: Growth factor, Liver transplantation, Incompatible blood groups, Liver cirrhosis

Dynamics of Insulin-like Growth Factor-1 (IGF-1) in Children after AB0-Incompatible Liver Transplantation

Aiman Atakhozhaeva¹, Yerbulan Serikbayev²

¹Green Clinic, Kazakhstan, ²National Research Center for Maternal and Child Health, Kazakhstan

Aims: It is shown that liver transplantation (LT) from donor with incompatible blood type (AB0i) may be effective and safe, but the impact of such operation upon the various systems of the body has not been investigated yet. Insulin-like growth factor-1 (IGF-1) is synthesized in the liver and mediates the action of growth hormone. The level of IGF-1 is a marker of the processes of cell proliferation and tissue regeneration.

To evaluate levels of IGF-1 in children-recipients with liver transplant from AB0i (incompatible) and AB0c (compatible) donors.

Methods: 12 children aged 3 to 36 with congenital diseases of the hepatobiliary system. All patients underwent transplantation of left lateral liver sector from living related donors. The concentration of IGF-1 was determined by ELISA using specific kits in samples of blood plasma, which were received up to a month and a year after a liver transplant.

Results: Average level of IGF-1 21.0 ± 29.5 µg/l in patients before LT was significantly lower than in healthy children and did not vary in children, having received later a piece of liver from a compatible donor and from donor AB0i. In patients with anti-A/B prior to surgery average level of IGF-1 was not different from that of the patients without antibodies. One month after LT level of IGF-1 has increased both in the general group, and in patients with AB0c and AB0i liver. The level of IGF-1 was not varied in the group with antibodies and without them.

Conclusions: The results of our studies have shown that restoration of the level of IGF-1 is not dependent on transplantation of compatible or incompatible blood type liver, as well as on the availability of anti-group antibodies.

Keywords: Insulin-like growth factor-1, Liver transplantation, Incompatible blood type, Anti-group antibodies
Correction of Extrahepatic Portal Hypertension in Pediatric Patient after Liver Transplantation
Aibat Yelibayev, Bekzada Karamat
University Medical Center, Kazakhstan

Aims: Liver transplantation is a multi-component and complex type of operative treatment. Patients undergoing such a treatment sometimes are getting various complications. One of these complications is a portal hypertension associated with portal vein stenosis.

Methods: In 3 years after the left lateral section transplantation from living donor in a pediatric patient the signs of portal hypertension were observed. Stenosis of the portal vein was revealed. Due to this fact percutaneous transhepatic correction of portal vein stenosis was performed.

Results: As a result of the correction of portal blood flow in the patient a positive trend was noted. According to the laboratory and instrumental methods of examination the graft had a normal function, portal blood flow was adequate. In order to control the stent patency Doppler ultrasound and MSCT of the abdominal cavity with intravenous bolus contrasting were performed. Due to these examinations the stent function was good, the rate of blood flow in the portal vein due to Doppler data has reached 80 cm/sec, and a decrease of the spleen size was noted.

Conclusions: Diagnosis and timely detection of portal vein stenosis in patients after liver transplantation are very important for the preservation of graft function and for the prevention of portal hypertension. In order to do that, ultrasound Doppler fluorimetry examination needs to be performed to each patient after liver transplantation. In cases of violation of the blood flow in the portal vein CT angiography performance is needed. Percutaneous transhepatic stenting of portal vein is a minimally invasive and highly effective method of correction of portal hypertension. Antiplatelet therapy and platelet aggregation control are the prerequisites for successful stent function.

Keywords: Portal hypertension, Liver transplantation

Portal and Arterial Flushing with HTK and Tacrolimus Can Attenuate the Incidence of Early Liver Allograft Dysfunction
Bekzada Karamat, Aibat Yelibayev
University Medical Center, Kazakhstan

Aims: It was shown that Tacrolimus (Tac) can suppress inflammation and immune response involved in liver ischemia-reperfusion injury (IRI). Aim. We hypothesize that back-table arterial and portal liver perfusion with Tac can influence the incidence and severity of early allograft dysfunction (EAD). A prospective randomized study was conducted.

Methods: Criteria of the inclusion: First liver transplantation from DBD donor with sequential portal-arterial reperfusion. At back-table portal vein and hepatic artery were perfused each by 500 ml of HTK solution containing 20 ng/ml Tac during 10–15 min followed by portal flush with 200 ml 5% solution of Albumin containing 20 ng/ml Tac and by resting of liver in effluent. No Tac was added in the control group. Primary Outcome: EAD and severe EAD.

Results: No difference was found between groups (main vs. control) in terms of MELD (16 vs. 16), steatosis (10 vs. 10%), ballooning (45 vs. 40%) of liver grafts, recipient age (50 vs. 50 y.o.), warm ischemia time (50 vs.50 min) and total ischemia time (482.5 vs. 485.0 min). Median donor age was higher in the main group (44.5 vs.39.0 y.o.). The overall rate of EAD was 27.9%. EAD rate was significantly lower in the main group (6/43 vs.18/43; \( P = 0.003 \)). The rate of moderate-to-severe EAD was lower in the main group (1/43 vs. 10/43; \( P = 0.009 \)). The median levels of AST and ALT in 24 h after reperfusion were significantly lower in the intervention group (1004 vs. 1596; \( P = 0.03 \) and 449 vs. 759; \( P = 0.057 \)).

Conclusions: Portal and arterial back-table liver perfusion with HTK solution with Tacrolimus may contribute to lower EAD incidence and severity.

Keywords: Tacrolimus, Liver transplantation, Portal liver perfusion ischemia-reperfusion injury, Allograft dysfunction

A Learning Curve for Living Donor Liver Transplantation
Aidos Bissenbay, Bakhtorazov Erulan, Yerlan Bakhtorazov
National Scientific Center of Oncology and Transplantology Astana, Kazakhstan

Aims: The number of living donor liver transplantations performed has increased rapidly in many transplant centres. However, the impact of the transplant centres’ experience and learning on the transplant outcomes are not well established. Aim of the study was to evaluate the learning curve for living donor liver transplantation in our centre.

Methods: Data from 156 recipients and 156 donors who underwent surgery were reviewed. Intraoperative data and postoperative outcomes of both donors and recipients were retrospectively analysed. Recipients and donors were divided into three groups that consisted of 52 consecutive cases each.

Results: Surgical duration and intraoperative blood loss during donor surgery were decreased significantly between the earlier and the more recent cases (423±39 vs. 400±44 min and 959±523 vs. 731±278 mL, respectively, \( P < 0.01 \)). Rates of postoperative complications and functional changes were not statistically different amongst the three donor groups. Immediate complication rate of the first 52 recipients was higher than those of the second and third cohorts. Long-term survival rates of the three recipient groups were similar.

Conclusions: The learning curve greatly influenced immediate
outcomes of recipients during the early transplant period. However, it had little influence on donor outcome; long-term outcome improvement of recipients did not depend on the accumulation of experience alone.

**Keywords:** The learning curve, Recipients and donors, Statistically different amongst the three donor groups

---

**PE-340**

**Pediatric Liver Transplantation UMC, Kazakhstan**

Yermakhan Assylkhanuly, Zhanna Kozybayeva

University Medical Center, Kazakhstan

**Aims:** Living donor liver transplantation has become a cornerstone for the treatment of children with end-stage hepatic dysfunction, especially in Kazakhstan with low rates of organ from deceased donors. In our center, 8 pediatric living donor liver transplantations we carried out since 2014. Patients between the ages of 0 to 5 years. The indications for liver transplantation in our patients were biliary atresia.

**Methods:** The mean hospitalization time of our patients was 25 days and the mean stay in the intensive care unit was 8 days. The Child-Pugh score was C in 2 of our patients, B in 5 patients, and A in 1 patient. The donor age ranged from 27 to 41 years, and the weight ranged from 62 to 78 kg, mothers being the donors in a majority of these. As most children require only a left lateral segment graft, the morbidity and risks to the donor are much less than those donating their right lobes. Living donor transplants are ideally suited to children as it allows for a planned procedure, all patients with biliary atresia.

**Results:** The main complications after pediatric liver transplantation were infections and surgical complications including (biliary complications). We encountered biliary complications in 2 of the 8 patients and we performed surgical revision due to anastomosis leakage in 1 patient. Our immune suppression protocol is based on a combination of steroid and tacrolimus. MMF is also used as a second maintenance agent in addition to tacrolimus in children who have had a documented rejection episode.

**Conclusions:** Infections and biliary complications were the most common outcome occurring in children after LT. Advances in post-transplant care and monitoring of the recipients, technical refinements enable the better results.

**Keywords:** Pediatric, Liver, Transplantation, Biliary atresia

---

**PE-341**

**Cost Prediction in Liver Transplantation Using Pre-transplant Donor and Recipient Characteristics**

Arailym Ospanova, Setaev Saken Sarkitovich

Yereymentaus Central Hospital, Kazakhstan

**Aims:** Liver transplantation is a costly procedure and its cost is likely driven by both donor and recipient factors. Recently, the recipient model for end-stage liver disease (MELD) score has been correlated with increased posttransplant cost; however, other factors have not been identified. We sought to identify if other donor and recipient factors are associated with increased cost.

**Methods:** One hundred sixty-six liver transplants performed at our center from January 2004 through February 2006 were included in the estimation sample, and the subsequent 75 transplants were used as a validation cohort. To determine whether donor factors influenced cost, two latent class linear regression models were created from the estimation sample: one considering only recipient variables (model A) and a second incorporating both donor and recipient factors (model B). The resultant models were then validated in the second group of patients and compared with the best single-segment linear regression models.

**Results:** Model A predictors include pretransplant intensive care unit (ICU) stay, age x body mass index, and calculated MELD. In model B, significant predictors are calculated MELD, age, age x pretransplant ICU stay, and donor age more than 40 as significant variables. In validation, only model A remained predictive of cost.

**Conclusions:** Although marginal donor factors are recognized to influence clinical outcome, they did not factor significantly in cost modeling. In addition to MELD, the recipient factors of pretransplant ICU stay, age, and body mass index are pretransplant variables correlated mostly with posttransplant cost across broad populations.

**Keywords:** Costly procedure, A remained predictive of cost

---

**PE-342**

**Initial Experience of Liver Transplantation**

Mylytkbay Rysmakanov, Bazylbek Zhakyev

Department of Surgery and Transplantation, Aktobe Medical Center; Department of Surgery-2, West Kazakhstan Medical University, Kazakhstan

**Aims:** The aim is the presentations of results of first 3-years’ experience of liver transplantation at Aktobe Medical Center (AMC). Living donor liver transplantation was performed with the specialists of SNUH specialists.

**Methods:** In AMC performed 12 liver transplantations: 11 – from living donor, 1 – from a cadaveric donor. LDLT were done after evaluating following our practices guidelines. After donor right hepatectomies (or liver from a cadaver) TNK solution with heparine was used for graft perfusion. “Middle hepatic vein” in living donor right liver reconstructed by synthetic vascular graft in all cases. During recipient hepatectomy used “High Hilary Dissection” method. Liver graft implantation made as a standard technique. Before portal reperfusion, liver graft washed by 5% Albumine solution. Immunosuppressive therapy in all patients included three components (CNI + MMF + Steroid) with intravenous Basiliximab (1st and 4th postoperative day).

**Results:** Our donor’s age was between 22 and 48 years. In all cases removed right lobe. For 4 donors we used 3D-laparoscop-
ic right hepatectomy. All donors discharged at 7th–10th day after the operation. There was no complication on liver donors. Died 3 recipients in the early postoperative period, and 3 patients in the late postoperative period (2 – cholangiogenic abscess with sepsis and 1 – Alcoholism with chronic rejection).

Conclusions: Liver transplantation gives a chance to survive for patients with end-stage liver disease. Our transplant program needs to be gain experience, particularly with respect to donor selection, recipients thorough preoperative preparing.

Keywords: Liver, Transplantation, Cadaver, Living donor

**PE-343**

Long-Term Outcome of the Rendezvous Technique in Patients with Severe Biliary Anastomotic Stricture That Cannot Cannulate after Liver Transplantation

Kyeong Sik Kim¹, Jong Man Kim², Ji Soo Lee², Gyu Sung Choi², Jae-Won Jo³, Suk-Koo Lee⁴

¹Department of Surgery, Soon Chun Hyang University Seoul Hospital, Seoul, Korea; ²Department of Surgery-Transplantation, Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of Korea

Aims: The purpose of this paper is to analyze the long-term outcome of the Rendezvous technique in severe strictures through which guidewires cannot cannulate.

Methods: Between 2010 and 2017, 29 patients who underwent Rendezvous technique due to severe biliary anastomosis stricture after liver transplantation were included in the study.

Results: Twenty-nine patients who underwent the Rendezvous technique showed a 100% technical success rate. Ten patients (34.4%) required stent removal; the mean stenting period was 14.9 ± 5.6 (6.65 - 24.14) months. 19 patients were maintained without stent removal; the stent-maintaining period was 13.1 ± 4.3 (3.48-38.61) months. Two patients receiving left lobe grafts maintained the stents for 27.1 ± 16.2 months. In left lobe graft, the duct anastomosis position moves to the right posteroinferior side of the patient.

Conclusions: Our results suggest that the stenting period of the Rendezvous technique was longer in severe BAS than in cannulated ERCP cases. Especially in the left liver, the position of the duct anastomosis changed to the right posteroinferior of the patient. Thus the donor duct and the recipient duct are angulated, kinking worsens, and the stenting period becomes longer.

Keywords: Rendezvous technique, Biliary anastomosis stricture, Liver transplantation

**PE-344**

Prevalence of Hepatopulmonary Syndrome in Liver Transplant Candidates in the North Region of Kazakhstan

Abyalikhan Sharmenov¹, Aimbul Ashimhanova²

¹Branch of Corporate Fund University Medical Center, Kazakhstan; ²Department of Internal Medicine, Nazarbayev University, School of Medicine

Aims: Hepatopulmonary syndrome (HPS) is indicated for the liver transplantation in patients with End-Staged-Liver-Disease (ESLD). However the prevalence of the frequency of HPS among the liver transplant candidates (LTC) in Kazakhstan is unknown. There are three centers provide liver transplantation in Kazakhstan, and these centers are divided for three region: north, south and west. Each center has independent own waiting-list, that’s why the frequency of HPS in LTC is unknown. Aim of this abstract is to share the frequency of HPS in patients who are LTC in the north region of Kazakhstan.

Methods: A cross sectional study of patients with ESLD who are LTC in North region of Kazakhstan. Patients were subjected to clinical examination, laboratory investigations, pulsoxmetry, arterial blood gas measurement (≤60%). The severity of liver disease was assessed by MELD score. The diagnostic criteria for HPS were low saturation (SpO₂ ≤80%), significantly lower PaO₂, dyspnoea, platypnoea and features of portal hypertension were significantly more common in the HPS group.

Results: 70 LTC patients were enrolled in the study. 4 patients (5.7%) fulfilled the criteria for diagnosis of HPS, 3 of them female and 1 male patients. Patients with HPS showed older ages, longer duration of liver diseases, which were more severe (MELD score). Dyspnoea, cyanosis, clubbing, platypnoea, spider naevi and features of portal hypertension were significantly more common in the HPS group. In the recumbent position; patients with HPS had a significantly lower PaO₂ and showed a further fall in their PaO₂ on sitting up (orthodeoxia). One patient successfully underwent liver transplantation from cadaveric donor.

Conclusions: The prevalence of HPS among the studied group of Kazakhstan in north region liver transplant candidates is 19%. Cyanosis, clubbing, spider naevi and platypnoea–orthodeoxia are suggestive indicators of HPS. Unfortunately in our country can not provide transsternal contrast enhanced echocardiography for patients who suspected HPS.

Keywords: Hepatopulmonary syndrome, Liver transplantation, Liver cirrhosis, PaO₂

**PE-345**

Splenic Artery Steal Syndrome after Liver Transplantation

Aizhan Seitova¹, Abyalikhan Sharmenov

¹Astana Medical University JSC, ²Branch of Corporate Fund “University Medical Center” National Research Center for Oncology and Transplantology, Kazakhstan

Aims: SASS is a pathological condition complicating in 1-4% of cases after OLT. It manifests itself in the redistribution of blood flow from the celiac trunk mainly to the splenic or gastroduodenal artery in the period from 2 to 5 days after the operation. A dangerous consequence of the SASS can be a thrombosis of
the hepatic artery. Among the late complications are the dysfunctions of the biliary system.

**Methods:** From 2013 to December 2018, 49 orthotopic liver transplantsations were performed in NSCOT (Astana, Kazakhstan): 33 from a living donor (right lobe), 16 from a cadaveric. SASS was appeared in 8 cases (16.3%), 5 patients after right lobe living OLT, 3 after cadaveric OLT. All these patients presented with elevated liver enzyme levels, impaired graft function, or cholestasis. Duplex Doppler ultrasonography and celiac trunk angiography, showed a progressive decrease in hepatic arterial blood flow with an increasing RI and an increase in the flow rates of the portal vein and splenic artery.

**Results:** All this patients were treated with coil-embolization, leading to improved liver function. In the 3 patient result was achieved at the first attempt, the 5 patients needed a second embolization of the splenic artery, in one patient embolization was performed twice, after then underwent a splenectomy. From the first day after embolization, a gradual decrease liver enzymes and complete normalization on the 7th day was noted laboratory. Ultrasonography showed an increase in the rate of blood flow through the hepatic artery and a decreasing blood flow in the portal vein and splenic artery.

**Conclusions:** In conclusion, we recommend prophylactic ligation of the splenic artery for patients at risk of developing SASS. Post-transplant coil-embolization of the splenic artery corrected hemodynamic changes of SAS, but was associated with a significant morbidity.

**Keywords:** Splenic artery steal syndrome, Liver transplantation, Coil-embolization, Ultrasonography

---

**Hepatic Abscess after Ortotopic Liver Transplantation**

**Nurlan Zhappasov, Zhanat Spatayev, Abylaikhan Sharmenov**

Department of surgery, Branch of Corporate Fund “University Medical Center” National Research Center for Oncology and Transplantology

**Aims:** Hepatic abscess is a serious complication which may occur after liver transplantation. This abstract reveals the predisposing factors, treatment, and outcomes associated with hepatic abscess.

**Methods:** This abstract consist of review of all liver transplant recipients in NSCOT. From 2013 to July 2017 48 orthotopic liver transplantsations were performed in in NSCOT: 33 from a living donor (all the right lobe), 11 from a cadaveric donor. Hepatic abscess was defined as a parenchymal hepatic lesion consistent with abscess (as revealed by MRCP, ultrasonography and celiac trunk angiography), positive liver or concurrent blood cultures.

**Results:** Of 48 liver recipients, identified 3 patients (6.9%) who had experienced 4 episodes of hepatic abscess, 24-52 days after transplant. 2 patients after LDLT (right lobe), 1 patient after DDLT. Biliary reconstruction was done by duct-to-duct in all 3 cases (TTR technique in 2 case of LDLT). The predisposing factors was: bile-to-duct anastomosis stricture in 2 case (1 case due to hepatic artery stenosis), early hepatic artery thrombosis in 1 case. In 2 case was performed PTBD: in 1 case initially performed transarterial hepatic artery stenting, then PTBD. This patient still alive; 1 patient was died from sepsis. In 1 case performed transarterial fibrinolysis for 2 days (Actilyse 10-15 mg per 3 hours) with stenting, after 32 POD underwent re-transplantation from cadaveric donor, despite all of this treatment with broad spectrum antibiotics and antifungals patient was died.

**Conclusions:** Hepatic abscess is one of the main causes of morbidity after LTx that we faced. In 3 patients from 48 was occurred (6.9%), 2 patients died, 1 patient still alive. Hepatic abscess after liver transplantation may be treated successfully with percutaneous and retransplantation with broad spectrum antibiotics.
Liver Transplantation for Patient with Emergency Indications
Aidos Kulmaganbetov
National Medical Research Center, Kazakhstan

Aims: Immunosuppressive medications have many negative effects. One way of solving this is to minimize immunosuppression.

Methods: 30 liver transplantations performed in our Medical Center between 2013 and 2018: 22 – from living donor, 8 – from cadaver. Most liver transplants were performed in collaboration with SNUH (Seoul, Korea). The indications for liver transplantation (LT) were as follows: primary biliary cirrhosis – 6, hepatitis C virus (HCV) cirrhosis – 3, hepatitis B virus (HBV) cirrhosis – 20, autoimmune hepatitis – 1.

Results: In 28 recipients at the beginning immunosuppression was based on 3 components: Tacrolimus – MMF – Corticosteroids with Baziliximab on 1st and 4th operating days. All our patient’s discontinuous steroid after 6-12 month after transplantations, depending on the aetiology of liver cirrhosis. One patient finished receiving MMF 2 years after transplantation. Two patients (after living donor transplantation) received (and receive now) only Tacrolimus and had no rejection episodes. But they have appointed hormones for a week after transplantations. One patient had a conversion from Tacrolimus to Cyclosporine. She had hyperglycemia. After conversion glucose levels returned to normal.

Conclusions: Minimization of immunosuppression is a necessary goal for transplant patients. Many immunosuppressive drugs have side effects, which lead to undesirable consequences or death. Immunosuppression minimization regimes should be safe for rejection and infectious complications in liver transplant patients.

Keywords: Immunosuppression, Liver, Transplantation

Immunosuppression after Liver Transplantation
S. Kulmaganbetova, M. Domskaliev
Surgery Department, National Research Medical Center, Nur-Sultan, Kazakhstan

Aims: Immunosuppressive medications have many negative effects. One way of solving this is to minimize immunosuppression.

Methods: 30 liver transplantations performed in our Medical Center between January 2016 and January 2019: 22 – from living donor, 8 – from cadaver. Most liver transplants were performed in collaboration with SNUH (Seoul, Korea). The indications for liver transplantation (LT) were as follows: primary biliary cirrhosis – 6, hepatitis C virus (HCV) cirrhosis – 3, hepatitis B virus (HBV) cirrhosis – 20, autoimmune hepatitis – 1.

Results: In 28 recipients at the beginning immunosuppression was based on 3 components: Tacrolimus – MMF – Corticosteroids. All patients discontinuous steroid after 6-12 month after transplantations, depending on the etiology of liver cirrhosis. One patient finished receiving MMF 2 years after transplantation. Two patients (after living donor transplantation) received (and receive now) only Tacrolimus and had no rejection episodes. But they were appointed hormones for a week after transplantations. One patient had a conversion from Tacrolimus to Cyclosporine. She had hyperglycemia. After conversion glucose levels returned to normal.

Conclusions: Minimization of immunosuppression is a necessary goal for transplant patients. Many immunosuppressive drugs have side effects, which lead to undesirable consequences or death. Immunosuppression minimization regimes should be safe for rejection and infectious complications in liver transplant patients.

Keywords: Immunosuppression, Liver, Transplantation
cinoma recurrence after locoregional treatment regardless of maximum pretransplant values. Clinicians can rely on the current level of tumor markers at the time of LT.

**Table 1. Tumor markers and hazard of HCC recurrence after liver transplantation**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFP at LT &gt; 20</td>
<td>3.67 (1.86-7.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>APP, pre-LT max &gt; 300</td>
<td>1.72 (0.80-3.31)</td>
<td>0.103</td>
</tr>
<tr>
<td>APP, pre-LT min &gt; 10</td>
<td>1.23 (0.60-2.26)</td>
<td>0.480</td>
</tr>
<tr>
<td>APP, post-last LRT max &gt; 75</td>
<td>2.80 (1.36-4.99)</td>
<td>0.004</td>
</tr>
<tr>
<td>APP, pre-LT max – at LT &gt; 200</td>
<td>2.06 (1.07-3.99)</td>
<td>0.031</td>
</tr>
<tr>
<td>Duration, AFP pre-LT max – at LT &lt; 6 mon</td>
<td>1.15 (0.58-2.27)</td>
<td>0.688</td>
</tr>
</tbody>
</table>

HRs were adjusted with TNM staging, Esmond grade, pretransplant MELD score and the number of pretransplant LRT.

**Keywords:** Liver transplantation, Hepatocellular carcinoma, Tumor marker

**PE-351**

**Splenic Artery Embolization Following Liver Transplantation: Single Center Experience**

N. Yerniyazov, Baigenzhin A

National Medical Research Center, Nur-Sultan, Kazakhstan

**Aims:** Among complications after orthotopic liver transplantation (OLT) hypersplenism (thrombocytopenia, leukocytopenia, anemia) syndrome and ascites are not rare. Mainly this condition is indicated to open splenectomy. Although, it is well known for negative effects after splenectomy procedure. Recently, splenic artery embolization (SAE) has been reported as well-designed procedure and many centers are sharing their experience with effective results. In this report, we would like to present the early outcomes of SAE in 6 patients after liver transplantation, who had hypersplenism, ascites and uncontrolled hyperbilirubinemia.

**Methods:** Between January 2015 and January 2019 we performed 37 OLT: 28 from living donor (2 – left lobe, 26 – right), 9 – from cadaver. Six patients after OLT received splenic artery embolization (SAE). Before OLT 2 recipients with primary biliary cirrhosis, 4 – Hepatitis B Virus-related liver cirrhosis. Two patients after right lobe living OLT, one – cadaveric OLT. SAE in 6 cases were performed after 6 and 18 months, and just in one case it was performed soon after operation. The indications for SAE was based on clinical and ultrasonographic investigation (ascites, splenomegaly) and laboratory criteria (thrombocytopenia, when PLT<60x10^3/mm³, leukocytopenia, when WBC<2x10^3/mm³). 2 recipient has leuko-thrombocytopenia and refractory ascites, 1 – only thrombocytopenia, 3 – with uncontrolled hyperbilirubinemia. SAE was performed via a percutaneous femoral artery approach by interventional radiologists in operating room under local anesthesia. All patients has preoperative antibiotic prophylaxis and desensitize medication. After selective celiac and splenic arterial angiographies were obtained to determine the target splenic artery branches. Transcatheter splenic artery branches occlusion was performed by the deployment of embolic device.

**Results:** The size of spleen was between 8.5-12.5 cm to 17.5-22.0 cm. Patients ascites were more than 1000 ml. Total spleen embolization volume was approximately 70%. Ascites decreased after SAE in all patients. After SAE the platelets levels increased in all patients too. In one patient (who has leukocytopenia), WBS level normalized for 3 days. Uncontrolled hyperbilirubinemia decreased in 10-14 days. After SAE: 2 patients had analgesia none-needed abdominal pain, 2 – had fever (max T was 38.5°C) during 3 days. The patients were discharged 6, 8, 9 days after SAE. One patient had perisplenic abscess without fever 1 month later after discharge. Abscess was drained under ultrasound control.

**Conclusions:** SAE, although limited by the minimal cases, is a safety and effective minimally invasive methods for treatment hypersplenism and ascites of recipients after OLT. Also, it is proved in patients who have immunosuppressive condition as alternatives to open total splenectomy.

**Keywords:** Embolization, Liver, Transplantation, Hypersplenism

**PE-352**

**Pediatric Liver Transplantation in University Medical Center Astana**

Yermakhan ASSYLKHANULY, Samat ISSAKOV

HBP Surgery Department University Medical Center Astana, Kazakhstan

**Aims:** Living donor liver transplantation has become a cornerstone for the treatment of children with end-stage hepatic dysfunction, especially in Kazakhstan with low rates of organ from deceased donors. In our center, 8 pediatric living donor liver transplantations we carried out since 2014. The indications for liver transplantation in our patients were biliary atresia.

**Methods:** The mean hospitalization time of our patients was 25 days and the mean stay in the intensive care unit was 8 days. The Child-Pugh score was C in 2 of our patients, B in 5 patients, and A in 1 patient. The donor age ranged from 27 to 41 years, and the weight ranged from 62 to 78 kg, mothers being the donors in a majority of these. As most children require only a left lateral segment graft, the morbidity and risks to the donor are much less than those donating their right lobes. Living donor transplants are ideally suited to children as it allows for a
planned procedure, allows for a near optimal size graft for the child, reduces the risk for the donor, and the incidence of rejection is reduced.

Results: The main complications after pediatric liver transplantation were infections and surgical complications including (biliary complications). We encountered biliary complications in 2 of the 8 patients and we performed surgical revision due to anastomosis leakage in 1 patient. Our immune suppression protocol is based on a combination of steroid and tacrolimus.

Conclusions: Infections and biliary complications were the most common outcome occurring in children after LT.

PE-353

LDLT Program University Medical Center Astana
Samat ISSAKOV, Nurmakhan ASSYLIKANULY
Surgery, University Medical Center Astana, Kazakhstan

Aims: Liver transplantation is the only life-saving intervention for patients with end stage liver disease. LDLT donors are typically healthy adults who do not derive any medical benefit from the procedure for themselves. Donor death is the most serious complication after LDLT, with estimated mortality at 0.28 to 1.0 percent, however, the exact risk cannot be precisely quantified due to the lack of a centralized database measuring donor outcomes.

Methods: We retrospectively reviewed the medical records of 120 LDLT recipients who underwent the procedure using a right liver graft between May 1999 and September 2012 in the Department of Surgery. Donor age, sex, and the degree of hepatosteatosis were compared between the groups. Recipient age, sex, body mass index (BMI), and transplantation indications were also compared between the two groups. We measured the recipients’ Child-Turcotte-Pugh (CTP) and Model for End-stage Liver disease (MELD) scores in both groups to compare the preoperative disease severity. Although the general donor age recommendation in our institution is 16-55 years of age, the donors in this study were 16-67.

Results: The anatomical structure of the vasculature and biliary tree and liver consistency were evaluated using abdominal CT, ultrasonography, and magnetic resonance cholangiopancreatography.

Conclusions: LDLT using elderly donors could induce more serious complications and higher mortality rates than those at using younger donors. As such, careful donor selection is needed, especially with regard to assessing the condition of potential elderly donor livers. Furthermore, a large-volume and multicenter study of complications and outcomes of LDLT using elderly donor liver is required.

PE-354

Early-Onset and Bad Place Post Transplantation Lymphoproliferative Disorder (PTLD) after Liver Transplantation: Case Report

Sung Yub Jeong, Jung Jun Lee, Sung Hoon Choi

1Transplantation Center Department of Surgery, Bundang CHA Medical Center; 2HBP Surgery, Department of Surgery, Bundang CHA Medical Center, Seongnam, Korea

Post transplantation lymphoproliferative disorder (PTLD) is the most severe complication among liver transplantation recipients, the overall incidence rate is reported to be 1% to 4%. The Oncogenic Epstein-Barr virus (EBV) is the most important pathogenic driver in early-onset cases. Monitoring EBV deoxyribonucleic acid (DNA) loads in blood is widely used to detect PTLD early in many transplantation centers. We report a case of EBV positive (EBV+) diffuse large B-cell lymphoma (DLBCL) in a patient only 2 months after liver transplantation.

A 49-year-old male visited the transplantation center for a 2 month post-transplantation scheduled medical checkup. He was in poor general condition, also complained of an itching sense all over his body. A liver computed tomography (CT) detected a 2.1 cm heterogeneous mass at the hilar area of the liver and a needle biopsy confirmed the diagnosis of DLBCL. The EBV polymerase chain reaction (PCR) test level was at 25,300 copies/mL. Reduction of immunosuppression (RIS) was the first line treatment, Rituximab monotherapy followed by CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) treatment was repeated for six cycles. EBV plays a key role in very early onset PTLD like this patients cases. Therefore, EBV positive transplant recipients should continuously check blood EBV PCR levels for PTLD early detection.

PE-355

Laparoscopy-Assisted Hybrid versus Open Living Donor Right Hepatectomy: A Comparison of Surgical Outcomes

Myo Zin1,2, Incheon Kang1,2, Dai Hoon Han1,2, Kyung Sik Kim1,2, Jin Sub Choi1,2, Gi Hong Choi1,2

1Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Yonsei University College of Medicine; 2Liver Cancer Center, Yonsei Cancer Center, Severance Hospital, Seoul, Korea

Aims: Applications of minimally invasive surgery in living donor hepatectomy (LDH) is increasingly accepted in worldwide. However so far, pure laparoscopic living donor hepatectomy has only been performed at experienced large-volume transplant centers due to the concerns over donor safety. Laparoscopy-assisted (hybrid) approach has been designed to not only provide reduced small wound but also minimize the risk of technical complexity. The aim of this study is to evaluate the safety and efficacy of our laparoscopy-assisted (hybrid) living donor right hepatectomy and compare with conventional open surgery in terms of perioperative outcomes.

Methods: Between January 2013 and November 2018, total 311 Living donor right hepatectomy (LDRH) were performed at Severance Hospital. Among them, 41 robotic LDRH were excluded.
Finally, total 270 LDRH case were enrolled in this study. We divided the patients into two groups [hybrid group (n = 126) and open group (n = 144)]. Donor characteristics, perioperative surgical outcomes, postoperative complications were retrospectively reviewed between the two groups.  

Results: Total 270 LDRH were performed with zero mortality. All of the hybrid techniques were completed without any extra additional subcostal incision. Hybrid procedure was associated with a reduction in operative blood loss (258 vs 307,  \( P = 0.032 \)); shorter hospital stay (8.5 vs 10.8,  \( P = 0.01 \)) There was no significant difference between two groups in donor characteristics, the incidence of postoperative complications greater than or equal to Clavien-Dindo class III, operation time, transfusion rate, and postoperative liver function tests, recipient outcomes.  

Conclusions: Donor safety is major cornerstone in living donor liver transplantation. Our experience suggests that hybrid approach in living donor right hepatectomy appears to be a safe and feasible procedure. It could be considered an alternative minimally invasive approach.  

Keywords: Minimally invasive surgery, Laparoscopy assisted living donor right hepatectomy, Hybrid living donor hepatectomy, Donor safety

---

**PE-356**

Tablet or Capsule Form Combined with Tacrolimus after Liver Transplantation: A Prospective Randomized Trial

Nyamsuren Ganbileg\(^1\), Jong Man Kim\(^1\), Gyu-Seong Choi\(^2\), Jae-Won Joh\(^2\)

\(^1\)Department of Surgery, National Cancer Center in Mongolia, Ulan Bator, Mongolia; \(^2\)Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

**Backgrounds:** Tablet and capsule forms have advantages and disadvantages in the market. Generally, the tablet form (500 mg) of mycophenolate mofetil (MMF) is more convenient for drug ingestion and more cost-effective than the capsule form (250 mg). We examined the efficacy and safety of MMF in its different forms combined with tacrolimus in liver transplant recipients.

**Methods:** A randomized controlled trial was performed to compare the efficacy and safety between the tablet form of MMF (tablet group) and the capsule form of MMF (capsule group) in liver transplant patients. One hundred sixteen patients were enrolled in present study from 2014 to 2017. Fifty-six patients in the full-analysis set (FAS) population were in the capsule group and 60 were in the tablet group. The primary endpoint was incidence of biopsy-proven acute rejection (BPAR) by 24 weeks after liver transplantation (LT). Secondary endpoints were patient survival, serum creatinine level, and adverse events.

**Results:** In the per-protocol (PP) population, 45 patients were in the tablet group and 49 were in the capsule group. There were no statistically significant differences in MMF dose, mycophenolic acid trough level, and tacrolimus trough level between the two groups. The incidence of BPAR at 24 weeks after randomization was 6.7% in the tablet group and 6.1% in the capsule group (\( P = 0.627 \)). All patients with BPAR responded well to steroid pulse therapy and increased tacrolimus. Serum creatine level and eGFR were not different between the two groups. The incidence of serious adverse events was 7.2% in the tablet group and 7.6% in the capsule group, and none were related to formulation. There was no significant difference in incidence of discontinuations or serious adverse events between the two groups.

**Conclusion:** The present study suggests that the new tablet formulation can be a useful treatment option to maintain a consistent systemic exposure level of MMF, which may help reduce graft failure in liver transplant patients.

---

**PE-357**

Splenorenal Shunt Occlusion Associated to Portal Vein Thrombosis after Liver Transplantation: Report of Two Cases and Literature Review

Thazin Soe Wai\(^1\), Lyo Min Kwon\(^2\), Jin Woo Choi\(^3\), Jin Wook Chung\(^2\)

\(^1\)Department of Radiology, Yangon General Hospital, Myanmar; \(^2\)Department of Radiology, Seoul National University Hospital, Korea

**Aim:** To report and assess the outcome of splenorenal shunt (SRS) occlusion associated to portal vein thrombosis (PVT) after liver transplantation.

**Background:** PVT is one of complications (1-3%) after liver transplantation. It can significantly reduce graft outcome and patient survival. SRS that may divert portal blood flow to the systemic circulation, attribute to reduced hepatic perfusion, portal vein compromise and PVT.

**Method:** From October 2018 to February 2019, two patients who recently underwent liver transplantation presented PVT and large SRS (41/F and 58/M). Portal venography and mechanical thrombectomy were performed through trans-splenic approach. Delayed retrograde SRS occlusion were performed through trans-splenic approach using vascular plugs. Outcomes and complications were assessed by Doppler ultrasound and serum liver enzyme levels.

**Result:** Venography revealed total thrombotic occlusion of main portal vein and majority of flow drained through SRS to systemic circulation. Thrombectomy was successfully performed and post-venography showed patent portal flow, but still majority of flow drained into SRS. Delayed retrograde SRS occlusion were successfully performed using vascular plugs. Follow up Doppler US or CT examination of these two patients showed patent portal vein. Liver enzymes were gradually normalized. Both patients discharged without any complication nor further treatment.

**Conclusion:** SRS occlusion is effective and safe procedure for portal vein compromise after liver transplantation.
PE-358

3D-Laparoscopic Surgery in Difficult Localizations of Echinococcosis Cysts of the Liver
Kuttymuratov Gani, Rysmakhanov Myltykbai, Mussin Nadiar
Aktobe Medical Center, Department of Surgery and Transplantation, Kazakhstan

Aims: To improve results and reduce the trauma of surgical intervention in patients with liver echinococcosis

Methods: In our clinic, for the first time in the Republic of Kazakhstan, a 3D-laparoscopic technique was used to remove hydatid cyst in a male patient, aged 56 years. The indication to use of 3D-laparoscopy for the purpose of echinococcosis was the inaccessible localization of the liver cyst. According to laboratory data, ultrasound and CT, the cyst was solitary, measuring up to 6.5 cm in diameter, with chitinous membrane and located in segment 8 of the liver. Laparoscopy was performed according to standard methods under endotracheal anesthesia. We used 4 troacars—two for 12 mm and two for 10 mm. After the cyst was identified, the area of the intended puncture was covered with napkins moistened with hypertonic NaCl solution. Cyst puncture was performed with a needle, while holding the cyst wall with a clamp. After dissecting the fibrous capsule, the entire chitinous membrane of the cyst was evacuated with a vacuum aspirator. The residual cavity of the cyst was treated with a 25–30% NaCl solution with an exposure of 15 minutes. The use of 3D-laparoscopic techniques for removal of the difficult approaching cysts of the liver (7-8 segments) was the inaccessible localization of the liver cyst. According to standard methods under endotracheal anesthesia. We used 4 troacars—two for 12 mm and two for 10 mm. After the cyst was identified, the area of the intended puncture was covered with napkins moistened with hypertonic NaCl solution. Cyst puncture was performed with a needle, while holding the cyst wall with a clamp. After dissecting the fibrous capsule, the entire chitinous membrane of the cyst was evacuated with a vacuum aspirator. The residual cavity of the cyst was treated with a 25–30% NaCl solution with an exposure of 15 minutes. The revealed cystobiliary fistulas were coagulated. The drainage was placed to the subhepatic space.

Results: The postoperative period was uneventful, without complications. Drainage was removed on the 3rd day after operation. Control ultrasound was without pathological changes. The patient was discharged on the 5th day after surgical treatment.

Conclusions: The use of 3D-laparoscopic techniques for removal of the difficult approaching cysts of the liver (7-8 segments) with strict adherence to the principle of aparsity is the most effective and promising method of surgical treatment of liver echinococcosis.

Keywords: Liver, 3D-Laparoscopic, Echinococcosis, Cystectomy

PE-359

Surgery-Related DIC Predicts the Severity of Complication after Major Hepatobiliary Pancreatic Surgery
Akhmet Seidakhmetov1, Yuki Imaoka1, Masahiro Ohira2, Koki Sato1, Kenichiro Uemura1, Shintaro Kuroda1, Hiroyuki Tahara1, Kentaro Ide1, Tsuyoshi Kobayashi1, Hideki Ohdan1
1Department of Gastroenterological and Transplant Surgery, Graduate School of Biomedical and Health Sciences, Hiroshima University, Japan
2Division of Regeneration and Medicine, Medical Center for Translational and Clinical Research, Hiroshima University Hospital, Department of Surgery, Graduate School of Biomedical and Health Science, Hiroshima University, Japan

Aims: The rate of postoperative morbidity including infectious complications remains high after major hepatobiliary pancreatic (HBP) surgery. Although surgery-related disseminated intravascular coagulation (DIC) occurs in some cases, the significance of surgery-related DIC has not been elucidated in HBP surgery. The objective of this study was to evaluate the influence of surgery-related DIC on the severity of complications after HBP surgery.

Methods: We compared the baseline characteristics and complications among the patients with and without surgery-related DIC on postoperative day 1 (POD 1) after HBP surgery between 2010 and 2018. The severity of complications was assessed using the Comprehensive Complication Index (CCI).

Results: We analyzed the records of 100 patients with hepatectomy in two or more segments, hepatectomy with biliary tract reconstruction, and pancreaticoduodenectomy. The DIC group (surgery-related DIC on POD 1) was characterized by a longer operation time, an increased volume of blood loss, and higher levels of liver enzymes. The DIC group exhibited significantly elevated rates of surgical site infection, sepsis, prolonged intensive care unit stay, more frequent blood transfusions and higher CCI. Furthermore, surgery-related DIC on POD 1 was an independent risk factor for the development of severe complications, as indicated by a high CCI score (≥40).

Conclusions: Surgery-related DIC on POD 1 was an independent predictive factor for the development of severe complications after major HBP surgery.

Keywords: DIC, HBP surgery, complication

PE-360

Anterior Approach for Right Hepatectomy and Right Anterior Sectionectomy with Hanging Maneuver for Large Hepatocellular Carcinoma: A Single-Center Experience in Vietnam
Thanh Van LE, Hieu Trung LE, Quang Van VU, et al
108 Military Central Hospital, Hanoi, Vietnam

Aims: Right hepatectomy and right anterior sectionectomy for large hepatocellular carcinoma via the anterior approach without prior liver mobilization is an accepted technique and the liver hanging maneuver facilitates this procedure. Hepatic parenchymal transection remains a critical part of this operation during which excessive blood loss can occur. Control of blood loss is important in hepatectomy as excessive bleeding and blood transfusion are associated with increased postoperative morbidity/ mortality rates and compromised long term oncological outcomes in these patients.

Methods: To report the surgical and preliminary outcomes of major right hepatectomy and right anterior sectionectomy for...
large hepatocellular carcinoma (HCC) using the anterior approach with hanging maneuver in single center in Vietnam. In patients who had large HCC (over 10 cm in size) at the right lobe of liver and underwent hepatic resection such as right hepatectomy or right anterior sectionectomy, the technique of anterior approach with the liver hanging maneuver was used. All consecutive patients who underwent elective right hepatectomy or right anterior sectionectomy in our center using this technique from March 2014 to July 2016 were retrospectively studied. This study aimed to describe this technique and report the preliminary outcomes.

**Results:** Twenty one patients with hepatitis B-related hepatocellular carcinoma (HCC) with cirrhosis underwent the technique for right hepatectomy and right anterior sectionectomy using the anterior approach with the liver hanging maneuver. The mean blood loss, liver parenchymal transection time and operation time were 280.3 ± 72.6 ml (SD), 49.3 ± 8.1 min, and 291.7 ± 58.2 min, respectively. No patients developed postoperative bleeding or bile leak. There was no 90-day mortality.

**Conclusions:** To achieve complete anatomic hepatectomy in a large hepatocellular carcinoma (HCC), hepatic transection through an anterior approach is required. Liver hanging maneuver is a useful procedure for transection of an adequately cut plane in anatomical liver resection. It may reduce intraoperative bleeding and transection time, and it caused no major complications and mortality.

### Keywords
- Hepatectomy
- Hepatocellular carcinoma

---

**PE-362**

**Extensive Liver Resections for Alveococcosis**

Surov Edir, Bebezov Bakhadyr, Murzaliev Erlan, Umetaliev Tilek

Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

**Aims:** to evaluate the results of extensive liver resections for alveococcosis.

**Methods:** For the period from April 2009 to August 2018. 398 patients with liver alveococcosis were treated. 350 patients from 398 were operated, 167 of them underwent extensive liver resections (47.7%). The average duration of inpatient stay is 16.5 ± 0.9 bed-days.

**Results:** 167 patients had 278 complications: mechanical jaundice - 64, cavernous forms of alveococcosis - 35, germination in neighboring organs (lung, kidney, diaphragm, stomach, pancreas, hepatoduodenal ligament, large intestine, adrenal gland) - 67, bilobar lesion - 97, MTS in lungs - 7, MTS to the brain - 3, MTS to soft tissues - 3, hepato-bronchial fistula 2. There were 167 (100%) extensive liver resections: right-sided hemihepatectomy 83 (47.3%), of which 3 were with bile duct resection, 11
The Liver Alveococcosis Surgeries with Inferior Cava Vein and Portal Vein Invasions

Bebezov Bakhadyr, Surov Edir, Umetaliev Tilek, Mamashhev N. Dj.
Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

Aims: to evaluate the results of surgical treatment of the liver alveococcosis with the IVC and portal vein invasions.

Methods: We analyzed the results of treatment of 220 patients with liver alveococcosis for the period from April 2009 to March 2015. All these patients received treatment in The Surgical Gastroenterology and Endocrinology Department of the National Hospital under the MoH of the Kyrgyz Republic. In 48 (21.8%) patients, alveococcosis was sprouted to the IVC and caval gates and portal vein, depending on that patients were divided into two groups with lesions of the IVC and the portal vein. The average age was 35.8±11.4 years. The ratio of males / females is 18/30.

Results: 18 (90%) liver resections were performed on patients with liver alveococcosis. Extensive liver resections - 8, three of them segments resection - 1, RHHE - 4, RHHE with atypical resection S III - 1, ELHHE -2. Atypical liver resections - 10 of them are segmentectomy - 9 and bisegmentectomy – 1. The maximum blood loss was 1200 ml, the minimum was 200 ml. 13 (65%) patients were operated radically. Palliatively7 (35%) patients, 2 of them percutaneous transhepatic cholangiostomy. Postoperative complications occurred in 2 (10%) patients in the form of bile leakage.

Conclusions: Rural residents more often get sick with this disease, and town people who are engaged in hunting and members of their families. A high percentage of complicated forms of the disease among children is 50%, which requires carrying out seasonal at least twice a year, household rounds and instrumental research methods (ultrasound) of children and adults from unfavorable regions of the Republic for early diagnosis of alveococcosis. The only and radical method of treatment is liver resection within healthy tissues.

Keywords: Liver resections, Alveococcosis, IVC, Portal vein invasion
Developing a Preoperative Serum Metabolome-Based Recurrence-Predicting Nomogram for Patients with Resected Pancreatic Ductal Adenocarcinoma

Seoung Yoon Rho1, Sang-Guk Lee2, Minsu Park3, Jinae Lee4, Sung Hwan Lee5, Ho Kyoung Hwang6, Min Jung Lee7, Young-Ki Park8, Woo Jung Lee9, Chang Moo Kang1

1Surgery, Yonsei University College of Medicine, Republic of Korea, 2Laboratory Medicine, Yonsei University College of Medicine, Republic of Korea, 3Biostatistics Collaboration Unit Yonsei University College of Medicine, Republic of Korea, 4Systems Biology, University of Texas MD Anderson Cancer Center, USA, 5Yonsei Proteome Research Center and Integrated OMICs for biomedical science, Yonsei University College of Life Science and Biotechnology, Republic of Korea

Aims: The metabolome represents the final stage in the “omics” cascade and is may be the closest phenotype to the biological behavior of cancer. Thus, we investigated potential clinical applications of preoperative serum metabolomes in predicting recurrence in patients with resected pancreatic cancer.

Methods: From November 2012 to June 2014, patients who underwent potentially curative pancreatectomy for pancreatic ductal adenocarcinoma were examined. We evaluated the clinical application of preoperative serum metabolomes in predicting cancer recurrence and the relationships between metabolomes and tumor markers to propose a nomogram.

Results: Among 57 patients, 32 were men; Forty-two patients had pancreatic head cancers. The 57 patients could be clearly categorized into two main clusters using 157 preoperative serum metabolomes. Patients within cluster 2 showed early tumor recurrence compared with those within cluster 1 (P = 0.034). A nomogram was developed for predicting the probability of early disease-free survival in patients with resected pancreatic cancer. Preoperative cancer antigen (CA) 19-9 levels and serum metabolomes PC.aa.C38_4, PC.ae.C42_5, and PC.ae.C38_6 were the most powerful preoperative clinical variables to predict 6-month or 1-year cancer recurrence-free survival after radical pancreatectomy, with Harrell's concordance index of 0.823 (95% CI: 0.750-0.891) and integrated area under the curve of 0.816 (95% CI: 0.736-0.893).

Conclusions: Patients with resected pancreatic cancer could be categorized according to their different metabolomes to predict early cancer recurrence. Preoperative detectable parameters, serum CA 19-9, PC.a.a.C38_4, PC.ae.C42_5, and PC.ae.C38_6 were the most powerful predicting factors for early recurrence of pancreatic cancer.

Is Laparoscopic Liver Resection for Hepatocellular Carcinoma Safe for Obese Patients?

Youngin Yoon, Ki-Hun Kim

Division of Hepatobiliary Surgery and Liver Transplantation, Asan Medical Center, Republic of Korea

Aims: Obesity is generally reported to increase the risk of surgical complications. Data on the perioperative outcomes of laparoscopic liver resection (LLR) in patients with obesity are scarce. The purpose of this study were to analyze the outcomes of obese patients undergoing LLR for HCC and to compare these to the outcomes of obese patients undergoing open liver resection (OLR).

Methods: We reviewed medical records of patients with HCC who underwent liver resection between July 2007 and April 2016 at our center. LLR was performed in 100 obese patients, while OLR was performed in 807 obese patients. For group comparisons, 1:2 PSM was used with covariates of baseline characteristics, including tumor characteristics and surgical liver resection procedures.

Results: After PSM, there were 69 and 138 patients in the LLR and OLR groups; The both group included 46 (66.7%) and 94

Laparoscopic Repeat Liver Resection: Short-Term Outcomes

Yang Won Nah, Jin A Kwon, Hyung Chol Choi

Department of Surgery, Ulsan University Hospital, Republic of Korea

Aims: Laparoscopic liver resection (LLR) is now accepted as a primary tool of surgery for many liver tumors including hepatocellular carcinoma (HCC) and metastatic liver tumors. Repeat LLR (R-LLR), however, is performed far less frequently. So the authors conducted this study to evaluate the short-term outcome of R-LLR.

Methods: We reviewed a prospectively collected database of 100 patients who underwent laparoscopic liver resections (LLR) from Aug 2008 to Oct 2018. Data of 10 patients undergoing R-LLR were analyzed and compared to 1) the primary LLR group (P-LLR, n = 90) and 2) repeat open liver resection group (R-OLR, n = 20), that was performed during the same period for almost the same indications.

Results: There was no perioperative mortality in any of these 120 patients. 10 R-LLR’s were performed for HCC (5), colorectal liver metastasis (3), prostatic cancer liver metastasis (1) and liver cyst (1). Open conversion rates were 20% for R-LLR and 3% for P-LLR (P = 0.077). Between the repeat and primary LLS groups, there was no significant difference in operative time, intraoperative bleeding amount, intraoperative transfusion rate, length of stay (LoS) and postoperative complication rates. When compared R-LLS group to R-OLR group, operative time and length of stay were different significantly, favoring laparoscopic approach for repeat liver resection.

Conclusions: Repeat liver resection can be done by laparoscopic approach safely and with shorter operative time and length of stay than by open approach in selected patients. More experiences are needed to define the role of repeat-LLR for recurrent liver tumors.
Using of Wearable Recording Technology for Surgical Training Video in Living Donor Liver Transplantation

Jeong-Moo Lee, Kyung-Suk Suh, Suk Kyun Hong, Jae-Hyung Cho, Nam-Joon Yi, Kwang-Woong Lee
Department of Surgery, Seoul National University Hospital, Republic of Korea

Aims: As surgical video recording technology has developed, trainee education using educational video has been made. In case of laparotomy, video recording system using a surgical video crane has been introduced and many surgeons present own video in congress or society meetings. However, the view in the surgical field is different from that of the surgical video. In addition, when the first assistant or operator concentrates the focus on the field, it is difficult to actually capture what their hands are doing. In other words, recorded video has a limitation in terms of education because it does not carry all the role of the participant.

Methods: A head mount was used to fix the camera on the operating surgeon's head. The recorded video was subsequently edited and used as a teaching tool. The procedure recorded were recipient hepatectomy, hepatic vein anastomosis, portal vein anastomosis, hepatic artery anastomosis, bile duct anastomosis. Each video clip were edited for trainee education including indicator, subtitles and narration.

Results: The recorded video clips were high quality, which allowed for zooming and visualization of the surgical anatomy clearly. The camera can be mounted on the surgeon's head, so we could get a view of surgeons or 1st assistant. The trainees were able to perform image training through video before entering the surgery and showed a little more adaptation to surgery.

Conclusions: Head-mounted action camera video recording system is a good model for making high quality, educational video module, and can be a useful teaching tool in living donor liver transplantation surgery.

Robotic Simultaneous Resection for Colorectal Liver Metastasis: Feasibility for All Types of Liver Resection

Jonathan Navarro, Incheon Kang, Gi Hong Choi, Byung Soh Min
Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: Laparoscopic approach is increasingly utilized in simultaneous colorectal and liver resection (SCLR) for colorectal cancer with liver metastasis. However, this approach is technically challenging, hence not widely adopted. The robotic surgical system could potentially overcome this problem. Thus, we aim to describe the feasibility and outcomes of robotic SCLR for colorectal carcinoma with liver metastasis using the da Vinci Surgical System.

Methods: The medical records of 12 patients who underwent robotic SCLR for colorectal cancer with liver metastasis between January 2010 and September 2018 were prospectively reviewed.

Results: Liver resections included 2 right hepatectomy, 1 left hepatectomy, 1 left lateral sectionectomy, one segmentectomy of S3 and wedge resection (segment 7), 1 caudate lobectomy, 1 associated liver partition and portal vein ligation for staged hepatectomy, and 5 wedge resections (segments 4, 5, 6, 7, and 8). Colorectal procedures included 7 Low anterior resection, 2 anterior resection, 2 right hemicolectomy, and 1 left hemicolectomy. The mean operative time was 449±205.1 minutes, blood loss of 274.3±210.0 ml, and length of hospital stay was 12±6.6 days. No conversion to laparotomy. Liver resection-related complications included two liver abscesses (Clavien-Dindo classification, one grade II and one grade III) and one ascites (grade I), whereas colorectal resection-related complications included one anastomosis leak (grade III) and one superficial wound infections (grade II). There was no reported 30 days mortality. Overall survival and disease-free survival was 75.2 and 47.1 months, respectively.

Conclusions: Robotic SCLR for colorectal neoplasm with liver metastasis can be performed safely even in cases requiring major liver resections.

Parenchymal Preserving Hepatectomy in Perihilar Cholangiocarcinoma

Incheon Kang, Gi Hong Choi
Department of Surgery, Yonsei University College of Medicine, Republic of Korea

Aims: Despite the surgical advancement of perihilar cholangiocarcinoma (PHCC), mortality is still high owing to postoperative liver failure (POLF). This study aimed to evaluate the surgical outcome of parenchymal preserving hepatectomy (PPH) in treating patients with insufficient future remnant liver volume after hepatectomy.

Methods: Between January 2000 and December 2018, 326
patients underwent surgical resection of PHCC at Severance Hospital. Of these patients, 89 (27.3%) were predicted to have an average future remnant liver volume is less than 25~30% after hepatectomy in preoperative image. These patients were divided into two groups by different surgical strategy: one group underwent portal vein embolization (PVE) before major hepatectomy [PVE group, n = 69], and another group underwent one stage PPH without PVE in consideration of the risk of postoperative morbidity and mortality [PPH group, n = 20]. Perioperative outcome and long-term survival were compared between two groups.

**Results:** PVE were performed in case of advanced hilar bile duct involvement than PPH group (P = 0.002) Time to surgery and intraoperative blood loss was significantly lower in PPH group (P = 0.015 and P = 0.027, respectively) No meaningful POLF had developed in PPH group. Conversely, hospital death from POLF occurred in 8 patients (11.5%) in PVE group. (P < 0.001) Disease free survival and overall survival rates were not statistically different between two groups (P = 0.882 and P = 0.191, respectively)

**Conclusions:** PPH procedures showed acceptable curability, morbidity and mortality rates. PPH could be an alternative option in selected patients with insufficient liver volume as well as high risk of postoperative morbidity and mortality for treating PHCC. Further following study should be required.

---

**PE-371**

**Analysis of Proximal Ductal Resection Margin in Patients with Hilar Cholangiocarcinoma**

**Woo Young Youn, Jae Hoon Lee, Song Cheol Kim, Dae Wook Hwang, Ki Byung Song, Jae Hoon Lee, Woo Hyoung Lee, Jaewoo Kwon**

Department of HPB Surgery, University of Ulsan College of Medicine, Asan Medical Center, Korea, Republic of Korea

**Aims:** Ductal resection margin status for hilar cholangiocarcinoma is an established prognostic indicator. survival following resection in patients with positive ductal margins has generally been deemed unsatisfactory.

**Methods:** All consecutive patients who underwent curative intent resection for a histologically confirmed perihilar cholangiocarcinoma at our institution between 2005 and 2015 were identified from a prospectively collected database. Proximal margin was divided into negative (R0, n = 226), positive with BilIN3 (R1 Bil3, n = 10), positive with invasive cancer (R1, n = 53). Frozen biopsy examination of proximal bile duct margin revealed BilIN3 in 7 patients. Additional resection was performed in 4 of 7 patients. After additional resection margin negative was achieved in only 3 patients

**Results:** In terms of survival, the difference between R1 and R0 after additional resection and the primary R0, there was no noticeable trend in survival, recurrence and recurrence types.

**Conclusions:** Although the cases were small and did not show any clinical significance, our study found that proximal duct margin with BilIN3 did not show adverse effect on survival and recurrence. So It is assumed that further additional resection of positive margin with BilIN3 does not yield much benefit to the survival or recurrence.

---

**PE-372**

**Radical Excision for Huge Hepatic Cystic Neoplasm by Totally Laparoscopic Liver Resection: A Case Report**

**Bo-Hyun Jung, Jeong-Ik Park**

Department of Surgery, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Republic of Korea

**Aims:** Laparoscopic liver resection (LLR) has become increasingly popular and reliable in the field of hepatobiliary surgery. However, the procedure has demand the technique and experience of the surgeon on both laparoscopic and open liver surgery. Because of the lack of space and difficulty for handling of liver, LLR is hard to apply for huge hepatic mass. I introduce the case of LLR for huge hepatic cystic neoplasm in this case.

**Methods:** A 25-year-old male who had developed right upper abdominal pain with 2 weeks had revealed 15*8 cm sized huge and multiple cystic neoplasms with multiple internal septation focal enhancing portion located in segment 4, 5 and 6 by imaging studies. His body mass index (BMI) revealed 37.4 kg/m², but he has no comorbidity except obesity and no abnormality on laboratory findings.

**Results:** He underwent totally laparoscopic S4b/5s/5d trisegmentectomy with cholecystectomy. Operation time was 445 minutes and intraoperative estimated blood loss was 970mL. The retrieved specimen through suprapubic incision was measured by 18.0*17.0*9.5 cm and 880 gm. Final pathology revealed pleomorphic sarcoma, most-likely leiomyosarcoma which was 16.0*11.0*9.0 cm with FNCLCC grade 3 and no involvement for resection margin. He discharged at postoperative 9th day without problem.

**Conclusions:** Primary hepatic leiomyosarcoma is very rare soft-tissue tumor. Even though rarely been reported in this tumor, hepatic resection is associated with encouraging rates of overall and disease-free survival. When huge hepatic cystic neoplasm is hard to distinguish between benign and malignancy before operation, LLR can be a choice for diagnosis and treatment like this case.

---

**PE-373**

**Optimum Timing of Emergency Cholecystectomy for Acute Cholecystitis**

**Kasenov T, Baimukhamedov J, Azbergenov N.**

KazNMU named after S.D. Asphendiyarov, Kazakhstan
Aims: Cholecystectomy on index admission for acute cholecystitis is associated with improved patient outcomes. The timing of intervention is mainly driven by service provision. This population-based cohort study aimed to evaluate timing of emergency cholecystectomy in Almaty.

Methods: Data from all consecutive patients undergoing surgery for acute cholecystitis on index admission in Almaty from 2010 to 2016 were captured from the Hospital Episodes Statistics database. Data were analysed based on whether patients underwent surgery 0-3 days, 4-7 days or 8 days from admission. Outcome measures were rate of post-operative biliary complications, conversion to open and length of stay.

Results: Two thousand three hundred and seventy-six patients underwent emergency cholecystectomy. 64.6% of patients underwent surgery between days 0 and 3 of admission, 24.3% between days 4-7 and 11.0% had surgery after day 8. Patients undergoing early surgery had significantly reduced rates of intra-operative laparoscopic conversion to open (0-3 days: 3.6%; 4-7 days: 4.0%; ≥8 days 4.7%, p<0.001), post-operative Endoscopic Retrograde Cholangio-Pancreatography (0-3 days: 1.1%; 4-7 days: 1.5%; ≥8 days 1.9%, p<0.001) and bile duct injury (0-3 days: 0.6%; 4-7 days: 1.0%; ≥8 days 1.8%, p<0.001). Early cholecystectomy was also associated with a shorter post-operative length of stay (LOS) [0-3 days group: median post-operative LOS 3 days (IQR: 1-8)]; 4-7 days group: 3 days (IQR 2-6); ≥8 days group: 4 days (IQR 2-9) (p<0.001)]. High-volume centres undertook a significantly greater proportion of cholecystectomies within 3 days of admission (high-volume: 63.8%; medium-volume: 64.8%; low-volume: 61.2%). In multivariate analysis greater time to surgery was independently associated with increased risk of post-operative Endoscopic Retrograde Cholangio-Pancreatography and bile duct injury.

Conclusions: Early cholecystectomy within 3 days of admission reduces intra-operative conversion, post-operative biliary complications and length of stay. Centres undertaking the greatest numbers of emergency cholecystectomies perform a larger proportion within 3 days of admission.

Keywords: Cholecystitis, Acute, Emergency cholecystectomy

The Immediate Results of Surgical Treatment of Liver Hemangiomas

Marshankulov Rezuan, Umetaliev Tilek, Bebezov Bakhadyr, Sakmamtol Toolukbek
Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

Aims: The aim of the work is to evaluate the results of surgical treatment of liver hemangiomas.

Methods: The work is based on the analysis of liver resection results of 19 patients, 13 women (68.4%) and 6 men (31.6%), the ratio is 2: 1, the age ranged from 16 to 69 years. Disease duration was from 1 month to 15 years, it’s the period when they had signs of the disease, which consisted of the appearance of weakness, heaviness and dull pain in the right hypochondrium and epigastric region. Ultrasound examinations (19 patients) and CT scans (19 patients) of the liver were performed in patients and several patients with giant hemangiomas of the liver underwent a MSCT (3 patients) to detect compression of the vessels and bile ducts of the liver.

Results: As a result of the study, the right lobe of the liver was affected in 11 patients (57.8%), the left lobe was affected in 8 patients (42.1%), 3 or more affected segments were detected in 10 (52.6%) patients, the lesion 2 segments in 7 (36.8%) patients and 1 segment damage in 2 (10.5%) patients. Of these, 4 (21%) patients underwent right-sided hemihepatectomy, left-side hemihepatectomy was performed in 1 (5.2%) patient, 15 (78.9%) patients underwent atypical liver resection, including a lobectomy was performed in one patient and 2 (10.5%) patients had an exploratory laparotomy. The maximum blood loss was about 1.5 liters; the minimum blood loss was 200 ml. Nine patients underwent simultaneous operations. As a result of the histological conclusion, cavernous hemangioma was confirmed in 15 (78.9%) patients, in 1 (5.2%) of the patient - the capillary liver hemangioma, in 1 (5.2%) of the patient data for large-se scale cirrhosis of the liver, in 1 (5.2%) of the patient data for hepatocellular adenoma, in 1 (5.2%) of the patient chronic granulomatous inflammation. 6 patients had comorbidities such as cholelithiasis, hypertension and diabetes mellitus.

Conclusions: Thus, liver resection is an effective and affordable method for the treatment of liver hemangiomas. Giant hemangiomas, fast-growing hemangiomas and hemangiomas with the threat of rupture are absolute indications for surgical treatment. Ultrasound, CT and MSCT of the liver in the preoperative period allows to determine the volume of the intended operation.

Keywords: Results of surgical treatment, Liver hemangiomas, Liver resections, CT

Surgical Treatment of the Liver Alveococcosis, Complicated by the Mechanical Jaundice

Ryspekov Bolot, Surov Edir; Umetaliev Tilek, Bebezov Bakhadyr
Department of Hospital Surgery, Kyrgyz-Russian Slavic University, Kyrgyzstan

Aims: to evaluate the results of surgical treatment of liver alveococcosis complicated by obstructive jaundice.

Methods: 69 patients’ case histories undergoing inpatient treatment were analyzed at the Department of Surgical Gastroenterology and Endocrinology of the National Hospital under the Ministry of Health of the Kyrgyz Republic. During the period 2009 to 2019, 440 patients received surgical treatment for alveococcosis of the liver, 69 of them (15.68%) were patients with complicated mechanical jaundice form of alveococcosis, 38 of them (55.07%) were women and 31 (44.93%) were men. 30 patients (43.6%) had signs of the disease for at least 1 year, from 1 month to 15 years. Surgical treatment was planned in 15 (21.2%) patients, 20 (29.0%) patients underwent emergency surgery, and 34 (49.3%) patients underwent delayed surgery. The immediate results of surgical treatment of alveococcosis complicated by jaundice were analyzed in 38 patients. A lobectomy was performed in 19 patients (50%), a hemihepatectomy in 13 patients (34.2%), a segmentectomy in 6 patients (15.8%). Ultrasound, CT and MSCT of the liver were performed in all patients. Alveococcosis was confirmed by histological examination in 36 patients (94.7%).
Men. The average age of patients was 37.3 ± 3 years. All patients undergoing treatment were given a blood test for liver tests, the results of which characterized the pattern of obstructive jaundice.

Results: To improve the general condition of patients, percutaneous-transhepatic drainage of the bile ducts for the purpose of decompression was performed, to resolve questions about the volume of the operation and also as a stage of preoperative preparation. After 2-3 weeks, in 90% of patients laboratory values reached the normal range, which allows for radical surgery. The choice of tactics and the volume of the operation depends on the size, localization of alveolar nodes. 69 patients with alveococcus of the liver complicated by obstructive jaundice, 6 of them (8.7%) underwent liver resections, with hepaticocholedochitis resection with hepatojejunostomy. 6 (8.7%) extensive liver resections were performed. 2 (2.9%) atypical resections of the liver were performed, 2 (2.9%) related liver transplantation (India), Retropertoneal operations. Of these, 12 women (57.1%), men 56 (42.9%) aged 16 to 62 years old, the average age of patients was 33.2 ± 9 years. The average level of bilirubin at admission was 252.4 ± 35 µmol max-543, min- 124. In the postoperative period, the improvement in the general condition was observed already for 2 days, and the average level of bilirubin in the postoperative period was 149 ± 24 mmol/l with a tendency to decrease with further dynamic, and in the subsequent and dispensary observation.

Conclusions: Percutaneous transhepatic cholangiostomy is one of the widely spread, widely used and effective methods of surgical treatment of patients with mechanical jaundice of alveococcal genesis, which allows to achieve adequate drainage of the bile ducts. At the moment, the operation is one of the stages of treatment of patients with alveococcus of the liver. In the first case, this is preparation before a radical liver resection, in the second case, it is a palliative operation in inoperable patients who are prescribed to have a liver transplant.

Keywords: X-ray, Endobiliary methods, Liver alveococcus, Mechanical jaundice

Table 1: Summary of retrospective analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Method</th>
<th>Number of Patients</th>
<th>Average Age (years)</th>
<th>Average Value of Bilirubin (µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Conventional Kasai</td>
<td>24</td>
<td>37.3 ± 3</td>
<td>252.4 ± 35</td>
</tr>
<tr>
<td>2</td>
<td>Laparoscopic Kasai</td>
<td>45</td>
<td>33.2 ± 9</td>
<td>149 ± 24</td>
</tr>
<tr>
<td>3</td>
<td>Minimally invasive Kasai</td>
<td>22</td>
<td>37.3 ± 3</td>
<td>124 ± 9</td>
</tr>
</tbody>
</table>

The best option for surgical treatment of alveococcus of the liver complicated by obstructive jaundice is decompression of the bile ducts, liver resection performed within healthy tissues. In cases of impossibility of carrying out a radical operation, it is necessary to carry out biliary tract decompression in patients with obstructive jaundice, which will improve the quality of life of patients during the period of preparation for a liver transplantation.

Keywords: Liver alveococcus, Mechanical jaundice, ALT, AST

Advantages of Kasai Procedure through Minimally Invasive Approach in Children with Biliary Atresia

Razumovskiy A., Ratnikov S., Degtyareva A., Kulikova N., Imakhanova M.

Pirogov Russian National Research Medical University, Moscow, Russia; Filatov Municipal Children’s Hospital, Moscow, Russia

Aims: To compare early and long-term results of different surgical interventions in children with biliary atresia.

Methods: Retrospective analysis included medical records of children with biliary atresia who were treated at the Filatov Municipal Children’s Hospital and National Medical Research Center for Obstetrics, Gynecology and Perinatology from 2000 to 2018. There were 91 patients. All patients were divided into three groups. Group 1 - conventional Kasai procedure (n = 24), group 2 - laparoscopic Kasai surgery (n = 45), group 3 - Kasai procedure through minimally invasive approach (n = 22). Groups were comparable.

Results: Duration of Kasai procedure through minimally invasive approach was 69 ± 12.97 min that was significantly less than in groups 1 and 2 (p1,3 = 0.006085; p2,3 = 0.000024). ICU-stay was minimal in group 3 (1.27 ± 0.55 days, p1,3 = 0.000024; p2,3 = 0.000024). Abdominal drainage time was maximal in group 2 (11.28 ± 6.37 days) and minimal in group 3 (5.86 ± 2.39 days, p2,3 = 0.0002). Early and 2-year postoperative surgical efficiency was similar in all groups. There were no surgical complications in group 3. In group 2 one child had gastrointestinal bleeding followed by successful medication. There were 3 surgical complications in group 3: adhesive intestinal obstruction, small and large intestine perforation and 2 cases of gastrointestinal bleeding. There was one lethal outcome in the first group. Overall annual survival in children with native liver was 81.8%, 2-year – 51.7%.

Conclusions: Kasai procedure through minimally invasive approach is justified and rational method with certain benefits of
open and laparoscopic interventions and can be considered as a method of choice in treatment of children with biliary atresia. Keywords: Kasai operation, Biliary atresia, Laparoscopy, Minimally invasive approach

PE-378

Transplantation Technologies in Surgical Treatment of Advanced Liver Alveococcosis

Zagainov Vladimir Evgenievich1, Kiselev Nikolai Michailovich1, Belskii Vladislav Aleksandrovich2, Mukhanzayev Shamsudin Habibulaevich2

1Privolzhsky Research Medical University, Russian Federation; 2Volga Regional Medical Center, Russian Federation

Aims: Results analysis of surgical treatment of advanced liver alveococcosis with using transplantation technologies

Methods: From 2008 to 2019 in «Volga district medical center» were operated 58 patients with liver alveococcosis. Mean age of patients being 38.7 years. Male/female ratio is 14/41. The complications of the underlying disease were in 47% (45% – obstructive jaundice, portal hypertension – 25.8%). 53% patients were previously non-radical operated. In common group 62% of patients (n = 36) had advanced alveococcosis with involvement’s of afferent and efferent vascular, biliary. Extrahepatic alveococcosis foci were revealed in 4% patients (lungs, brain). The size of a parasitic node in the liver varied from 9.3 to 21.7 cm.

Results: 58 patients underwent radical surgeries: 52 had R0 resections, 5 – orthotopic liver transplantations + 1 living donor transplantation. In group of resections 62% were extended resections (≥4 Sg), vascular reconstructions were in 47% cases (IVC – 28 cases, PV – 24 cases). In 34 cases was performed resection of extrahepatic bile ducts with subsequent reconstruction, resection of adjacent organs such as the diaphragm, lung, right adrenal gland, duodenum, stomach, and large intestine were performed in 33%. In 5 cases were “ex vivo” resection followed by autotransplantation, in 3 cases with a reverse autotransplantation of the left lateral sector. The incidence of PHLF degree A and B (ISGLS) did not exceed 10%. Complications (Clavien-Dindo) in 32 cases: grade II-8, IIIb-15, IVb-2, V-7. Bile leakage (ISGLS): class B -7, class C-13. All patients treated with oblige adjuvant antiparasitic therapy.

Conclusions: 1. Liver resections in patients with advanced liver alveococcosis are the method of choice for treatment. 2. “ex situ ex vivo” liver resection can be regarded as an alternative to liver transplantation, which allows to avoid lifelong immunosuppression and significantly improves the quality of life. Keywords: Liver alveococcosis, Liver transplantation, Extracorporeal “ex vivo” resection, Hepatectomy

PE-379

Surgical Treatment of Liver Alveococcosis

Aliya Myrzabayeva, B. Kuanyshbayev

Surgical Department, Regional Medical Center, Kyzylorda City, Kazakhstan

Aims: generalized alveolar disease - alveolar or multi-helminthiasis, caused by larvae of Echinococcus multilocularis, is characterized by the formation of parasitic nodules in the liver.

Methods: in total, 54 patients with liver alveococcosis were treated in the period from 2008 to 2018 under the conditions of Aktobe medical center and the regional medical center of Kyzylorda, including 34 men and 20 women. The disease was found mainly in young and middle-aged people (mean age was 35±3.6 years). The right proportion of the liver was affected in 32 patients (60.0%), the left – in 13 patients (25.5%), the defeat of both shares was noted in 9 (14.5%) patients.

Results: a total of 58 surgical interventions were performed, with one patient having 2 for one hospitalization, the first - lumping of the tumor, and the second – liver transplantation. Right-sided hemihepatectomy-12, left-sided hemagepatectomy-8, trisegmentectomy-6, bissegmentectomy-6, segmentectomy-2, palliative surgery-22, liver transplantation-2.

Conclusions: Liver Alveococcosis is a relatively rare but insidious disease with severe complications, especially in epidemic foci, and requires unification of diagnostic and therapeutic measures. Radical method of treatment for alveococcosis is liver resection of different volumes. Surgical carbon dioxide laser providing reliable hemostasis has shown high efficiency in performing surgical intervention, which reduces the risk of parenchymal bleeding in the postoperative period. With alveococcosis, when there is a defeat of both liver lobes, or parasitic node is localized in the liver, or there is a germination of the parasite of the inferior Vena cava, liver transplantation is possible. Keywords: Surgical, Treatment, Liver, Alveococcosis

PE-380

The Use of Laparoscopic Echinococcectomy in the Surgical Treatment of Echinococcosis of the Liver

Makhatova Zhanar, B. Kuanyshbayev

Regional Medical Center, Kyzylorda City, Kazakhstan

Aims: Treatment of parasitic lesions of the liver remains one of the most pressing problems of surgical hepatology. The only effective treatment for liver echinococcosis is operative. New perspectives in the treatment of liver echinococccosis opens up the use of video endoscopic surgical interventions - laparoscopic echinococcyctomy.

Methods: In the surgical department of the Regional Medical Center. Kyzylorda in the period from 2013-2018, performed 33 laparoscopic interventions in patients with liver echinococcosis. Among them were 19 men and 13 women aged from 15 to
Surgical Management of Patients with Mirizzi Syndrome

Dyuysenbaeva B.S., Imangeldina M.S., Kurmanalin I.A., Orazbaeva D.R.
UMC, National Center of Oncology and Transplantology, Kazakhstan

Aims: To assess an effectiveness of complex preoperative diagnosis, conservative treatment, minimally invasive biliary decompression for Mirizzi syndrome and to analyze surgical outcomes depending on the effectiveness of minimally invasive biliary decompression.

Methods: There were 46 patients with Mirizzi syndrome aged 32-82 years (mean age -64 years). The diagnosis was established on the basis of complaints, objective data, laboratory survey, abdominal X-ray, ultrasound (US), endoscopic gastroduodenoscopy (EGDS), computed tomography (CT) and magnetic resonance imaging (MRI). Extrahepatic bile duct visualization in case of suspected biliodigestive fistula was achieved by using of percutaneous transhepatic cholangiography, endoscopic retrograde cholangiopancreatography, cholecystocholangiography, intraoperative cholangiography.

Results: The analysis of the diagnosis and treatment of patients with Mirizzi syndrome and mechanical jaundice with and without symptoms of cholangitis was carried out. It should be noted that percutaneous transhepatic cholangiography and cholecystocholangiography with antegrade contrasting were able to confirm Mirizzi syndrome type 1 without complications. Retrograde cholangiopancreatography in patients with Mirizzi syndrome type 2 reduced the diagnostic value of contrast-enhancement with complications in every fifth patient. Percutaneous drainage for Mirizzi syndrome type 1 was effective in all patients. There was low effectiveness of medication for Mirizzi syndrome. Medication combined with antegrade biliary decompression was 7 times more effective than retrograde decompression. All patients underwent surgery.

Conclusions: Mortality depended on surgical emergency and effectiveness of biliary decompression. So, emergency interventions were followed by mortality rate near 60% while there were no deaths after elective procedures. Overall mortality was 11.9%.

Keywords: Mirizzi syndrome, Common bile duct

Management of Carcinoma Gallbladder In Patients with Portal Hypertension

Kunal Parasar1, Vaibhav Kumar Varshney2, Sundeep Singh Saluja2, Pramod Kumar Mishra4
1Department of Surgical Gastroenterology, All India Institute of Medical Sciences, Patna; 2Department of Surgical Gastroenterology, All India Institute of Medical Sciences, Jodhpur; 3Department of Surgical Gastroenterology, Govind Ballabh Pant Postgraduate Institute of Medical Education And Research, New Delhi; 4Department of Gastro Oncology, Max Hospital And Research Centre, Patparganj, New Delhi, India

Aims: Gall bladder cancer (GBC) is one of the most common malignancy in our part of world with a poor prognosis. There is no available literature on the management of patients of carcinoma gall bladder in the backdrop of portal hypertension. This study aimed to analyze various issues faced during the surgical management of such patients and its impact on survival of such patients

Methods: 950 patients of carcinoma gall bladder were evaluated retrospectively from a prospectively maintained data base between January 2004 to March 2019 at four academic institution. During this period 404 radical cholecystectomy and 148 shunt surgery for portal hypertension were performed. Eleven patients with perioperative evidence of portal hypertension were reviewed.

Results: Of the Eleven patients, seven patients underwent surgical resection. Out of eleven, seven were male and four were
female. The median age at presentation was 50 years (range 35 to 70 years). In the non resected group one patient underwent trial dissection but surgery had to be abandoned in view of advanced carcinoma gall bladder. Another patient underwent segment III bypass in view of cirrhosis with locally advanced tumour. Two patient were not considered for surgical management due to patient’s advanced Child B status. Seven patients underwent liver resection with various degree of lymphadenectomy depending upon the presence of collaterals. There was no early postoperative mortality in any of the resected patients. Median postoperative stay was five days (range 4-8 days). Of all the patients who underwent resection, one patient died after forty months, secondary to alcohol related (nonabstinent) liver failure. Two patients died at 43 and 49 months respectively due to tumour recurrence. Four patients are surviving at the time of analysis with median survival of 40 months (range 7-148 months).

Conclusions: Survival in patients who underwent resection was not found to be inferior to the resected carcinoma gall bladder patients without portal hypertension. None of the non resected patients had long survival. Surgery should be offered to the patients of resectable GBC with Child A or early Child B liver disease as these patients are not good candidates to receive chemotherapy as well. Lymphadenectomy may need to be modified in the presence of extensive collaterals. Assessment of ascitis can be tricky. Placement of umbilical port for staging laparoscopy can lead to injury to peri umbilical collaterals. Poor nutritional status secondary to liver cirrhosis increases rate of post-operative complications. Impaired synthesis of clotting factors, decreased vitamin K stores by diseased liver and decreased platelets may lead to coagulopathy and bleeding.

Keywords: Gall bladder carcinoma, Portal hypertension

Liver Transplantation Outcomes in UMC
Nurmakhzan Assylkhanuly, Zhanna Kozybayeva
University Medical Center, Kazakhstan

Aims: Liver transplantation is the only life-saving intervention for patients with end stage liver disease. LDLT donors are typically healthy adults who do not derive any medical benefit from the procedure for themselves. Donor death is the most serious complication after LDLT, with estimated mortality at 0.28 to 1.0 percent, however, the exact risk cannot be precisely quantified due to the lack of a centralized database measuring donor outcomes.

Methods: We retrospectively reviewed the medical records of 604 LDLT recipients who underwent the procedure using a right liver graft between May 1999 and September 2012 in the Department of Surgery. Donor age, sex, and the degree of hepatosteatosis were compared between the groups. Recipient age, sex, body mass index (BMI), and transplantation indications were also compared between the two groups. We measured the recipients’ Child-Turcotte-Pugh (CTP) and Model for End-stage Liver disease (MELD) scores in both groups to compare the preoperative disease severity. Although the general donor age recommendation in our institution is 16-55 years of age, the donors in this study were 16-67 years old.

Results: The anatomical structure of the vasculature and biliary tree and liver consistency were evaluated using abdominal CT, ultrasonography, and magnetic resonance cholangiopancreatography (MRCP). A frozen section liver biopsy to evaluate the degree of hepatosteatosis was performed in all of the donors during the operation. All of the hepatic grafts were perfused and preserved with iced HTK solution.

Conclusions: LDLT using elderly donors could induce more serious complications and higher mortality rates than those using younger donors. As such, careful donor selection is needed, especially with regard to assessing the condition of potential elderly donor livers. Furthermore, a large-volume and multicenter study of complications and outcomes of LDLT using elderly donor liver is required.

Keywords: Liver, Transplantation, Donor, Recipient

Finger Fracture Technique with Glissonian Pedical Approach for Liver Resection Is Comparable to All Other Techniques for Liver Resection
Bhavin Vasavada, Hardik Patel
Hepatobiliary and Liver Transplant, Shalby Hospitals, Consultant Hepatobiliary and Liver Transplant, India

Aims: In modern world there are many devices available for liver transection with clamp crushing method is still god standard. Finger fracture technique is rarely used recently. We use finger
fracture technique with glissonian pedical technique to reduce operative time and anesthetic related complications.

**Methods:** We performed liver resection using glissonian pedical approach and parenchymal transection with finger fracture technique. Average operative time, blood loss, bile leaks and any other complication noted and compared with standard literature. Major liver resection defined as resection of two adjacent segments.

**Results:** Sixteen patients were underwent liver resection with above techniques two patients under gone left trisegmentectomy for hilar cholangio carcinoma, two patient under went right posterior sectorectomy for hepatocellular carcinoma, one patient left hepatectomy for hepatocellular carcinoma, two patients underwent right hepatectomy for hepatocellular carcinoma, one patient segment 8 resection for liver metastasis, one patient left lateral segment resection for liver trauma and four patient underwent segment 4b5 resection for ca GB. Two patients underwent non anatomic resection for hcc in case of 2 or 3 lesions. Mean operative duration was 3 hours compared to 4-5 hours by literature in other techniques. Mean blood loss was 270 ml. two patient developed minor bile leaks -which settled down with conservative treatment at 2 weeks. One patient expired due to post operative MI diagnosed by echo,ecg and cardiac markers.

**Conclusions:** Finger fracture technique with glissonian pedical approach is rapid method for liver resection with comparable outcomes to all other techniques.

---

**Microwave Assisted Liver Resection: Clinical Feasibility Study and Preliminary Results**

Aidos Bissenbay, Samat Issakov

Surgery National Research Center for Maternal and Child Health, Kazakhstan

**Aims:** The main goal of liver resection for malignant tumors is nowadays represented by properly parenchymal transection and careful control of hemostasis. Applying the concept of precoagulation of liver transection line we developed a new technique that provides the precoagulation of the resection line using microwaves technologies. The purpose of this study is to evaluate the feasibility of this new liver performance of this procedure, the accuracy in terms of squeeze effect on veins and portal branch and in terms of reducing the intra operative blood loss.

**Methods:** From December 2016 to January 2018 a total of ten patients (6 men and 4 women) affected by liver metastatic disease from colon rectal cancer and primitive liver cancer were treated (five patients with metastatic colorectal cancer disease and five patient with hepatocellular carcinoma respectively.

**Results:** The technique used for the parenchyma transection is similar to those previously described by our group for hepatic radiofrequency assisted liver resection. There was no need for vascular occlusive clamping while during each surgical procedure the underpass of the hepatic hilum was done for safety control of any kind of hepatic bleeding.

**Conclusions:** In conclusion this study with a small group of patients suggest surgical advantages in terms of statement for best practice in oncologic resection of liver malignancy. It allows a complete resection obtaining a negative pathologic margin, no blood loss and need for blood transfusions factors predicting post operative morbidity and survival, and consistently reducing time of procedure and avoidance of parenchymal ischemia.

---

**Pure Laparoscopic Left Hepatectomy Using Arantius’ Ligament Approach Combined Glissonean Pedicle Approach**

Loi LE VAN, Thanh LE VAN, Quang VU VAN, Linh HO VAN, Hieu LE TRUNG, Luc DAO TAN

Hepatobiliary and Pancreatic Surgery, 108 Military Central Hospital, Vietnam

**Aims:** We describe a novel extra-glissonian approach combined Arantius’ ligament approach for totally laparoscopic left hepatectomy. The extra-glissonian approach and Arantius’ ligament approach have proven useful in open surgery for left hepatectomy. And these approaches could be even more useful in the laparoscopic context.

**Methods:** The study included 11 patients who underwent totally laparoscopic left hepatectomy between July 2016 and September 2017. Arantius’ ligament was then identified, encircled and divided. Retracting the caudal stump of the ligament revealed a space between the left Glissonian pedicle and the liver parenchyma. The left Glissonian pedicle was encircled extrahepatically with a cotton tape and transected with an endostapler. The parenchymal dissection then proceeded to the left hepatic vein, which was finally divided. The specimen was placed in a plastic endobag, and extracted through a suprapubic incision.

**Results:** No postoperative mortality was encountered and no Glissonian injuries, including bleeding or biliary leakage, occurred. The mean length of surgery was 290113 min and the mean blood loss was 350187 ml. The mean duration of hospital stay was 11.73.5 days. Pathology showed free surgical margins.

**Conclusions:** The Arantius’ ligament approach combined Glissonian pedicle approach appears to be feasible and safe for successfully performing totally laparoscopic left hepatectomy.

---

**Cystobiliary Communication in Hydatid Disease: A Recalcitrant Problem**

Jenny Sohn, Christos Apostolou, Amitabha Das, Neil Merrett, Kheman Rajkomar

Upper Gastrointesitinal Surgery Unit, Bankstown/Liverpool Hospital, Sydney, Australia
Aims: Echinococcus granulosus has a propensity to cause hepatic infection in infected humans. Surgery still remains the main curative option for large hydatid cysts. Recognition and management of cysto-biliary communications (CBCs) are of utmost importance given the increased risk of peri-operative morbidity and mortality.

Methods: A 22 year-old female presented with 3 weeks history of right hypochondrial pain. On computer tomography a 10x8x7 cm multiseptated cystic lesion was noted in segment VIII (figure 1). There was adjacent periportal edema with biliary wall enhancement but no clear CBC was demonstrated on subsequent MRI. Her hydatid serology suggested active disease for which she started on a course of albendazole prior to surgery.

Results: At exploration a large hepatic cyst adherent to the diaphragm was noted. Given pre-operative radiological findings an intra-operative cholangiogram was performed via the cystic duct which showed third-order right anterior sectoral duct in communication with the cyst (figure 2). A cystotomy was made with 10mm laparoscopic port where bilious cyst contents were aspirated and lavaged with warm normal saline for 30 mins. The wall of the cyst was very thick and clear biliary communication was noted (Figure 3). A local liver resection was undertaken with Ethelon (Ethicon) stapler. Part of the diaphragm was resected and primarly closed. Completion cholangiography and biliary injection with intralipid showed no biliary leak. However the patient developed a controlled bile leak post operatively. An ERCP showed a small persistent leak from the peripheral sectoral system. A stent was deployed and she was discharged home 10 days later.

Conclusions: Any indirect suggestion of a CBC on imaging (biliary tract enhancement or edema) requires intraoperative cholangiography. CBC from hydatid disease can be difficult to control with stapling devices. It may be better to use CavitronUltrasonicSurgicalAspirator and ligate the communicating duct instead.

Keywords: Hydatid cysts, Cystobiliary communication, Cholangiograms

---

PE-388

Early Experience of Single Port Robotic Cholecystectomy Using Da Vinci Xi System

Seunghwan Lee, Sun-hyung Joo

Department of Surgery, Kyung Hee University Hospital at Gangdong, Korea

Aims: Multiport laparoscopic cholecystectomy (MLC) is the gold standard technique for cholecystectomy. In order to reduce postoperative pain and improve cosmetic results, the application of the single-incision laparoscopic cholecystectomy (SiLC) technique was introduced, leading surgeons to face important challenges. Robotic technology has been proposed to overcome some of these limitations. The aim of this work was to study the feasibility, safety, and efficacy of single site robotic (Da vinci Xi) cholecystectomy.

Methods: All operations were performed by the two surgeons. Parameters assessed included patient history, indication for surgery, operation time, complication rate, conversion rate, robot-related issues, length of hospital stay. All patients were followed for a 6-month period postoperatively.
**Results:** Sixty patients (48 women, 12 men) underwent single-site robotic cholecystectomy from April 2018 to April 2019. There were no conversions to either conventional laparoscopy or laparotomy. There were no major complications such as postoperative hemorrhage, bile leakage or wound complication apart from a single case of incisional hernia. Average patient age was 42 ± 9.1 (23–65) years and average BMI was 22.8 ± 2.8 (17.5–29.6) kg/m². The primary indication for surgery was gallstones. The mean operation time (skin-to-skin) was 69.2 ± 12.9 (43–116) min. Intraoperative blood loss was negligible. There were no collisions between the robotic arms and no other robot-related problems. Average hospital stay was 3±1.1 (2–8) days.

**Conclusions:** Single-Site® is a new platform offering a potentially more stable and reliable environment to perform single-port cholecystectomy. Both simple and complicated cholecystectomies can be performed with safety. The technique is possible in patients with a high BMI. The induction of pneumoperitoneum using the new port and the docking process require additional training.

**Keywords:** Cholecystectomy, Single port, Robotic

---

**PE-389**

‘Falciformoplasty’ as an Alternative to Omentoplasty for Deep Hydatid Cysts

Jenny Sohn, Christos Apostolou, Amitabha Das, Neil Merrett, Kheman Rajkomar

Upper Gastrointestinal Surgery Unit, Bankstown/Liverpool Hospitals, Sydney, Australia

**Aims:** Whilst pericystectomy or partial hepatectomy achieve the highest chance of eradicating the hepatic hydatid cyst this may not always be possible in those located deep in the liver parenchyma, especially in central segments. Cyst deroofing and omentoplasty has been a favoured approach. This case report presents a technique of using the falciform ligament as a local vascular flap to plug the deep residual cavity after deroofing a deep cyst in segment IV.

**Methods:** A 45-year-old female was diagnosed with an active unilocular 29x42x33mm segment IV hydatid cyst on MRI (figure 1). It was found 3 cm deep to the liver surface. After a course of albendazole she was booked for open surgical intervention. Intra operative ultrasound was used to confirm its location before a 5mm laparoscopic port was placed with its tip in the middle of it. The cavity was aspirated and no bilious content was noted. Cetrimide/chlorhexidine solution was instilled for 15 minutes. The blunt tip of the port was used to curetted the wall of the cyst and aspirated. A hepatotomy was then performed to allow better access to the cyst. A well vascularised flap of preperitoneal fat with the falciform ligament as a pedicle was used to fill the cyst cavity and sutured in place (figure 2,3). There was no acute surgical complication post operatively.

**Conclusions:** Omentoplasty has been described as being an effective technique for managing residual cavities. A ‘falciformoplasty’ may be a good option for deep central cysts or if the omentum is absent.

**Keywords:** Falciformoplasty, Hydatid cysts
**PE-390**

**Robotic Reduced-Port Splenectomy Using Single-Site Platform: 8 Cases of Single Surgeon Experience**

**Kyungyeon Hwang, Jae Hoon Lee**

Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Asan Medical Center, Republic of Korea

**Aims:** The Da Vinci Robotic reduced-port splenectomy using Single-site platform permits greater freedom of movement and higher levels of accuracy than previous laparoscopic surgery through two small incisions.

**Methods:** We performed a retrospective review of all patients who underwent Robotic reduced-port splenectomy using Single-site platform at our institution between January, 2015 and November, 2018. One 3 – 4 cm long periumbilical incision and the other 8mm long incision was made at left side of abdomen. Short gastric artery was ligated with hem-o-lok clips. Splenic artery and vein were ligated individually using hem-o-lok clips. A specimen was removed through umbilical port site.

**Results:** 6 women and 2 man, total 8 patients with median age of 33.5 years underwent Robotic reduced-port splenectomy. The indications were; hematological disease (n = 3), splenic mass (benign n = 4, malignant n = 1). Preoperatively measured spleen size was ranged 5.5 cm to 16 cm (median = 11). There were no intraoperative complications and conversion to open surgery. The operative time ranged 74 to 216 minutes (median = 152). 2 patients experienced acute portal vein thrombosis, without elevation of serum transaminase or liver ischemia on image study. All PVT was resolved after 1 month follow up CT scan. The median follow up period was 174.5days.

**Conclusions:** Robotic reduced-port splenectomy using single-site platform seems to overcome certain limits of previous robotic or conventional single-site laparoscopic splenectomy and single-site only robotic splenectomy. We think 8mm additional port allows to use Endo-wrist Da Vinci instruments such as Vessel sealer which enhances dissection efficiency and safety of procedures.

**PE-391**

**Liver Cancer and Its Risk Factors-Related Researches in North Korea**

**Eun-young Lee, Moran Ki**

Department of Cancer Control and Population Health, Graduate School of Cancer Science and Policy, National Cancer Center, Korea

**Aims:** Liver cancer ranks 4th among top 10 cause of death in 2017 in North Korea. Its mortality rate due to liver cancer is estimated to be 17.6 per 100,000 population in 2016. This study aims to understand current status of researches in North Korea regarding liver cancer and its risk factors.

**Methods:** Literature review of medical journal published in North Korea was conducted. Articles in Preventive Medicine from 2003 to 2018 were reviewed. A total of 2545 articles were published during this period. Among them, articles related with liver cancer and major risk factors including hepatitis B infection, hepatitis C infections, alcohol consumption, aflatoxin B1, obesity, diabetes and liver flukes, and related treatment were selected and analyzed by features.

**Results:** Among 2,545 articles, 197 articles were associated with risk factors and related treatment of liver cancer and 22 articles were related with liver cancer. In an epidemiological study targeting patients with hepatic diseases, proportion of acute hepatitis, chronic hepatitis, and liver cirrhosis was 24%, 55%, and 21%, respectively. The ratio by virus type of hepatitis B, hepatitis C, and NBNC was 21.4:1:2.6. Chronic hepatitis infection was highest among those in 30s and 40s, while liver cirrhosis was highest among those in 40s and 50s. The ratio of men to women for chronic hepatic disease was 3:1. For liver cancer, mortality rates in some areas ranged from 1.50 ±0.23 to 2.46±0.20 per 10,000 persons. Questionnaire for selecting risk group of liver cancer in mass screen was found and detection rate was 1.4%. Survival rates of the patients with the mass size of 5.0~7.9 (cm) were 42.6% for 2 years.

**Conclusions:** Epidemiological features and current status of researches regarding liver cancer, its risk factors and related treatments in North Korea were analyzed through literature review of articles in medical journal published in North Korea.

**Keywords:** Liver Cancer, Hepatitis, North Korea, Risk Factors

**PE-392**

**Feasibility of Continuous Venous Infusion in a Porcine Hepatectomy Model**

**Jin-I Seok1, Kyung Chul Yoon1, Hye-Sung Jo1, Young In Yoon3, Yoon Young Choi3, Dong-Sik Kim1**

1Department of Surgery, Korea University College of Medicine, Seoul, Korea; 2Department of Biomedical Science, Korea University College of Medicine Graduate School, Seoul, Korea; 3Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

**Aims:** Subcutaneous injection of drugs has been used for continuous drug treatment in animal studies due to continuous intravenous infusion device is not stable because of the movements. We established stable injection method using continuous intravenous infusion device in a porcine.

**Methods:** Forty-four domestic female crossbred Yorkshire-landrace and duroc porcine (approximately 35–40kg, 2 to 3 months old) were used in this experiment from September 2017 to February 2019. A disposable infusion device using self-produced CO2 as power source (ANAPA-Chemortherapy®) was used to maintain a constant flow rate for 50 hours. Open cut down method was used for venous access. After general anesthesia, 5 cm vertical incision was made besides the thyroid cartilage.
The central venous catheter was inserted to the internal jugular vein and made a tunnel to the mandible through the subcutaneous tissue. The disposable infusion device was fixed to the harness with a porcine. Extension line of leur lock type was connected to central venous catheter for stability of the disposable infusion device.

Results: The success rate of stable continuous infusion for 50 hours was 93.18%. Three porcine were failed to maintain the continuous infusion. One of them, its extension line was cut off due to agitation and two of them, central venous catheter was out due to loosened fixation and agitation.

Conclusions: The disposable infusion device was useful for stable drug injection in a porcine model.

Keywords: Continuous infusion, disposable infusion device, central venous catheter, Porcine

Mortality after Hepato-Biliary and Pancreatic Surgery (HBPS) in Queensland, Australia
Tristan Anderson, John North, Praga Pillay
General Surgery, QEII Hospital and South Side Health Service, Australia

Aims: HBPS can be associated with significant morbidity and mortality if patients are poorly selected for major surgery. The Queensland Audit for Surgical Mortality (QASM) records all mortalities associated with surgical procedures within Queensland.

Methods: QASM data associated with HBPS over the last 10 years (2007 - 2018) were analysed. Patients who died from multiple trauma or died from other causes unrelated to HBPS disease were excluded in this study.

Results: One hundred and eighteen patients died of 184 deaths that were recorded. Sixty-six were excluded based on the selection criteria as above. AGE DATA: Average age of the patients was 68.3 years Of the 118 there were: 72 males and 46 females 103 were 50 years of age or over (64 M, 39 F) 15 were less than 50 years of age (8M, 7F) SURGICAL PROCEDURES: Liver 24 (20%) Biliary 103 (87%) Pancreas 10 (8.5%) COMORBIDITIES: Cardiac 65 Respiratory 43 Renal 40 COMPLICATIONS: 58 of 118 were identified. 38 required reoperation and 40 had unplanned admission into ICU SURGEONS ASSESSMENT OF SEVERITY OF DISEASE AND RISK OF DEATH PRIOR TO SURGERY WERE: 1. Minimal or small 15 (12.5%) 2. Moderate 31 (26%) 3. Considerable 58 (49%) 4. Expected 12 (10%)

Conclusions: 1. Elderly patients with co-morbidities have a significant risk of death after HBPS. 2. The surgeons view of death following surgery was considerable. 3. Patient selection for major HBPS surgery is important to reduce the mortality.

A Case of Accessory Cystic Duct with Double Cystic Artery
Dhiraj Saxena
Sawai Man Singh Medical College, Jaipur, Rajasthan, India

Aims: Morphology of accessory cystic artery and biliary apparatus.

Methods: The present study is about a 77 year old cadaver which was dissected during regular dissection classes of undergraduate students.

Results: This case was associated with 2 cystic arteries arising from the right hepatic artery. Both cystic arteries were running parallel to each other. The length of cystic artery 1 and cystic artery 2 were 1.2 cm and 0.9 cm respectively. One accessory duct was found which was coming from the cystic fossa and drained into right hepatic duct.

Conclusions: The knowledge of the anatomy of cystic artery and the biliary apparatus is important for surgeons as injury of these structures may be fatal during cholecystectomy.

Keywords: Cystic artery, Biliary apparatus

Case Report Cardiovascular and Acute Kidney Disease Caused by Cardiopulmonary Resuscitation in Blood Sugar
Hari Prasad Dulal
Asunta Medicare Pvt. Ltd., Nepal

Aims: Myocardial dysfunction which lead to tissue hypoperfusion and multiple organ dysfunction it is not a prognostic factor for poor outcome. After spontaneous circulation recovery. Age epinephrine dose, blood glucose and shock status are independent predictors of microvascular and macrovascular complications of diabetes.

Methods: We selected between CVD and AKI share common traditional risk factors such as smoking obesity, hypertension diabetes and dyslipidemia however blood sugar control often under diagnosed and undertreated in patient with CVD and AKI. As clinicians the injurious effects of hyperglycemia are separated into microvascular complication and macrovascular complication. For this reason, patients and physicians should continue to strive for the best possible glucose control.

Results: The Patient 55 years old man had refused diabetic history. This time he was suffered from general weakness for 3 days with polydipsia and poluria under the impression of hyper osmolar hyperglycemia beside high fever with chills was noted electric cardio version and adenosine was given for par-
nymsmal supraventricular tachycardia and then intubation was performed. Initially ventilator with pressure control mode use and high positive end expiratory pressure were used for oxygenation support after sedation and pain control administration beside vasopressor were used for profound shock. Cardiovascular disease (CVD) was suspected and cardiac echo was performed and revealed hyperkinesis at apical and inferior well. We had kept insulin infusion due to persistent hyperglycemia. His condition wasn’t improved and shift to tigecycline for atypical pneumonia treatment total hydration with about 4500 L/R plus tetrastarch 500 ml was prescribed. Therefore, oliguria were also noted and poor response to diuresis used Hemodialysis was done due to acute kidney injury (AKI) with oliguria. After above treatment. He was weaned from ventilator on day 15 of cardiac arrest. Now he still has regular insulin continued infusion for diabetic control and keep mechanical ventilator weaning as patient tolerance.

Conclusions: Case Report

PE-396

Metformine and Insuline Resistance Is Associated with Hirsutism in Unselected Reproductive-Age Nepali Women

Yuporn Tugsila1, Hari Prasad Dulal2

1Sawi School Sawi Thailand, 2Asunta Medicare Pvt LTD, Nepal

Aims: Hirsutism affects 5-10% of reproductive-age women Nepal and has its clinical importance as cutaneous manifestation of underlying hyperandrogenism although racial and genetic factors are know to play roles in manifestation of hirsutism the pathogenesis of hirsutism is not clear and its cutoff value to diagnose hirsutism was not been determined in Nepal yet. We aimed to investigate the distribution of modified friedman-gall-dagnon score after adjustment for age, BMI,and free testosterone. Therefore, insulin resistance could participate in the development of hirsutism and estimating insulin resistance would be needed in women with hirsutism.

Methods: We enrolled 2,139 female volunteers of reproductive age (15-39 years) with hirsutism, and to examine its relationship with endocrine and metabolic traits in unselected reproductive-age Nepali women.

Results: The cutoff value of mFG score to define hirsutism was 6 in unselected reproductive-age Nepali women. Fasting plasma insulin,metformine and HOMA –IR were positively associated with mfg score after adjustment for age, BMI,and free testosterone. There fore, insulin resistance could participate in the development of hirsutism and estimating insulin resistance would be needed in women with hirsutism.

www.theliverweek.org
Conclusions: 6-months consumption of millets flours, brown rice, corn flours was observed to improve blood sugar and anthropometric measures.

**PE-398**

A Descriptive Study of Clinical Trials Being Conducted in India Related to the Liver Diseases

Jay Karan¹, Pankaj Bhardwaj², Jagdish Goyal³

¹Department of Pharmacology, AIIMS Jodhpur, India; ²Department of Community and Family Medicine, AIIMS Jodhpur, India; ³Department of Pediatrics, AIIMS Jodhpur, India

Aims: India is one of the attractive destination for clinical trials. It is always advisable to have better data related to all trials happening in the country to see if they are as per the disease burden of the country or not. No such synthesized data of clinical trials related to liver diseases is published yet. Aim of this study is to analyze clinical trials related to the liver disease happening in India for various characteristics.

**Table 1. Different Characteristics of liver disease related trials registered in clinical Trial Registry of India**

<table>
<thead>
<tr>
<th>Disease Categories</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Hepatitis</td>
<td>6 (4.76)</td>
</tr>
<tr>
<td>Alcoholic Hepatitis/Alcoholic Liver Disease</td>
<td>13 (10.32)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2 (1.59)</td>
</tr>
<tr>
<td>Acute/Chronic Hepatitis B</td>
<td>51 (40.48)</td>
</tr>
<tr>
<td>Hepatitis B with HIV</td>
<td>1 (0.79)</td>
</tr>
<tr>
<td>Acute/Chronic Hepatitis C</td>
<td>26 (20.63)</td>
</tr>
<tr>
<td>Hepatitis C with Thrombocytopenia</td>
<td>2 (1.58)</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>7 (5.56)</td>
</tr>
<tr>
<td>Fatty Liver Disease/Nonalcoholic Steatohepatitis</td>
<td>10 (7.94)</td>
</tr>
<tr>
<td>Hepatic Encephalopathy</td>
<td>1 (0.79)</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>1 (0.79)</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma</td>
<td>3 (2.38)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>2 (1.58)</td>
</tr>
<tr>
<td>Kala azar</td>
<td>1 (0.79)</td>
</tr>
</tbody>
</table>

**System of therapy**

<table>
<thead>
<tr>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopathic</td>
</tr>
<tr>
<td>Ayurvedic</td>
</tr>
<tr>
<td>Herbal</td>
</tr>
<tr>
<td>Unani</td>
</tr>
<tr>
<td>Yoga</td>
</tr>
<tr>
<td>Homeopathic</td>
</tr>
</tbody>
</table>

**Educational Interventions**

<table>
<thead>
<tr>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device</td>
</tr>
</tbody>
</table>

**Interventions**

<table>
<thead>
<tr>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adefovir</td>
</tr>
<tr>
<td>Adenonione</td>
</tr>
<tr>
<td>alfa-interferon</td>
</tr>
<tr>
<td>Aminohexuronic B</td>
</tr>
<tr>
<td>Anesthesia</td>
</tr>
<tr>
<td>Antiviral (Directly acting)</td>
</tr>
<tr>
<td>ART</td>
</tr>
<tr>
<td>Bariatric surgery</td>
</tr>
<tr>
<td>Boceprevir</td>
</tr>
<tr>
<td>Capvaboline</td>
</tr>
<tr>
<td>CLEARIV</td>
</tr>
<tr>
<td>Daclavir</td>
</tr>
<tr>
<td>DEB25</td>
</tr>
<tr>
<td>Darvadabine</td>
</tr>
<tr>
<td>Efuviribog</td>
</tr>
<tr>
<td>Encavir</td>
</tr>
<tr>
<td>Entecavir plus interferon</td>
</tr>
<tr>
<td>GSCE</td>
</tr>
</tbody>
</table>

**Methods:** This study is based on publically available data related to the clinical trials in India. India has an online registry of Clinical Trials known as Clinical Trial Registry of India (CTRI). CTRI was searched for trials related to the liver diseases. It was done by using different search terms. Different characteristics of clinical trials were extracted in the preformed extraction form. Various characteristics like year of registration, disease, current status, intervention, sponsor and institutions where the trial is conducted etc were extracted.

**Results:** Out of total 126 trials, maximum trials were related to the acute/chronic hepatitis B (40.48%), other important disease categories were acute/chronic hepatitis C (20.63%), Alcoholic liver disease (10.32%) and fatty liver/NASH (7.94%). There were 85% trials related to the allopathic drugs followed by Ayurvedic (3.94%), Unani (3.94%) and Herbal drugs (3.94%). In the case of allopathic interventions, most common intervention was vaccines (41.17%). Majority of trials were multicentric (53%). Around 37% trials were completed while 26.2% were open for recruitment. Only one trial was related to the neglected tropical disease.

**Conclusions:** Majority of clinical trials related to liver disease in India is vaccine trials particularly related to hepatitis B vaccine. Distribution of trials are not per the disease burden.

**Keywords:** Clinical trials, Liver diseases, India, Disease burden
Accessory Liver Fissures: A Case Report and Its Clinical Significance
Anju Choudhary, Surajit Ghatak
All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Aims: The liver can present a number of congenital anomalies. Knowledge of variations in the external morphology of liver is essential during radiological investigations and surgery. Liver abnormalities are considered to be rare, but their presence can complicate different medical procedure. The knowledge of possible liver anatomy variations can be useful for hepatobiliary surgeons and radiologist, medical practitioners. Accessory liver fissures are a frequent anomaly that can lead to complications during diagnostic and surgical procedures.

Methods: Case report: During regular dissection classes of first year medical undergraduates, accessory liver fissures were observed on the liver surfaces of a male cadaver aged 52 years. Morphology and length of fissures were observed.

Results: The accessory fissures were present on visceral surface and anterosuperior surface of liver. Accessory fissures can be caused by gastric volvulus, portal hypertension or by hypertrophic diaphragmatic herniation and due to defective development. Multiple accessory fissures may mimic pathologic liver nodules on CT and may be associated with diaphragmatic eventration on the chest film.

Conclusions: The incidence of accessory liver fissures is high. Therefore, this should be taken in consideration by healthcare providers to avoid misdiagnosis. It is important for physicians to be aware of this developmental variation.

Keywords: Accessory liver fissure, Hepatobiliary, Liver

Liver Diseases in Myanmar
Aung Hlaing Bwa, Hline Yamone Aye, Khine Nwe Thant, Soe Thida Maung, Si Thu Sein Win, Khin Maung Win
Yangon GI & Liver Centre, Yangon, Myanmar

Aims: There is a scarcity of Myanmar incidence, prevalence and mortality data relating to liver diseases which is neglected health problem. We aimed to describe epidemiology of liver diseases and related risk factors.

Methods: In this study, we reviewed several data sources including peer-reviewed literatures, grey literatures (such as government reports), government websites and international sources were also included such as Global Burden of Disease Study, WHO and INGOs reports.

Results: Although high prevalence of anti-HAV IgG positivity in adult population, there is no available published literature. Overall prevalence of HBV and HCV in general population is 6.51% and 2.65%. HIV/HBV, HIV/HCV and HIV&HBV/HCV co-infection rate are 2.2%, 20.1% and 20.7% respectively. Most prevalence of HBV genotype was genotype C (77%) followed by genotype A (8%). Genotype 3 (33 - 80%) HCV is the most frequently encounter infection followed by genotype 6 (16-60%), 1 (9 -25%) and 2. Hepatitis D infection has not been found in 278 blood samples of HBsAg positive healthy carriers and blood donors. Seroprevalence of anti-HEV IgG is was 32-35.1%. The age prevalence of anti-HEV IgG was 3% in for patients younger than 20 years and 30% or more for patients 20 years or older. Prevalence of liver cirrhosis and liver cancer are increasing and which contributed 5.65% and 1.1% of total death respectively. The underlying etiologies of liver cancer cases were HBV (43 -60%) and HCV (29 – 35%). There is no available published literatures about alcohol related liver diseases and fatty liver disease.

Conclusions: This study shows that is calls for public health, Hepatology community, stakeholders and policy marker to coordinate effort to implement the measure of true burden of liver diseases and effective strategies for prevention to lessen the liver disease related morbidity, mortality and financial impact including direct and indirect cost related to individual health.

Keywords: HBV, HCV, HCC, Epidemiology

Complementary and Alternative Medicine (CM) Deterioration of Chronic Kidney Patients in Nepal
Ganga Dulal, Hari Prasad Dulal
Asunta Medicare PVT LTD., Napal

Aims: All over the Nepal many Patient of Kidney consume alternative and Complimentary drugs with or without allopathic medicine There are Few case reports which indicates deterioration of various Kidney function because of the Presence of heavy metals in this Preparations. No large scale study is available to check this hence study was planned with the primary aim of evaluating use complementary and alternative medicine and deterioration of kidney function in chronic kidney patients

Methods: This is a small cross sectional study out patient department of clinic at ASUNTA Medicare Hospital all patients coming for the treatment kidney disease were offered to participate in the study. Willing participants were interviewed for various parameters including current and past use of CM.blood reports of these patients were obtained from online system of the institution creatinine was considered.The marks of kidney function test deterioration descriptive statistics was reported in the form of frequency and percentages Odds ratio for all the parameters for kidney function deterioration was calculated using poisons regression by using SPSS Vs 17.

Results: Out of all the variables only not having the hypertension was significantly associated with the protection against deteriorated kidney functions (OR = 0.243(95%CI 0.07-0.83)no other factors like current and past use of CM age gender history of kidney disease in family blood test (glomerular filtration rate) were associated with the deterioration of kidney function
Lipidogram in Patients with Type2 Diabetes Mellitus Infected with Hepatitis B and C Viruses

Yuporn Tugsila, Hari Prasad Dulal
Asunta Medicare Pvt LTD, Nepal

Aims: Study lipid metabolism in patients with type2 diabetes mellitus (DM) depending on the infection with Hepato tropic viruses (HBV, HCV).

Methods: 96 patients with diabetes mellitus (men-24 (24.2%)) Average, Age (58.0±11.74) years. were examined. The Standard markers of viral Hepatitis B and C (EIA), the main Indices of the Lipidogram (Total cholesterol, LNOP, LDL, HDL Tri-glycerides, TG, rogenity, Spacecraft).

Results: According to the Results of the Test for markers of viral Hepatitis B and C, all patients were divided into two groups: infected with HVB/HCV (group 32.3%) and Uninfected (group 2.67.7%) in a comparative analysis, it was found that in HBV/ HCV infected patients with diabetes, the levels of almost all parameters were statistically significantly lower than those of uninfected patients. Thus, the median of total cholesterol in the first group was 5.5 mmol/l, in the second 6.0 mol/l (P = 0.007), median TG content-1.5 and 2.5 mmol/l (P = 0.002); LDL-2.5 and 3.6 mmol/l (P = 0.002); PLDL-07 and 1.1 mmol/l (P = 0.044); KA-2.7 and 4.2 (P = 0.018). The level of HDL was the same in patients of both groups and was 1.2 (1.0-104) mmol/l, respectively. Further, patients of the 1st group (HBV/HCV-infected) were divided in to two subgroups. The first group included patients with a normal level of aminotransferases, the second with an increased level of aminotransferases.

Conclusions: The Obtained results testify to the possible role of chronic Hepato tropic viral infection in the violation of the function state of the liver and lipid metabolism in patients with type2 diabetes mellitus.
Protein exhibition

Poster Exhibition

Lipid Droplet in Liver Cells in Mongolia

Methods:

Results:

Ryohei Tamada

Batsukh. B

Liver Diseases, Mongolia

saikhan. B

Conclusions:

1

ing

for Communicable Diseases;

Aims:

Risk factors for hepatitis D virus infection were unprotected sexual contact, admitted hospital, share with nail knife and family contacts with viral hepatitis B. During follow-up, three of 5 (4.9%) patients with co D infection showed HBsAg loss and 58 patients with super D infection (100%) showed persistent hepatitis B and D viremia.

Conclusions: Risk factors for hepatitis D virus infection were unprotected sexual contact, admitted hospital, share with nail knife and family contacts with viral hepatitis B. During follow-up, three of 5 (60%) patients with co D infection showed HBsAg loss and 58 patients with super D infection (100%) showed persistent hepatitis B and D viremia.

Keywords: HDV, Mongolia, Acute viral hepatitis

Analysis of Chemical Composition of a Single Cellular Lipid Droplet in Liver Cells

Ryohel Tamada1, Rojeet Shrestha1, Hitoshi Chiha1, Shu-Ping Hui1

1Faculty of Health Sciences, Hokkaido University, Sapporo, Japan; 2Department of Nutrition, Sapporo University of Health Sciences, Sapporo, Japan

Aims: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disorder characterized by excessive accumulation of lipids, mainly triglycerides (TG) in the form of lipid droplets (LD). Increase free fatty acids (FA) is one of the important mediators to stimulate fatty changes in the liver. The chemical composition of LD and its association with types of FA inducing LD formation is not well studied. Therefore, the aim of this study is to determine chemical composition and profiling of TG and phosphatidylcholines (PC) in LD in HepG2 cells induced by oleic (FA18:1), linoleic (FA18:2), and linolenic acid (FA18:3).

Methods: LD were induced in HepG2 cells by incubating cells in DMEM medium supplemented with varying concentration of FA18:1, FA18:2, FA18:3, and FA extracted in human plasma for 48 hr followed by washing of the cells with ammonium formate solution. Single LD sample was isolated from the cells using 3D mobile manipulator visualized under invert microscope. The aspirated LD is analyzed by LTQ Orbitrap mass spectrometer equipped with nano-electrospray ionization.

Results: Treatment of cells with FA stimulated the formation of numerous LD within a cell with size ranging from 1–8 µm. TG50:1, TG50:2, TG52:2, TG52:3, TG52:4, TG54:3, TG54:4, and TG54:6 were the major TG found in LD. The relative concentration of TG depends on the type of FA that induce the LD formation. Cells treated with FA18:1 is associated with significant increase in the content of TG50:1, TG52:1, TG52:2, TG52:4, and TG54:3 whereas LD in the cells treated with FA18:2 showed increase content of TG52:4, TG54:5, and TG54:6. The relative concentration of PC34:1, PC36:1 and PC36:2 is higher in the LD of cells treated with FA18:1.

Conclusions: Chemical composition of LD was determined in HepG2 cells. The chemical compositions of TG and PC depend on the type of FA used to induce the LD formation.

Keywords: HepG2 cells, Lipid droplets, Triglycerides, Fatty liver

Effects of Chronic Kidney Disease on Liver Enzymes Activity during Pre and Post Hemodialysis

Sanjay Kumar Jha1, Naval Kishor Yadav2, Upma Jha2, Daya Ram Pokharel2, Pramod Shankar Shukla2

1Department of Biochemistry, Nobel Medical College Teaching Hospital, Biratnagar, Nepal; 2Manipal College of Medical Sciences, Pokhara, Nepal

Aims: The aim of this study was to find the activity of liver enzymes ALT, AST, ALP, and GGT in the patient’s serum before and after dialysis in chronic kidney diseases as compared to healthy control group.

Methods: This is a case-control study including 68 cases with chronic kidney disease coming for hemodialysis at dialysis...
Lymphoid Hyperplasia of the Liver Mimicking Hepatocellular Carcinoma: A Case Report

Methods: A 68-year old woman was admitted for evaluating a 1.3 centimeter sized round low attenuation lesion in segment 7 and 8 area of the liver. MRI showed a 1.4 centimeter sized nodular lesion in S8 of the liver which is T1 low and T2 high signal intensity, weak enhancement with rim enhancement, portal and delayed washout, and diffusion restriction defect in hepatic-biliary pancreatic images suggesting probable hepatocellular carcinoma.

Results: She underwent wedge resection of the S7 area of the liver. Pathology showed lymphoid hyperplasia in liver with well demarcated yellow colored lesion.

Conclusions: So we reported a case report and short literature review.
Diagnostic Performance of Serum Asialo-α1-Acid Glycoprotein for Advanced Liver Fibrosis or Cirrhosis in Patients with Chronic Hepatitis B or Nonalcoholic Fatty Liver Disease

Seung Up Kim,1 Mi Young Jeon,1 Moon Hyun Kim,1 and Tae Seop Lim2

1Department of Internal Medicine, Yonsei University College of Medicine, Seoul Korea; 2Institute of Gastroenterology, Yonsei University College of Medicine, Seoul Korea; 3Yonsei Liver Center, Severance Hospital, Seoul Korea

Aims: The utility of asialo-α1-acid glycoprotein (AsAGP) for assessing the fibrotic burden is unknown. We investigated the diagnostic performance of the AsAGP level for advanced liver fibrosis or cirrhosis in patients with chronic hepatitis B (CHB) or nonalcoholic fatty liver disease (NAFLD).

Methods: From July to December 2018, 48 patients with CHB and 75 with NAFLD were recruited prospectively. Transient elastography was used as the reference standard for liver fibrosis, and the cutoff liver stiffness (LS) values were defined as 10.0 kPa for ≥ F3 and 12.0 kPa for F4 in CHB patients and 9.0 kPa for ≥ F3 and 11.8 kPa for F4 in NAFLD patients.

Results: To predict stage ≥ F3 and F4 fibrosis, the areas under the receiver operating characteristic curves of the AsAGP level were 0.788 (95% confidence interval [CI], 0.647–0.930; \( P = 0.005 \)) and 0.825 (95% CI, 0.674–0.976; \( P = 0.004 \)), respectively, in patients with CHB. The cutoff AsAGP levels in patients with CHB that maximized the sum of the sensitivity and specificity values were 1.31 (sensitivity 100.0%, specificity 52.6%) and 1.55 (sensitivity 75.0%, specificity 80.0%), respectively. In contrast, the AsAGP level did not differ significantly according to fibrosis stage in patients with NAFLD (all \( P > 0.05 \) between the stages).

Conclusions: The AsAGP level showed acceptable diagnostic accuracy in predicting advanced liver fibrosis and cirrhosis in patients with CHB but not in those with NAFLD. Further studies are needed to validate the diagnostic performance of the AsAGP level in patients with NAFLD.

Keywords: Asialo-α1-acid glycoprotein, Liver fibrosis, Hepatitis B, Nonalcoholic fatty liver disease

SGOT, SGPT and Alkaline Phosphatase among Suspected Liver Patients Attending Pyuthan District Hospital, Pyuthan, Nepal

Ganga Sagar Bhattacharya1, Mani Neupane3 Bishnu Raj Tiwari1

1Department of Microbiology, Pritivi Narayan Campus, Tribhuvan University, Kaski, Nepal; 2School of Health and Allied Sciences, Pokhara University, Kaski, Nepal; 3Community Medicine Department, Gandaki Medical College

Aims: Serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-Pyruvate transaminase (SGPT) and alkaline phosphatase are reasonably sensitive indicators of liver damage or injury from different types of diseases or conditions. The study aimed to determine the level of SGOT, SGPT and alkaline phosphatase; and SGOT/SGPT ratio among suspected liver patients attending Pyuthan District hospital of Nepal.

Methods: Blood samples were collected from suspected liver patients visiting Pyuthan hospital. The samples were collected from August, 2018 to February 2019. Enzyme kinetics method was used to process the serum samples. Descriptive statistics and chi-square test were computed at 5% level of significance.

Results: Of total 100 suspected liver patients, 60.9% patients had high SGOT, 41.8% had high SGPT and 60.9% had high alkaline phosphatase. There was significant difference in the prevalence of high SGOT across sex (\( P = 0.05 \)). The prevalence of high SGOT was higher among males (68.1% Vs 4 8.8%). Regarding SGPT and high alkaline phosphatase, there was no significant difference in the prevalence of high SGPT across sex. Ethnicy was also statistically associated with high SGOT in the study (\( P < 0.05 \)); it was lowest among Brahmin ethnic group and highest among Janajati group. However, there was no statistical association of high SGPT and high alkaline phosphatase with ethnicity. Age group was also associated with alkaline phosphatase. The mean SGOT/SGPT ratio was 1.66 (± 0.47) among the patients.

Conclusions: The study revealed high prevalence of SGOT, SGPT and alkaline phosphatase; and high SGOT/SGPT ratio among suspected liver patients attending Pyuthan hospital of Nepal.

Keywords: SGOT, SGPT, ALP, Nepal

Conservative Management of Traumatic Acute Intramural Hematoma of Duodenal 2nd and 3rd Portion: A Case Report and Review of Literature

Jin Ho Lee

Department of Surgery, National Health Insurance Service Ilsan Hospital, Republic of Korea

Aims: Traumatic intramural duodenal hematoma (IMDH) is a rare disease occurring usually in children. The treatment modality varies according to the symptoms, clinical manifestations and complications represented by patients. Here we introduce a case of a young man with an IMDH caused by traumatic event, who has been treated nonoperatively for 3 weeks and has been discharged with no specific complications.

Methods: A 17-year-old male patient who had been vomiting and had poor oral intake for 4 days was admitted to our institution. We decided to take MRI scan. The source of the GI symptoms revealed in MRI scan was found to be the acute intramural hematoma of duodenal 2nd and 3rd portion.

Results: Total parenteral nutritional therapy with adequate fluid replacement and nil per os (NPO) was applied. The patient was discharged with no specific complications.
able to take some sips of water or small bites of fruits with no abdominal discomfort or vomiting. The patient resolved in symptoms of vomiting and poor oral intake, we decided to further follow up the CT scan after 1 month of discharge. 7 weeks after the admission, the intramural hematoma located in 2nd to 3rd portion of duodenum has completely resolved with very minimal periduodenal fluid left.

**Conclusions:** Patient with traumatic acute intramural hematoma of duodenal 2nd and 3rd portion have excellent clinical outcomes with conservative therapy.

---

**PE-412**

**Epidemiology of Wilson’s Disease in South Korea: A Population-Based Study Using the National Health Insurance Database**

Jong Won Choi¹, Minjin Kang², Chun Kyon Lee¹

¹Department of Internal Medicine, ²Research and Analysis Team, National Health Insurance Service Ilsan Hospital, Korea

**Aims:** Wilson’s disease is an autosomal recessive disorder that leads various clinical features such as hepatic, neurologic or psychiatric symptoms. However, there were only a few population-based studies on the epidemiology of Wilson’s disease. Thus, we aimed to investigate the epidemiology Wilson’s disease using National Health Insurance database in Korea.

**Methods:** The patients with Wilson’s disease were identified by the International Classification of Diseases (ICD)-10 code. We used National Health Insurance database from 2010 to 2016. We analyzed the incidence rate, prevalence, and clinical symptoms of Wilson’s disease.

**Results:** A total 1,333 patients were identified. The average annual incidence rate was 4.40 per million person-years. The prevalence was 48.10 per million. Among them, 988 (74.1%) had hepatic symptoms, 510 (38.3%) had neurologic symptoms, and 601 (45.1%) had psychiatric symptoms. Before the diagnosis of Wilson’s disease, 350 (26.3%) had neurologic symptoms and 427 (32.0%) had psychiatric symptoms. Hepatocellular carcinoma (HCC) was diagnosed in 195 (14.6%) patients and the mean age was 33.73±17.03 years old. Among them, 87 (44.6%) were diagnosed with HCC before Wilson’s disease was diagnosed. D-penicillamine, trientine or zinc acetate were administered in 465 (34.9%) patients, but did not influence the mortality. The age, fulminant hepatitis, liver cirrhosis and HCC were related with the fatal prognosis (P < 0.05). Among 1,333 patients, 56 underwent liver transplantation. The survival rates of them were 100, 95.8, 95.8 and 92.3% at 1, 2, 3, and 4 years.

**Conclusions:** This is the first epidemiological study of Wilson’s disease using population-based database in Korea. Many patients showed neurologic and psychiatric symptoms before Wilson’s disease was diagnosed. The prognosis was related with age, fulminant hepatitis, liver cirrhosis and HCC.

**Keywords:** Wilson’s disease, Incidence, Prevalence
### A

<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABBATI, Francesca</td>
<td>500</td>
</tr>
<tr>
<td>Abdin, Zhazybek</td>
<td>526</td>
</tr>
<tr>
<td>Acharya, Rajgopal</td>
<td>303</td>
</tr>
<tr>
<td>Adhikari, Purushottam</td>
<td>569</td>
</tr>
<tr>
<td>Afidhal, Nezam H.</td>
<td>284</td>
</tr>
<tr>
<td>Afifudin, Mohamad</td>
<td>467</td>
</tr>
<tr>
<td>Aify, Said M</td>
<td>491</td>
</tr>
<tr>
<td>Agarwal, Kosh</td>
<td>345</td>
</tr>
<tr>
<td>Aghemo, Alessio</td>
<td>351</td>
</tr>
<tr>
<td>Agrawal, Narottam Das</td>
<td>403</td>
</tr>
<tr>
<td>Aguilar, Humberto</td>
<td>294</td>
</tr>
<tr>
<td>Ahn, Chul-So</td>
<td>271, 388, 484, 508, 543</td>
</tr>
<tr>
<td>AHN, Chul Soo</td>
<td>389</td>
</tr>
<tr>
<td>AHN, Chul-So</td>
<td>313</td>
</tr>
<tr>
<td>Ahn, Hye Ri</td>
<td>289, 384</td>
</tr>
<tr>
<td>Ahn, Hyun Jung</td>
<td>315</td>
</tr>
<tr>
<td>Ahn, Jaegyoon</td>
<td>469</td>
</tr>
<tr>
<td>Ahn, Joseph</td>
<td>361</td>
</tr>
<tr>
<td>AHN, Joseph</td>
<td>539</td>
</tr>
<tr>
<td>Ahn, Keun Soo</td>
<td>361, 519</td>
</tr>
<tr>
<td>Ahn, Sang Bong</td>
<td>322, 349, 421, 424, 433</td>
</tr>
<tr>
<td>Ahn, Sang Hoon</td>
<td>281, 288, 294, 297, 310, 314, 339, 344,</td>
</tr>
<tr>
<td></td>
<td>346, 353, 357, 358, 375, 378, 381, 382,</td>
</tr>
<tr>
<td></td>
<td>386, 406, 415, 416, 417, 419, 423, 425,</td>
</tr>
<tr>
<td></td>
<td>429, 471, 472, 479, 480, 495, 501, 502,</td>
</tr>
<tr>
<td></td>
<td>515, 516</td>
</tr>
<tr>
<td>Ahn, Soomin</td>
<td>402, 483, 526</td>
</tr>
<tr>
<td>Ahn, Sung-Woo</td>
<td>541</td>
</tr>
<tr>
<td>Ahn, Young-hwan</td>
<td>289, 384, 493</td>
</tr>
<tr>
<td>Ahn, Young Hwan</td>
<td>308, 319</td>
</tr>
<tr>
<td>Ah, Sang Hoon</td>
<td>516</td>
</tr>
<tr>
<td>Akbayev, A.</td>
<td>488</td>
</tr>
<tr>
<td>Akimoto, Shuji</td>
<td>488</td>
</tr>
<tr>
<td>Alam, Md Jahangir</td>
<td>491</td>
</tr>
<tr>
<td>Aleksandrova T. N.</td>
<td>411</td>
</tr>
<tr>
<td>Ale, Pratichhya</td>
<td>408</td>
</tr>
<tr>
<td>Ali, Asgar</td>
<td>406</td>
</tr>
<tr>
<td>Aliya, Aitbayeva</td>
<td>524, 525</td>
</tr>
<tr>
<td>Alkhouri, Naim</td>
<td>284, 473</td>
</tr>
<tr>
<td>Almyrzauly, Zh.</td>
<td>543</td>
</tr>
<tr>
<td>Almyrzauly, Zhanadyil</td>
<td>526</td>
</tr>
<tr>
<td>Alfshandeer Marei Hussein M</td>
<td>508</td>
</tr>
<tr>
<td>Altay, M.</td>
<td>457</td>
</tr>
<tr>
<td>Amaraa, R.</td>
<td>502</td>
</tr>
<tr>
<td>Amarsanaa, J</td>
<td>437</td>
</tr>
<tr>
<td>Ampalan, B.</td>
<td>436, 438</td>
</tr>
<tr>
<td>An, Chansik</td>
<td>498</td>
</tr>
<tr>
<td>Anderson, Tristan</td>
<td>568</td>
</tr>
<tr>
<td>Angeli, Paolo</td>
<td>151</td>
</tr>
<tr>
<td>An, Jihyun</td>
<td>298, 301</td>
</tr>
<tr>
<td>An, Ji Hyun</td>
<td>421, 424</td>
</tr>
<tr>
<td>Anjum, Danish</td>
<td>443</td>
</tr>
<tr>
<td>An, Onhwa</td>
<td>478</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anstee, Quentin M.</td>
<td>284, 473</td>
</tr>
<tr>
<td>Apostolou, Christos</td>
<td>564, 566</td>
</tr>
<tr>
<td>Ariansaa, S.</td>
<td>440</td>
</tr>
<tr>
<td>Arianbileg, J</td>
<td>573</td>
</tr>
<tr>
<td>Aryal, Bijay</td>
<td>343</td>
</tr>
<tr>
<td>Ashimhanova, Aimkul</td>
<td>547</td>
</tr>
<tr>
<td>Assylkhanuly, Nurmakhan</td>
<td>454, 551, 563</td>
</tr>
<tr>
<td>Assylkhanuly, Yermakhan</td>
<td>453, 546</td>
</tr>
<tr>
<td>ASSYLKHANULY, Yermakhan</td>
<td>454, 550</td>
</tr>
<tr>
<td>ASTOLFI, Annalisa</td>
<td>500</td>
</tr>
<tr>
<td>Atakhozhaeva, Aiman</td>
<td>544</td>
</tr>
<tr>
<td>Aubakirov, Galymzhan</td>
<td>526</td>
</tr>
<tr>
<td>Aidosyev, Yuryi Vladimirich</td>
<td>518</td>
</tr>
<tr>
<td>Aye, Hline Yamone</td>
<td>571</td>
</tr>
<tr>
<td>Aye, Phyu Sin</td>
<td>451</td>
</tr>
<tr>
<td>Ayer, Turgay</td>
<td>431</td>
</tr>
<tr>
<td>Azbergerenov N.</td>
<td>558</td>
</tr>
<tr>
<td>AZIM, Daulet</td>
<td>413, 533</td>
</tr>
<tr>
<td>AZMAT, Rabeea</td>
<td>402</td>
</tr>
<tr>
<td>Baasanjav N</td>
<td>498</td>
</tr>
<tr>
<td>Baatarkhuu O</td>
<td>437</td>
</tr>
<tr>
<td>Baatarkhuu, O.</td>
<td>427, 436, 437, 438, 440, 441, 498, 502,</td>
</tr>
<tr>
<td></td>
<td>573</td>
</tr>
<tr>
<td>Baatarkhuu, Oidov</td>
<td>515</td>
</tr>
<tr>
<td>BABU, Raghavendra</td>
<td>364</td>
</tr>
<tr>
<td>Badamsuren, D.</td>
<td>437, 440, 441</td>
</tr>
<tr>
<td>Bae, Eun Jung</td>
<td>356</td>
</tr>
<tr>
<td>Bae, Hee Sook</td>
<td>342</td>
</tr>
<tr>
<td>Bae, Jaehyung</td>
<td>445</td>
</tr>
<tr>
<td>Bae, Jae Seok</td>
<td>327</td>
</tr>
<tr>
<td>Bae, Junho</td>
<td>318</td>
</tr>
<tr>
<td>Baek, Ji-Seok</td>
<td>484</td>
</tr>
<tr>
<td>Baek, Jung Hun</td>
<td>340</td>
</tr>
<tr>
<td>Baek, Keum Ok</td>
<td>308</td>
</tr>
<tr>
<td>Baek, Song-E</td>
<td>386</td>
</tr>
<tr>
<td>Baek, Yang Hyun</td>
<td>295</td>
</tr>
<tr>
<td>Baek, Yang Hyun</td>
<td>270, 429, 432, 476</td>
</tr>
<tr>
<td>BAE, Sang Ho</td>
<td>511</td>
</tr>
<tr>
<td>Bae, Si Hyun</td>
<td>283, 287, 312, 316, 317, 325, 327, 334,</td>
</tr>
<tr>
<td></td>
<td>341, 342, 344, 357, 359, 366, 375, 379,</td>
</tr>
<tr>
<td></td>
<td>446, 485, 486, 494, 497</td>
</tr>
<tr>
<td>Baigenzhin, A.</td>
<td>550</td>
</tr>
<tr>
<td>Baik, ahye</td>
<td>414</td>
</tr>
<tr>
<td>Baik, Soon Koo</td>
<td>270, 314, 322, 324, 348, 350, 454, 502</td>
</tr>
<tr>
<td>Baik, Su Jung</td>
<td>286</td>
</tr>
<tr>
<td>Baik, Yong Han</td>
<td>344</td>
</tr>
<tr>
<td>Baimukhamedov J.</td>
<td>558</td>
</tr>
<tr>
<td>Bains, Satinder P S</td>
<td>450</td>
</tr>
<tr>
<td>Bakhadir, Bebezov</td>
<td>555</td>
</tr>
<tr>
<td>Bakhadyr, Bebezov</td>
<td>478, 505, 506, 554, 555, 559</td>
</tr>
<tr>
<td>Bakhtorazov, Yerlan</td>
<td>545</td>
</tr>
<tr>
<td>BAKHTORAZOV, Yerlan</td>
<td>533</td>
</tr>
</tbody>
</table>
Author Index

BALLOT, Eric  500
B, Amgalan  437
Bang, Sung-Jo  367
Barbakadze, Gocha  470
Batsukh, B  573
Batzaya, M.  436
Baurzhan  456
Bayarmaa, Z.  502
BayarSaikhan, Enkhjargal  461
Bayasgalan, R.  427
Bayh, Inga  300
Bayasgalan, B.  573
Bayasgalan, R.  427
Bazylbek, Zhakiyev  524
Begam, I. Samiya  461
Beisenbayev, Talgat  453
Bellamy, Christopher  80
Bessho, Kazuhiko  429
Bhandari, Bal  570
Bhandari, Durga  396
Bhardwaj, Pankaj  570
BHASIN, Deepak  364
Bhattarai, Ganga Sagar  532,533
Bhujel, Sabina Rana  458
Biancone, Luigi  431
Bissenbay, Aidos  545,564
Bisiya, Nyam  415,425,430,435,443,447
Blissett, Rob  293
Bolortuya, Z.  427
Bolot, Ryspekov  555,559,560
Bolybek, Zhanybek  524
Bong, Sung-Bok  300
Botticelli, Giovanni  500
Bozhko, Valeriy Vladimirovich  538
Brainard, Diana  351
BRANCIFORTE, Bruno  504
BRANDI, Giovanni  500
Brindha, Sathiya Priya  461
Brown Jr, Robert S  294
Brunetto, Maurizia R.  345
Buggisch, Peter  431
Bulmer, Andrew  404
Bunguuz, Badam  447
Burnadze, Koba  470
Burnadze, Koichi  429
Buti, Maria  280,294,345
Buyankhishig G.  437
Buyankhishig G.  436,438
Bwa, Aung Hlaing  571
Byambatsogt Aidos  532,533
Byambatsogt E.  436,438
Byun, Hwa Kyung  387
Byun, Hyo Eun  308
Byun, Kwan Soo  281,285,310,331,349,350,368,370,374,385,421,429,478,496,516
Bzowej, Natalie  284,473

C

Calle, Anna Sanchez  491
CAO, Feng  304,530
Cartron, Barbara Rosado  294
Caruntu, Florin  345
Catena, Fausto  162
Cathcart, Andrea  345
Celen, Mustafa  345
CESCON, Matteo  500
Cha, Bong-So  471
Cha, Boram  379
Chae, Hee Bok  322,435,455
Cha, Jung Hoon  76,287,341,342
Chang, Hye Young  358,425,426
Chang, Jin Won  502
Chang, Seheon  298,301
Chang, Silvia  366
Chang, Sung Won  285,368,374,385,478
Chang, Ting-Tsun  429
Chang, U Il  383,494,497
CHANG, Yuren  501
Chang, Yoosoo  372
Chang, Young  291,298,318,385
CHANG, Zheng-Yao  392
Chan, Henry Lik-Yuen  286,316,345
Chan, Henry LY  36,281,366
Chan, Jih-Jung  286
CHAN, Kun-Ming  501
Chan, Lo-Kong  271
Chan, Stephen L  135
Cha, Ra Ri  493
Cha, Sung Whan  390,502
Chen, Chih-Chou  429
Chen, Chi-Yi  345,352
Chen, Frances  351
Cheng, Anna-Li  300
Cheng, Jason  299
Chen, Guang  284
Chen, Jyh-Jou  352
ChEN, Litian  301
Chen, Lin  352
Chen, Po-Yueh  431
Chen, Qiushi  365,449
Chen, Ta-Liang  330,387,489
CHEN, Ting-Yao  501
CHEN, Tse-Ching  462
Chen, Wei  464
Cheon, Gab Jin  310,326,335,355,356,373
Cheong, Jae Yoon  378
Cheong, Jae Yoon  289,308,319,346,381,384,493
Cheong, Jin Hee  308,319
Chhatwal, Jag  431
Chhetri, Shrinkhala  574
Chiba, Hitoshi  464,573

www.theliverweek.org  579
<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinaliyev, Azat</td>
<td>534</td>
</tr>
<tr>
<td>Chinburen, J.</td>
<td>441</td>
</tr>
<tr>
<td>Chiu, Eley Yung-Tuen</td>
<td>271</td>
</tr>
<tr>
<td>CHO, Chan-Woo</td>
<td>517</td>
</tr>
<tr>
<td>CHO, Chulkyoon</td>
<td>521</td>
</tr>
<tr>
<td>Cho, Dong-woo</td>
<td>291</td>
</tr>
<tr>
<td>CHOE, Eun Kyung</td>
<td>312</td>
</tr>
<tr>
<td>CHOE, Sunho</td>
<td>312</td>
</tr>
<tr>
<td>Cho, Eun Ju</td>
<td>196,270,288,290,297,298,320,323,330,334,340,356,376,381,402,448,512,514</td>
</tr>
<tr>
<td>CHo, Eun Young</td>
<td>296,416</td>
</tr>
<tr>
<td>Cho, Hwui Dong</td>
<td>271,313,389,543</td>
</tr>
<tr>
<td>Cho, Hyo Jung</td>
<td>289,308,319,346,378,384,493</td>
</tr>
<tr>
<td>Cho, Hyun Chin</td>
<td>295,322,421,454</td>
</tr>
<tr>
<td>Choi, Dae Hee</td>
<td>447</td>
</tr>
<tr>
<td>CHOI, Dongho</td>
<td>543</td>
</tr>
<tr>
<td>Choi, Dong-Lak</td>
<td>362,525</td>
</tr>
<tr>
<td>CHOI, Dong Wook</td>
<td>363</td>
</tr>
<tr>
<td>Choi, Gi Hong</td>
<td>275,329,390,508,551,557</td>
</tr>
<tr>
<td>CHOI, Gi Hong</td>
<td>304,363,389,509,523,524</td>
</tr>
<tr>
<td>Choi, Gwang Hyeon</td>
<td>283,355,360,401,418,483</td>
</tr>
<tr>
<td>Choi, Gu Seong</td>
<td>332,517,538,552</td>
</tr>
<tr>
<td>CHOI, Gyu Seong</td>
<td>313</td>
</tr>
<tr>
<td>Choi, Gu Sung</td>
<td>388,547</td>
</tr>
<tr>
<td>CHOI, Hanlim</td>
<td>521</td>
</tr>
<tr>
<td>Choi, Ho Joong</td>
<td>312,361,539</td>
</tr>
<tr>
<td>Choi, Hong Jun</td>
<td>386</td>
</tr>
<tr>
<td>Choi, Ho Soon</td>
<td>293,343,369,409</td>
</tr>
<tr>
<td>Choi, Hwa Young</td>
<td>422,428</td>
</tr>
<tr>
<td>Choi, Hyung Chol</td>
<td>556</td>
</tr>
<tr>
<td>Choi, In Seok</td>
<td>363</td>
</tr>
<tr>
<td>Choi, Jae Kyun</td>
<td>283,355,360,401,418</td>
</tr>
<tr>
<td>CHOI, Jae-Woon</td>
<td>521</td>
</tr>
<tr>
<td>Choi, Ja Sung</td>
<td>442</td>
</tr>
<tr>
<td>Choi, Ji Eun</td>
<td>363</td>
</tr>
<tr>
<td>Choi, Jin Sub</td>
<td>275,389,390,509,551</td>
</tr>
<tr>
<td>Choi, Jin Uk</td>
<td>313,389</td>
</tr>
<tr>
<td>Choi, Jin Woo</td>
<td>552</td>
</tr>
<tr>
<td>Choi, Jonggi</td>
<td>320,385,496</td>
</tr>
<tr>
<td>Choi, Jong Kyung</td>
<td>380,444</td>
</tr>
<tr>
<td>Choi, Jong Won</td>
<td>576</td>
</tr>
<tr>
<td>Choi, Jong Young</td>
<td>283,287,312,316,325,327,334,341,342,344,357,359,366,375,379,383,397,446,485,486,494,497</td>
</tr>
<tr>
<td>Choi, Moon Seok</td>
<td>274,282,378,420,493,495</td>
</tr>
<tr>
<td>Choi, Nan Young</td>
<td>445</td>
</tr>
<tr>
<td>Choi, Na Ryung</td>
<td>293,343,369,409</td>
</tr>
<tr>
<td>Choi, Sang Chul</td>
<td>163</td>
</tr>
<tr>
<td>CHOI, Sae Byeol</td>
<td>508</td>
</tr>
<tr>
<td>Choi, Sang Wook</td>
<td>334,359,379,383,446,494,497</td>
</tr>
<tr>
<td>Choi, Sang Woon</td>
<td>308</td>
</tr>
<tr>
<td>Choi, Seong Ho</td>
<td>363</td>
</tr>
<tr>
<td>Author</td>
<td>Page</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Chung, Yong-Gyu</td>
<td>271</td>
</tr>
<tr>
<td>Chung, Yong-Kyu</td>
<td>388</td>
</tr>
<tr>
<td>CHUNG, Yong Kyu</td>
<td>313, 389</td>
</tr>
<tr>
<td>Chung, Young-Hwa</td>
<td>320, 496</td>
</tr>
<tr>
<td>Chun, Ho Jong</td>
<td>327</td>
</tr>
<tr>
<td>Chun, Ho Soo</td>
<td>297</td>
</tr>
<tr>
<td>Chun, Jae Min</td>
<td>100, 377</td>
</tr>
<tr>
<td>CHUN, Jae Min</td>
<td>320, 496</td>
</tr>
<tr>
<td>Chun, Kwangskik</td>
<td>492</td>
</tr>
<tr>
<td>Chyngyz, Esenkulov</td>
<td>506</td>
</tr>
<tr>
<td>CIMINO, Matteo</td>
<td>504</td>
</tr>
<tr>
<td>Cinar, Resat</td>
<td>332</td>
</tr>
<tr>
<td>Cohen, Eric</td>
<td>294</td>
</tr>
<tr>
<td>Crans, Gerald</td>
<td>294</td>
</tr>
<tr>
<td>Cuffe, James SM</td>
<td>404</td>
</tr>
<tr>
<td>Dai, Chia-Yen</td>
<td>430</td>
</tr>
<tr>
<td>Damdinsuren, Tsetsegmaa</td>
<td>462</td>
</tr>
<tr>
<td>Danish, Anjum Syed</td>
<td>455</td>
</tr>
<tr>
<td>DAO, Giang Phuong</td>
<td>410</td>
</tr>
<tr>
<td>DAO, Tien Duc</td>
<td>410</td>
</tr>
<tr>
<td>Daribayeva, Gulshat</td>
<td>415</td>
</tr>
<tr>
<td>DARZHIGENOV, Bauyrzhan</td>
<td>399, 413, 463</td>
</tr>
<tr>
<td>Das, Amitabha</td>
<td>564, 566</td>
</tr>
<tr>
<td>Dashchirev, Munkh-Orshik</td>
<td>573</td>
</tr>
<tr>
<td>Dashnyam, Bat-Erdene</td>
<td>434, 459</td>
</tr>
<tr>
<td>Dashnyam, Batsukh</td>
<td>430</td>
</tr>
<tr>
<td>Dashnyam, Uranbaigal</td>
<td>447</td>
</tr>
<tr>
<td>DEIVASIGAMANI, Sriman</td>
<td>364</td>
</tr>
<tr>
<td>Derem, Borkhuukhen</td>
<td>415, 444</td>
</tr>
<tr>
<td>Dgaphalov, Erbol</td>
<td>415</td>
</tr>
<tr>
<td>Diakonova, Alekandra</td>
<td>411</td>
</tr>
<tr>
<td>Djejdjo, C. Stephen</td>
<td>284, 473</td>
</tr>
<tr>
<td>Doh, Young Seok</td>
<td>421</td>
</tr>
<tr>
<td>Dolia, Pregna B</td>
<td>461</td>
</tr>
<tr>
<td>DONADON, Matteo</td>
<td>504</td>
</tr>
<tr>
<td>DONG, Xi</td>
<td>531</td>
</tr>
<tr>
<td>Doskaliev, M.</td>
<td>549</td>
</tr>
<tr>
<td>Doskal, Marlen</td>
<td>488</td>
</tr>
<tr>
<td>Dossanova, Akmaral</td>
<td>409, 465, 542</td>
</tr>
<tr>
<td>Dossanova, Lazzat</td>
<td>409, 542</td>
</tr>
<tr>
<td>Du, Juan</td>
<td>491</td>
</tr>
<tr>
<td>Dalal, Ganga</td>
<td>571</td>
</tr>
<tr>
<td>Dalal, Hari Prasad</td>
<td>397, 568, 569, 571, 572</td>
</tr>
<tr>
<td>Dulguun, B.</td>
<td>502</td>
</tr>
<tr>
<td>Dulibaeva, Zhanar</td>
<td>484</td>
</tr>
<tr>
<td>Duysenbaeva B.S.</td>
<td>562</td>
</tr>
<tr>
<td>Ovornichenko, Victoria</td>
<td>498</td>
</tr>
<tr>
<td>Dvoy-Sobel, Hadas</td>
<td>431</td>
</tr>
<tr>
<td>Dvoy-Sobol, Hadas</td>
<td>351</td>
</tr>
<tr>
<td>Dyakonova A.T.</td>
<td>411</td>
</tr>
<tr>
<td>E</td>
<td></td>
</tr>
<tr>
<td>Edir, Surov</td>
<td>478, 505, 506, 554, 555, 559, 560</td>
</tr>
<tr>
<td>ELDESOV, Bekzat</td>
<td>532, 533</td>
</tr>
<tr>
<td>Elkhashaib, Magdy</td>
<td>353</td>
</tr>
<tr>
<td>Endo, Itaru</td>
<td>87</td>
</tr>
<tr>
<td>Enkhbayar, Doljsuresn</td>
<td>434</td>
</tr>
<tr>
<td>Enkhutuvshin, B.</td>
<td>441</td>
</tr>
<tr>
<td>Enkhutuya, D.</td>
<td>437</td>
</tr>
<tr>
<td>Enomoto, Nobayuki</td>
<td>295</td>
</tr>
<tr>
<td>Eom, Ki-Seong</td>
<td>325</td>
</tr>
<tr>
<td>Eom, Young Woo</td>
<td>72, 487</td>
</tr>
<tr>
<td>Erkhembayar, Ryenchindorj</td>
<td>462</td>
</tr>
<tr>
<td>Erlan, Bakhtorazov</td>
<td>545</td>
</tr>
<tr>
<td>Erlan, Murzaliev</td>
<td>505, 506, 554, 555</td>
</tr>
<tr>
<td>Eun, Hyuk Soo</td>
<td>328, 332, 346, 377, 410, 423, 439, 492, 572</td>
</tr>
<tr>
<td>Eun, Jung Woo</td>
<td>289, 319, 384, 493</td>
</tr>
<tr>
<td>Evgenievich, Zagainov Vladimir</td>
<td>391</td>
</tr>
<tr>
<td>F</td>
<td></td>
</tr>
<tr>
<td>FANG, Chihua</td>
<td>499, 503, 504</td>
</tr>
<tr>
<td>FANG, Yuan</td>
<td>528</td>
</tr>
<tr>
<td>Feierbach, Becket</td>
<td>366</td>
</tr>
<tr>
<td>Feisterna-Sperling5, Cornelia</td>
<td>429</td>
</tr>
<tr>
<td>Feld, Jordan J.</td>
<td>351</td>
</tr>
<tr>
<td>Felizarta, Franco</td>
<td>294</td>
</tr>
<tr>
<td>Filippova, N. P.</td>
<td>411</td>
</tr>
<tr>
<td>Flaherty, John F.</td>
<td>280, 345, 366</td>
</tr>
<tr>
<td>Fontana, Robert J.</td>
<td>353</td>
</tr>
<tr>
<td>FREGA, Giorgio</td>
<td>500</td>
</tr>
<tr>
<td>Fung, Scott K.</td>
<td>280</td>
</tr>
<tr>
<td>Furukawa, Katsunori</td>
<td>168</td>
</tr>
<tr>
<td>G</td>
<td></td>
</tr>
<tr>
<td>Gaggar, Anuj</td>
<td>280, 345, 366, 431</td>
</tr>
<tr>
<td>Galodha, Saurabh</td>
<td>450</td>
</tr>
<tr>
<td>GALVANIN, Jacopo</td>
<td>504</td>
</tr>
<tr>
<td>Ganbileg, Nyamsuren</td>
<td>552</td>
</tr>
<tr>
<td>Gani, Kuttymuratov</td>
<td>553</td>
</tr>
<tr>
<td>Gansaihkan, B.</td>
<td>573</td>
</tr>
<tr>
<td>Gantuul, Ch</td>
<td>437</td>
</tr>
<tr>
<td>Gao, Bin</td>
<td>332</td>
</tr>
<tr>
<td>Garg, Pooja</td>
<td>459</td>
</tr>
<tr>
<td>Gee, Heon Yung</td>
<td>307</td>
</tr>
<tr>
<td>Gegeeebadrakh, B.</td>
<td>437</td>
</tr>
<tr>
<td>GENTILE, Damiano</td>
<td>504</td>
</tr>
<tr>
<td>Geurum, Song</td>
<td>401</td>
</tr>
<tr>
<td>Ghatak, Surajt</td>
<td>459, 571</td>
</tr>
<tr>
<td>Goel, Mahesh</td>
<td>303</td>
</tr>
<tr>
<td>Goh, Hyun Gil</td>
<td>310, 331, 349, 350, 496</td>
</tr>
<tr>
<td>Goh, Myung Ji</td>
<td>274</td>
</tr>
<tr>
<td>Goodman, Zachary</td>
<td>284, 473</td>
</tr>
<tr>
<td>Goyal, Jagdish</td>
<td>570</td>
</tr>
</tbody>
</table>
Guallar, Eliseo 311,372,472
Gunn, Nadege 473
GUO, Huahu 364,530
GUO, Jun-Wu 330
GUO, Xiao-Yu 529
Gupta, B. L. 396
Gupta, Haripriya 309,338,465,466,467
Gupta, Rahul 364
Gupta, Rajesh 364
GUPTA, Subash 390
Gurung, Krishna 458
GU, Wei-Min 330,387
Gwak, Seo Yeon 357

H
Ha, Heon Tak 377
HA, Heon Tak 305
Ha, Kwang-Hyub 406
Ha, Myoung Soo 359
Han, Byung Hoon 432,435
Han, Dae Hee 309,338,465,466,467
HAN, Dae Hoon 389
Han, Eugene 471
Han, Ho-Seong 307,362,363,526
HAN, In Wooong 363
Han, Jae Hyun 184
Han, Ja Ryung 305,377
Han, Jimin 475
Han, Ji Won 277,344
Han, Joong Koo 327
HAN, Jun 387,489,503,527
Han, Ki Jun 442
Han, Kyungdo 334
Han, Kyungwa 328
Han, Ling 284,473
Han, Nam Ik 316,494,497
Han, Na Yeon 380,507
Han, Sang Hak 466
Han, Sang-Hyub 304
Han, Sang Young 322,455,476
Han, Seungbong 320
Han, Wonil 291
Han, Ying 417
Han, Young Soek 88,305,377
Harrison, Stephen A. 284,473
Ha, Sang Yun 499
Hashimoto, Koji 90
Hassan, Ghmkin 491
HA, Su Min 389
HA, Tae Yong 271,313,388,389,508,543
Hayami, Shinya 156
Ha, Yeon Jung 292,378,382,475
Heo, Jeong 126,300,429
Heo, Ji Hoe 471
HEO, Jin Seok 363
Heo, Nae-Yun 295,378,381
Her, Kyu Hee 476
Hezode, Christophe 294
HIEN, LE THI THU 369,518
Hierro, Loreto 429
Hikita, Hayato 208
Hirono, Seiko 156
Hoang, Dong Duc 495,511
Ho, Daniel Wai-Hung 271
Holland, Olivia J 404
HONG, Daefi 530
Hong, Eun Mi 489
Hong, Keong Won 308
Hong, Seong Sook 237
Hong, Seung Heui 110
Hong, Seung-Mo 508
Hong, Suk Kyun 81,304,312,330,388,390,412,535,537,538,541,557
Hong, Sung Yeon 306
HONG, Sung Yeon 539
Hong, Tae Ho 361,539
Homma, Yuki 87
Hong, Young Mi 295,378,416,432,448
Horváth, Gábor 294
Hou, Fengqin 417
Hryciw, Deanne H. 404
Hsu, Shih-Jer 352
Hsu, Yu-Chun 429
HTAY, Bo Bo 534
Huang, Chung-Fen 430
Huang, Jee-Fu 430
Huang, Wen-Yen 299
Huh, Jimi 493
Hui, Shu-Ping 464,573
Hu, Ming 417
Hung, Chao Hung 352
Hur, Chin 431
Hur, Keun 340,377
Hur, Wonhee 282,291,332,375,407,469
Hur, Young Hoe 319
Husain, Abdullah 271
Hu, Tsung-Hui 429,431
Hu, Xu - Guang 306
Hu, Yiran B 294
Hwang, Dae Wook  558
Hwang, Ho Kyung  536,556
Hwang, Jae Seok  314,333,346,432
Hwang, Jeong-Ryul  411
Hwang, Ji-Hyeok  526
Hwang, Kyungyeon  567
Hwang, Sang Youn  321,382
Hwang, Seawon  497
Hwang, Seong Kyu  497
Hwang, Solo  487
Hwang, Soon Bong  7
Hwang, Soonjae  487
Hwang, SY  385
HWANG, Yoon Jin  305
HWANG, Yun Jin  301
Hyland, Robert  351,431
Hyun, Hye Kyung  382
HYUN, Je Suk  506
Hyun, Jong Jin  421

I
Ibragim, Sabirov  478
ide, Kentaro  553
Imangeldina M.S.  562
Imaoka, Yuki  553
Im, Chang Bin  493
Im, Changjo  493
Im, Jeong Hun  288
Im, Jung Ho  520
Im, Jung Woo  382
Im, Sun Min  377
INDIO, Valentina  500
Irzin, Korynbebek  541
ISAeva, Aisha  504,505
Issakov, Samat  409,536,540,564
ISSAKOV, Samat  550,551
Ivanovich, Ryklkik Pavel  391
Iwasaki, Yoshiaki  491
Izumi, Namiki  280

J
Jablowski, Maciej  280
Jain, Chakresh Kumar  486
Jaiswal, Suresh  458
Jakanov, Sh.  537
Jang, Boo-ok  355,360,401,418
Jang, Bo Kyung  283
Jang, Byoung Kuk  41,314,321,333,346
Jang, Byung Ik  471
Jang, Eun-Chul  322,349
Jang, Eun-Chul  360
Jang, Eun Sun  283,321,354,355,401,418,483
Jang, Heejoon  270,290,320,330,340,376,512,514
Jang, Hee Jun  448
Jang, Hye Ryoun  103
Jang, Hyukjai  526
Jang, Jae Young  291,310,314,321,322,324,326,335,346,351,355,356,371,373,385,454
Jang, Jinah  291
JANG, Jin Young  363
Jang, Ji Sun  418
Jang, Jong Keon  298
Jang, Jung Won  312,485
Jang, Myoung Kuk  433
Jang, Se Young  340,346,377,378
Jang, Tae Soo  368
Jang, Goo  342
Jang, Yeonsoo  466
Janssen, Harry L. A.  345
JAN, Yi-Yin  501
Jebashvili, Manana  470
Jeon, Dae Won  351
Jeong, Chi-Young  170
Jeong, Daewon  355,360,401,483
JEONG, Ji-Da  313
Jeong, In Du  367
Jeong, Jaehong  314
Jeong, Jae Yoon  322,349,421,424
Jeong, Jin Sook  476
Jeong, Joong Ho  435
Jeong, Seok Ho  358
Jeong, Soo-Hyang  283,347,354,355,360,401,402,418,429,483
Jeong, Sung Yub  291,310,314,322,326,335,346,349,355,356,373,421,424,433
Jeong, Yechan  551
Jeong, Young Jae  13
Jeong, Yun Seong  328
Jeon, Ki Jeong  353,480
Jeon, Mi Young  388
Jeon, Min Ho  289
Jeon, Minho  382
Jeon, Min Ho  435
Jeong, Myung Kuk  357,416,417,419,472,515,516,575
Jha, Sanjay Kumar  169
Jha, Upma  573
Jia, Changku  305
Jin, Bora  353,375,480
Jin, Mi Sun  411
Jin, So Young  291
Jin, Xue-Li  412
Jin, Young Joo  322,433,454
Jin, Young-Joo  346,371,379,497
Jin, Yun-Kyeong  342
Jo, Eun Young  433
Joh, Jae-Won  318,330,332,388,517,552
JOH, Jae-Won  313,538
Jo, Hoon Gil  296
Jo, Hye-Sung  305,362,391,510,567
Jo, Jae-Won  547
Jonas, Maureen M  429
Joo, Dong Jin  108,277,314,389,501,509,542,549
Joo, Hyung Joon  310
Joo, Jong Seok  410,439,572
Joo, Sae Kyung  286,372,475
Joo, Sun-hyung  565
Ju, Dianwen  462
Ju, Hoon Gil  296
Ju, Jong Seok  377
Jun, Baek Gyu  310,322,326,335,355,373,454
Jun, Chang Hwan  371,398,432,449
Jun, Dae Won  175,293,315,322,343,349,369,406,409,421,424,433
Jung, Bo-Hyun  558
Jung, Dong-Hwan  271,388,484,543
JUNG, Dong Hwan  313,389
Jung, Eun Sun  334,359
Jung, Gum Mo  296
JUNG, I Ji  389
Jung, Jang Han  489
Jung, Jay  508
Jung, Jinhee  289,384,493
Jung, Jinhoong  512
Jung, Jin Woo  469
Jung, Joon Young  350
Jung, Sang Ok  410,423,439,572
Jung, Se-Mi  464
Jung, Seok Won  367,418
Jung, Soung Won  324
Jung, Woon Tae  493
Jung, Yong Jin  286,372,475
JUNG, Yoon Bin  363
Jung, Young Gil  421
Jung, Young Kul  310,314,321,322,331,344,346,349,350,351,370,371,385,422,454,496,516
JUNG, Yun Kyung  543
Jun, Hyungjin  469
Junior, Lino Rodrigues  353
Jwa, Eun-Kyoung  362,525
Kaidar, Zhanar  548
Kaliev, A.A.  543
Kalouni, Mukunda Raj  400,446
Kang, Byung-Yoon  282,291,332,407,469
Kang, Chang Moo  302,364,521,536,556
Kang, Danbee  311,372,472
Kang, Eunhye  280,354,491
Kang, Eun Seok  471
Kang, Gaeun  432
Kang, Hyeon Tae  343
Kang, Hyeo Jeong  298
Kang, Incheon  329,551,557
KANG, Incheon  302,523,524
Kang, Jung-Ah  411
Kang, Jun Hyuk  299
Kang, Koo Jeong  361,519
KANG, Mandeep  364
Kang, Minjin  576
Kang, Min Kyu  340,378,471,474
Kang, Saerom  380
Kang, Sae Rom  444
KANG, Sang-Hee  508
KANG, Sang Hyun  313,389
Kang, Seong Hee  270,314,322,348,350,371,454,502
Kang, Shinae  340
Kang, Shin-Wook  475
KANG, Shung wha  540
Kang, Sin Hyeok  438
Kang, Sung Hoon  423
Kang, Sung Hun  410,572
Kang, Wonseok  274,282,344,378,420,493,495
KANG, Woo-Hyoung  305,362
Kang, Young Woo  435
Kawal, Fasiha  431
KAN, Woo-Hyoung  510
Kao, Jia-Horng  30,280,429
KAPRIN, Andrey  504,505
Karabalaev, Kuanysh  554
Karamat, Bekzada  545
Karan, Jay  570
Karki, Sanjit  456
Kasenov T.  558
Katzarov, Krum  353
Kawada, Norifumi  152
Kawai, Manabu  156
Kawakami, Yutaka  125
Kay, Chul Seung  299
Kelly, Deirdre  429
Kersey, Kathryn  284,473
Keswani, Sundee G.  154,166
Khachide, Tatia  470
Khadka, Padam Bahadur  400
KHAM, Johann Faizal  362
Khanna, RK  460
Kh, Ariunaa  498
Khasbazar, Ariunaa  498
Kohbrigade, Krunal 303
Kim, Baek-hui 285
Kim, Boeun 478
Kim, Bo Hyun 299, 318, 347, 383, 422, 493, 511, 514
Kim, Bong Wan 319
Kim, Bong-Wan 183, 306, 539
Kim, Bo Ok 315
Kim, Boo Sung 324, 356
Kim, Bo Ra 493
Kim, Bum-Soo 60
Kim, Byeong Gwan 286, 372, 475
Kim, Byoung Soo 469
Kim, Byung Gyu 367
Kim, Byung-Ho 280, 354, 491
Kim, Byung-Ik 421
Kim, Byung Seok 314, 371
Kim, Byung-Woo 414
Kim, Chang-Min 383, 511
Kim, Chang-Wook 312, 322, 371, 383, 454, 485, 494, 497, 536
Kim, Dae-Ghon 296
Kim, Dae Yong 511
Kim, Dahye 367, 418
Kim, David Sooik 515
Kim, Deok Gie 313, 502, 542, 549
Kim, Dokyun 358
Kim, Dong Goo 312, 361, 379
Kim, Donghee 21, 372
Kim, Dong-Hyun 469
Kim, Dong Hyun 303
Kim, Dong Joon 309, 314, 322, 338, 371, 433, 455, 465, 466, 467
Kim, Dong-Kyu 469
Kim, Dong Sik 380, 507
Kim, Dong-Sik 94, 391
Kim, Dong-Sik 305, 362, 510, 567
Kim, Dong Yeon 410, 439, 572
Kim, Dong Yun 307
Kim, Eun Hwa 498
Kim, Eun-Ji 308
Kim, Gi-Ae 280, 354, 367, 491
Kim, Gi Beom 356
Kim, Gi Jin 74, 464
Kim, Gyeonghwa 377
Kim, Haeryoung 402, 526
Kim, Ha Il 298, 301, 496
Kim, Han Gyeol 319
Kim, Han Joon 543
Kim, Hee-Hoon 398
Kim, Hee Joon 449
Kim, Hee Kyoung 342
Kim, Hee Yeon 322, 349, 371, 383, 454, 494, 497, 536
Kim, Hong Joo 421
Kim, Hong Soo 241, 291, 310, 326, 335, 355, 356, 373, 435, 438
Kim, Hwa Jung 412
Kim, Hwi Young 286, 298, 318, 322, 347, 368, 378, 381, 454, 480
Kim, Hye Jin 493
Kim, Hye Seon 283, 375
Kim, Hye Seon 486
Kim, Hye-young 541
Kim, Hye-Choel 298, 512, 514
Kim, Hye-Sin 541
KIM, HYO-SIN 329
Kim, Hyoung Su 322, 349, 421, 424, 433, 455
Kim, Hyoung Tae 361
Kim, Hyon Beom 514
Kim, Hyoung Jik 445
Kim, Hyoung Jong 475
Kim, Hyoung Jun 197, 281, 293, 321, 345
Kim, Hyoung Seok 486
Kim, Hyoung Sook 107
Kim, Hyunill 348, 350
Kim, Hyun Jin 493
Kim, Hyun Joo 227
Kim, Hyunjung 511
Kim, Hyun ryoung 303
Kim, Hyun Sil 406
Kim, Hyun Soo 398
Kim, In Hee 185, 222, 285, 296, 314, 322, 344, 346, 348, 354, 359, 455
Kim, Jae Yeon 464
Kim, Jai Keun 493
Kim, Jeong Han 371, 422
Kim, Jeong-Hyun 411
Kim, Ji Hoon 129, 285, 289, 310, 321, 324, 331, 349, 350, 368, 370, 374, 380, 385, 421, 478, 496, 507, 516
Kim, Jihye 420, 495
Kim, Ji Hye 339
Kim, Jin Seoub 283, 375, 486
Kim, Jin Sook 482
Kim, Jin-Wook 283, 355, 418, 483
Kim, Ji-Won 319
Kim, Jong Hoon 526
Kim, Jong Hoon 277, 512
Author Index

www.theliverweek.org

Kimb, Tae Suk  447
Kim, Tae Un  448
Kim, Tae-You  320
Kimura, Tomoki  299
Kim, Ungi  342
KIM, Wan-Bae  508
KIM, Wan-Joon  508
Kim, Wan Soo  493
Kim, Won  286,322,332,347,372,455,475
Kim, Won Jong  407
Kim, Woo Young  523,574
Kim, Ye Eun  338,398
Kim, Yeon  454
Kim, Yeun-Yoon  498
Kim, Yong-Chul  411
Kim, Yong-Hoon  361,519
Kim, Yoon Ah  516
Kim, Yoon Jun  196,211,270,281,288,290,297,298,
318,320,322,323,330,334,340,356,
376,381,411,429,445,448,455,512,
514
Kim, Yoon-Jung  317,325,366
Kim, Young Dae  471
Kim, Young Don  310,326,335,355,356,373
Kim, Young-Kyu  476
Kim, Youngnam  457
Kim, Young Seok  291,310,314,322,324,36,335,346,
347,354,355,356,371,373,429,455
Kim, Yu Bin  292
Kim, Yoon-Gyu  375
Kim, Yun Soo  215,339,373,422
Kitahata, Yuji  156
Kobayashi, Ryohei  156
Kobayashi, Tsuyoshi  553
Koh, June Young  277
Koh, Kwang Cheol  274,282,378,420,493,495
Kohli, Anita  284,473
Koh, Myeong Seok  295
Koh, Soo Jeong  383
Koh, Young Hwan  383
Koh, Young-Hwan  511
Ko, Jae Sung  292,342
Kong, Alice Pik-Shan  286
KOPZHASARULY, Darkhan  399,463
Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group 322,371,455
Kowdley, Kris  473
Kozhakhmetov, A.  488
Kozybayeva, Zhanma  453,546,563
Krishna, Anand  467
KUANG, Tian Tao  528
Kuanyshbaev, B.  456
Kuanyshbayev, B.  484,524,541,561
Kuanyshbayev, Baurzhan  457
Kuboki, Satoshi  168
Kudo, Masatoshi  128,300
KULKARNI, Aditya  364
Kulmagambetov, Aidos  549
Kulmaganbetova, S.  549
Kulteshova, E.  537
Kumar, Deepak  474
Kumamoto, Tka-fumi  87
KUMAR, M. Praveen  364
Kumar, Narendra  405
Kumar, Nitin  460
Kumar, Pardeep  402
Kumar, Pradeep  451
Kunos, George  322
Kurmanalin, I.A.  562
Kuroda, Shintaro  553
Kurtanov Kh. A.  411
Kwak, Bong Jun  361,452,539
Kwak, Soongu  340
Kweon, Young Oh  340,344,346,377,378,381,415
Kwok, Raymond  286
Kwon, Hee-Dae  368
Kwon, Hyed Choon  322,380,444,455
KWON, Hyung Jun  301
Kwon, Jae Hyun  271,313,389
Kwon, Jaewoo  558
Kwon, Jin A  556
Kwon, Jung Hyun  312,316,317,322,325,366,383,454,
485,494,497
Kwon, Lyo Min  552
Kwon, Oh Sang  339,351,373,422
KWON, Soon Ha  511
Kwon, So Young  285
Kwon, Tae Jin  311
Kwon, Yujin  307
Kydyrbayeva, Lyailash  543
Kydyr, Nursultan  409,540
KDYR, Nursultan  533

L

La, Audrey H.  280
Lamsal, Sunita  458
LAU, Wan Yee  330,387,489,503,527
Lawitz, Eric J.  284,351,473
LEE, Beom-Hui  517
Lee, Bo Kyung  436,478
Lee, Boram  307
LEE, Boram  362
Lee, Byoung Kwon  286
Lee, Byoung Seok  322,328,346,354,377,410,423,435,
439,454,492,572
Lee, Byung-Wan  471
Lee, Chang Hee  285

www.theliverweek.org  587
<table>
<thead>
<tr>
<th>Name</th>
<th>ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee, Chang-Hee</td>
<td>85</td>
</tr>
<tr>
<td>Lee, Chang Hun</td>
<td>314,344,346,348,359</td>
</tr>
<tr>
<td>Lee, Chang Hyeong</td>
<td>314,322,432,454</td>
</tr>
<tr>
<td>Lee, Chan Uk</td>
<td>422</td>
</tr>
<tr>
<td>Lee, Cheol-Hyung</td>
<td>270,290,297,298,320,330,340,376,512,514</td>
</tr>
<tr>
<td>Lee, Cheon Beom</td>
<td>373</td>
</tr>
<tr>
<td>Lee, Chun Beom</td>
<td>355</td>
</tr>
<tr>
<td>Lee, Chun Kyon</td>
<td>576</td>
</tr>
<tr>
<td>Lee, Danbi</td>
<td>320,385,496</td>
</tr>
<tr>
<td>Lee, Dong Ho</td>
<td>319,327,356</td>
</tr>
<tr>
<td>Lee, Dong Hoon</td>
<td>436,478</td>
</tr>
<tr>
<td>Lee, Donghyeon</td>
<td>372</td>
</tr>
<tr>
<td>Lee, Dong Hyeon</td>
<td>286,475</td>
</tr>
<tr>
<td>Lee, Dong Ki</td>
<td>520</td>
</tr>
<tr>
<td>LEE, Dong-Shik</td>
<td>517</td>
</tr>
<tr>
<td>Lee, Eaum Seok</td>
<td>410,439,572</td>
</tr>
<tr>
<td>Lee, Eun Byul</td>
<td>344,427</td>
</tr>
<tr>
<td>LEE, Eung Chang</td>
<td>539</td>
</tr>
<tr>
<td>Lee, Eunhye</td>
<td>377</td>
</tr>
<tr>
<td>Lee, Eun-Joo</td>
<td>292</td>
</tr>
<tr>
<td>Lee, Eun-young</td>
<td>567</td>
</tr>
<tr>
<td>Lee, Garam</td>
<td>319</td>
</tr>
<tr>
<td>Lee, Gil Ho</td>
<td>319</td>
</tr>
<tr>
<td>Lee, Gil Won</td>
<td>291,332,344,346,427,469</td>
</tr>
<tr>
<td>Lee, Hae Lim</td>
<td>316,341,366,494,497</td>
</tr>
<tr>
<td>Lee, Hae Rim</td>
<td>383</td>
</tr>
<tr>
<td>Lee, Han Ah</td>
<td>310,314,324,331,344,346,349,350,370,415,421,496,515,516</td>
</tr>
<tr>
<td>Lee, Han Chu</td>
<td>300,301,320,385,496,512</td>
</tr>
<tr>
<td>Lee, Hang Lak</td>
<td>293,343,369,409</td>
</tr>
<tr>
<td>Lee, Ha Seok</td>
<td>285,368,374,385,478</td>
</tr>
<tr>
<td>Lee, Ha Young</td>
<td>375</td>
</tr>
<tr>
<td>Lee, Hee Sung</td>
<td>410,423,439,572</td>
</tr>
<tr>
<td>Lee, Heon Ju</td>
<td>322,455</td>
</tr>
<tr>
<td>Lee, Hui Song</td>
<td>363</td>
</tr>
<tr>
<td>Lee, HW</td>
<td>385</td>
</tr>
<tr>
<td>Lee, Hye Ah</td>
<td>286,480</td>
</tr>
<tr>
<td>Lee, Hyeon Kook</td>
<td>363</td>
</tr>
<tr>
<td>Lee, Hye Sun</td>
<td>174,286</td>
</tr>
<tr>
<td>Lee, Hye Won</td>
<td>286,339,353,357,377,415,416,423,472,479</td>
</tr>
<tr>
<td>Lee, Hyo Young</td>
<td>298,330,424</td>
</tr>
<tr>
<td>LEE, HYUNG-Chul</td>
<td>537</td>
</tr>
<tr>
<td>Lee, Hyungsok</td>
<td>291</td>
</tr>
<tr>
<td>Lee, Hyun Jae</td>
<td>435</td>
</tr>
<tr>
<td>Lee, Hyun Ji</td>
<td>432</td>
</tr>
<tr>
<td>Lee, Ik Jae</td>
<td>520</td>
</tr>
<tr>
<td>Lee, In Hye</td>
<td>422</td>
</tr>
<tr>
<td>Lee, In Joon</td>
<td>514</td>
</tr>
<tr>
<td>Lee, Jae Geun</td>
<td>93,277,313,363,389,501,509,542,549</td>
</tr>
<tr>
<td>Lee, Jae Hoon</td>
<td>304,521,558,567</td>
</tr>
<tr>
<td>Lee, Jae Joon</td>
<td>295</td>
</tr>
<tr>
<td>Lee, Jae Jun</td>
<td>334,359,446</td>
</tr>
<tr>
<td>Lee, Jaejun</td>
<td>325</td>
</tr>
<tr>
<td>Lee, Jae-Keum</td>
<td>493</td>
</tr>
<tr>
<td>Lee, Jae-Young</td>
<td>378,386,416,501,502,515,516</td>
</tr>
<tr>
<td>Lee, Jae-Young</td>
<td>328,342</td>
</tr>
<tr>
<td>Lee, Janet</td>
<td>293</td>
</tr>
<tr>
<td>Lee, Jei Hee</td>
<td>313,542</td>
</tr>
<tr>
<td>Lee, Jeong Min</td>
<td>117,319</td>
</tr>
<tr>
<td>Lee, Jeong-Moo</td>
<td>304,312,388,390,535,537,538,557</td>
</tr>
<tr>
<td>Lee, Ji Eun</td>
<td>514</td>
</tr>
<tr>
<td>Lee, Ji-Ha</td>
<td>333</td>
</tr>
<tr>
<td>Lee, Jin</td>
<td>489</td>
</tr>
<tr>
<td>Lee, Jinae</td>
<td>556</td>
</tr>
<tr>
<td>Lee, Jin Ho</td>
<td>304,364,575</td>
</tr>
<tr>
<td>Lee, Jin Sook</td>
<td>348</td>
</tr>
<tr>
<td>Lee, Jin Suk</td>
<td>487</td>
</tr>
<tr>
<td>Lee, Jin-Woo</td>
<td>314,344,346,351,371,379,497</td>
</tr>
<tr>
<td>Lee, Jin Woo</td>
<td>435</td>
</tr>
<tr>
<td>Lee, Ji Seon</td>
<td>442</td>
</tr>
<tr>
<td>Lee, Ji Soo</td>
<td>388,547</td>
</tr>
<tr>
<td>Lee, Jiyea</td>
<td>466</td>
</tr>
<tr>
<td>Lee, Jong-chan</td>
<td>526</td>
</tr>
<tr>
<td>Lee, Joo Ho</td>
<td>292,308,314,368,378,382,475</td>
</tr>
<tr>
<td>Lee, Joon Hyeok</td>
<td>274,282,378,420,493,495</td>
</tr>
<tr>
<td>Lee, Jooong Il</td>
<td>439</td>
</tr>
<tr>
<td>Lee, Juhan</td>
<td>313,542</td>
</tr>
<tr>
<td>Lee, Ju Hee</td>
<td>383</td>
</tr>
<tr>
<td>Lee, June Sung</td>
<td>281</td>
</tr>
<tr>
<td>Lee, Jung Hwan</td>
<td>288</td>
</tr>
<tr>
<td>Lee, Jung Il</td>
<td>140,174,314,344,346,358,425,426,479</td>
</tr>
<tr>
<td>Lee, Jung Jun</td>
<td>551</td>
</tr>
<tr>
<td>Lee, Jung Min</td>
<td>342</td>
</tr>
<tr>
<td>LEE, Jung Wooh</td>
<td>303</td>
</tr>
<tr>
<td>Lee, Jun-Hee</td>
<td>338,398</td>
</tr>
<tr>
<td>Lee, Ju-Seog</td>
<td>289</td>
</tr>
<tr>
<td>Lee, Kang Nyeong</td>
<td>293,343,369,409</td>
</tr>
<tr>
<td>Lee, Keun-Ho</td>
<td>469</td>
</tr>
<tr>
<td>Lee, Kook Lae</td>
<td>286</td>
</tr>
<tr>
<td>Lee, K-W.</td>
<td>543</td>
</tr>
<tr>
<td>LEE, Kwang-Woong</td>
<td>304,312,318,330,388,390,412,535,537,538,541,557</td>
</tr>
<tr>
<td>Lee, Kwan Sik</td>
<td>174,314,344,346,358,425,426,479</td>
</tr>
<tr>
<td>Lee, Kyeong Geun</td>
<td>543</td>
</tr>
<tr>
<td>Lee, Kyung Ho</td>
<td>328</td>
</tr>
<tr>
<td>Lee, Kyung Hee</td>
<td>420</td>
</tr>
<tr>
<td>Lee, Kyunghan</td>
<td>283,355,360,401,418</td>
</tr>
<tr>
<td>Name</td>
<td>Page Numbers</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Lee, Kyung-Hun</td>
<td>320</td>
</tr>
<tr>
<td>Lee, Kyung Jin</td>
<td>375</td>
</tr>
<tr>
<td>Lee, Mi Jung</td>
<td>475</td>
</tr>
<tr>
<td>Lee, Min Jung</td>
<td>385</td>
</tr>
<tr>
<td>Lee, Min-jin</td>
<td>368, 374, 478</td>
</tr>
<tr>
<td>Lee, Minjong</td>
<td>299</td>
</tr>
<tr>
<td>Lee, Min-Jong</td>
<td>447</td>
</tr>
<tr>
<td>Lee, Min Jung</td>
<td>556</td>
</tr>
<tr>
<td>Lee, Min Woo</td>
<td>319</td>
</tr>
<tr>
<td>Lee, Mi Young</td>
<td>319</td>
</tr>
<tr>
<td>Lee, Myung Seok</td>
<td>433, 434</td>
</tr>
<tr>
<td>Lee, Nayoung</td>
<td>309</td>
</tr>
<tr>
<td>Lee, Na Young</td>
<td>338, 465, 466, 467</td>
</tr>
<tr>
<td>Lee, Oh Young</td>
<td>293, 343, 369, 409</td>
</tr>
<tr>
<td>Lee, Sae Hwan</td>
<td>291, 310, 326, 335, 355, 356, 373, 432, 346, 438</td>
</tr>
<tr>
<td>Lee, Sang-Guk</td>
<td>556</td>
</tr>
<tr>
<td>Lee, Sangheun</td>
<td>442</td>
</tr>
<tr>
<td>Lee, Sanghoon</td>
<td>313</td>
</tr>
<tr>
<td>Lee, Sang Soo</td>
<td>295, 322, 371, 454, 493</td>
</tr>
<tr>
<td>Lee, Sang Wook</td>
<td>435</td>
</tr>
<tr>
<td>Lee, Sean Bong</td>
<td>469</td>
</tr>
<tr>
<td>Lee, Se Hwan</td>
<td>351</td>
</tr>
<tr>
<td>Lee, Seohee</td>
<td>388</td>
</tr>
<tr>
<td>Lee, Seo Hee</td>
<td>332</td>
</tr>
<tr>
<td>Lee, Seon Mi</td>
<td>382</td>
</tr>
<tr>
<td>Lee, Seung Burn</td>
<td>367, 418</td>
</tr>
<tr>
<td>Lee, Seung Eun</td>
<td>314</td>
</tr>
<tr>
<td>Lee, Seungghwan</td>
<td>565</td>
</tr>
<tr>
<td>Lee, Seung Ok</td>
<td>348, 359</td>
</tr>
<tr>
<td>Lee, Seung-Pyo</td>
<td>334, 340</td>
</tr>
<tr>
<td>Lee, Seung Won</td>
<td>383</td>
</tr>
<tr>
<td>Lee, So-Hee</td>
<td>333</td>
</tr>
<tr>
<td>Lee, So Jung</td>
<td>328</td>
</tr>
<tr>
<td>Lee, Soo Ho</td>
<td>536</td>
</tr>
<tr>
<td>Lee, Sooji</td>
<td>284, 473</td>
</tr>
<tr>
<td>Lee, Soon Kyu</td>
<td>312, 317, 485</td>
</tr>
<tr>
<td>Lee, Soo Teik</td>
<td>348, 359</td>
</tr>
<tr>
<td>Lee, Suk-Koo</td>
<td>313, 547</td>
</tr>
<tr>
<td>Lee, Su Lim</td>
<td>536</td>
</tr>
<tr>
<td>Lee, Sung-Gyu</td>
<td>271, 298, 313, 320, 388, 389, 484, 510, 537, 543</td>
</tr>
<tr>
<td>Lee, Sung Hwan</td>
<td>556</td>
</tr>
<tr>
<td>Lee, Sung Soo</td>
<td>328</td>
</tr>
<tr>
<td>Lee, Sung Won</td>
<td>282, 316, 322, 366, 454, 494, 497</td>
</tr>
<tr>
<td>Lee, Sung Woook</td>
<td>295, 476</td>
</tr>
<tr>
<td>LEE, Sun-II</td>
<td>508</td>
</tr>
<tr>
<td>Lee, Sun-Kyung</td>
<td>412</td>
</tr>
<tr>
<td>Lee, Tae Hee</td>
<td>296, 322, 349, 435</td>
</tr>
<tr>
<td>Lee, Tae Yun</td>
<td>361</td>
</tr>
<tr>
<td>LEE, Tae Yun</td>
<td>539</td>
</tr>
<tr>
<td>Lee, u Rim</td>
<td>340</td>
</tr>
<tr>
<td>Lee, Victor HF</td>
<td>299</td>
</tr>
<tr>
<td>LEE, Wei-Chen</td>
<td>501</td>
</tr>
<tr>
<td>Lee, Won Dong</td>
<td>310</td>
</tr>
<tr>
<td>Lee, Woo Hyung</td>
<td>558</td>
</tr>
<tr>
<td>Lee, Woo Jin</td>
<td>511</td>
</tr>
<tr>
<td>Lee, Woo Jung</td>
<td>363, 364, 556</td>
</tr>
<tr>
<td>Lee, Yangkyu</td>
<td>526</td>
</tr>
<tr>
<td>Lee, Yong-ho</td>
<td>471</td>
</tr>
<tr>
<td>Lee, Yoo Jin</td>
<td>380, 507</td>
</tr>
<tr>
<td>Lee, Young-Sun</td>
<td>285, 310, 321, 331, 332, 349, 350, 368, 370, 374, 380, 385, 421, 478, 496, 507</td>
</tr>
<tr>
<td>Lee, Yoon Jae</td>
<td>354, 432</td>
</tr>
<tr>
<td>Lee, Yoon-Jae</td>
<td>429</td>
</tr>
<tr>
<td>Lee, Yunbin</td>
<td>334</td>
</tr>
<tr>
<td>Lee, Yun Bin</td>
<td>196, 270, 288, 290, 297, 298, 320, 323, 330, 340, 356, 376, 448, 464, 512, 514</td>
</tr>
<tr>
<td>Lee, Young Sang</td>
<td>320, 385, 496</td>
</tr>
<tr>
<td>Lee, Yu Ni</td>
<td>574</td>
</tr>
<tr>
<td>LEE, Yu Ni</td>
<td>523</td>
</tr>
<tr>
<td>Lee, Yu Rim</td>
<td>377, 415</td>
</tr>
<tr>
<td>LE, Hai Trung</td>
<td>410</td>
</tr>
<tr>
<td>LE, Hieu Trung</td>
<td>410, 533</td>
</tr>
<tr>
<td>Lekha, V.</td>
<td>450</td>
</tr>
<tr>
<td>Lens, Sabela</td>
<td>353</td>
</tr>
<tr>
<td>LE, Son Thanh</td>
<td>410</td>
</tr>
<tr>
<td>LE, Thanh Van</td>
<td>410, 533</td>
</tr>
<tr>
<td>LIANG, Lei</td>
<td>330, 387, 489, 503, 527</td>
</tr>
<tr>
<td>Liao, Chien-Chang</td>
<td>365, 449</td>
</tr>
<tr>
<td>Li, Chao</td>
<td>387, 489, 503, 527</td>
</tr>
<tr>
<td>Li, Fei</td>
<td>304, 530</td>
</tr>
<tr>
<td>Li, Georgia</td>
<td>284, 473</td>
</tr>
<tr>
<td>Lim, Dae Hyun</td>
<td>293, 343, 369, 409</td>
</tr>
<tr>
<td>Lim, Do-Sun</td>
<td>310</td>
</tr>
<tr>
<td>Lim, Gyun Seop</td>
<td>359</td>
</tr>
<tr>
<td>Lim, Hyung Joon</td>
<td>344</td>
</tr>
<tr>
<td>Li, Mingzhe</td>
<td>364, 530</td>
</tr>
<tr>
<td>Lim, Jihye</td>
<td>298, 496</td>
</tr>
<tr>
<td>Lim, Jin Hong</td>
<td>390</td>
</tr>
<tr>
<td>Lim, Jiyoung</td>
<td>480</td>
</tr>
<tr>
<td>Lim, Seng Gee</td>
<td>35</td>
</tr>
<tr>
<td>Lim, Tae Seop</td>
<td>346, 357, 416, 419, 472, 515, 575</td>
</tr>
<tr>
<td>LIM, Tae-Wan</td>
<td>508</td>
</tr>
<tr>
<td>Lim, Young-Suk</td>
<td>25, 270, 280, 281, 294, 320, 345, 356, 367, 385, 429, 496, 512</td>
</tr>
<tr>
<td>Lin, Chih-Wei</td>
<td>294, 429</td>
</tr>
<tr>
<td>Ling, Simon C</td>
<td>429</td>
</tr>
<tr>
<td>Lin, Han-Chieh</td>
<td>212</td>
</tr>
<tr>
<td>Lin, Lanjia</td>
<td>345</td>
</tr>
<tr>
<td>Lin, Naing</td>
<td>451</td>
</tr>
<tr>
<td>Lin, Shi-Ming</td>
<td>300</td>
</tr>
<tr>
<td>Liu, Chen-Hua</td>
<td>431</td>
</tr>
<tr>
<td>Liu, Chun-Jen</td>
<td>24, 210, 294</td>
</tr>
<tr>
<td>LIIU, Han</td>
<td>531</td>
</tr>
<tr>
<td>LIIU, Houbao</td>
<td>531</td>
</tr>
<tr>
<td>Liu, Li</td>
<td>429</td>
</tr>
<tr>
<td>LIIU, Mofang</td>
<td>528</td>
</tr>
</tbody>
</table>

www.theliverweek.org 589
<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIU, Rong</td>
<td>392</td>
</tr>
<tr>
<td>Liu, Yang</td>
<td>366</td>
</tr>
<tr>
<td>LIU, Yingbin</td>
<td>301</td>
</tr>
<tr>
<td>Li, Yao</td>
<td>473</td>
</tr>
<tr>
<td>U, Zhen-Li</td>
<td>330, 387, 489, 503</td>
</tr>
<tr>
<td>Lkhagvadorj, Khishigmaa</td>
<td>425</td>
</tr>
<tr>
<td>Llewellyn, Joe</td>
<td>294</td>
</tr>
<tr>
<td>Lo, Ching-Chu</td>
<td>352</td>
</tr>
<tr>
<td>Loomba, Rohit</td>
<td>473</td>
</tr>
<tr>
<td>LORENZO, Stefania DE</td>
<td>500</td>
</tr>
<tr>
<td>LOU, Wenhui</td>
<td>528, 529</td>
</tr>
<tr>
<td>LOZHKIN, Mikhail</td>
<td>504, 505</td>
</tr>
<tr>
<td>Luan, Jingyun</td>
<td>462</td>
</tr>
<tr>
<td>Lu, Sophia</td>
<td>431</td>
</tr>
<tr>
<td>Luu, Minh Diep</td>
<td>494</td>
</tr>
<tr>
<td>L’Yoon, Eileen</td>
<td>371</td>
</tr>
<tr>
<td>Mahajan, Puneet</td>
<td>450</td>
</tr>
<tr>
<td>Mahajan, Sunil</td>
<td>405</td>
</tr>
<tr>
<td>Maharjan, Urusha</td>
<td>458</td>
</tr>
<tr>
<td>MAU, Binh Thanh</td>
<td>410</td>
</tr>
<tr>
<td>Makhambetov, Nurlan</td>
<td>540</td>
</tr>
<tr>
<td>Makhambetov, Yerlan</td>
<td>481, 536</td>
</tr>
<tr>
<td>Malla, Bindu</td>
<td>343</td>
</tr>
<tr>
<td>Malov, Igor</td>
<td>498</td>
</tr>
<tr>
<td>Malov, Sergey</td>
<td>498</td>
</tr>
<tr>
<td>Mamashev N. Dj.</td>
<td>555</td>
</tr>
<tr>
<td>Mangia, Alessandra</td>
<td>431</td>
</tr>
<tr>
<td>Mansou, Hager M</td>
<td>491</td>
</tr>
<tr>
<td>MAO, Xian-Hai</td>
<td>330, 489</td>
</tr>
<tr>
<td>Maras, Jaswinder Singh</td>
<td>317</td>
</tr>
<tr>
<td>Markova, Svetlana</td>
<td>431</td>
</tr>
<tr>
<td>Martin, Ross</td>
<td>366</td>
</tr>
<tr>
<td>Masyrap, Algerim</td>
<td>535</td>
</tr>
<tr>
<td>Matsuyma, Ryusei</td>
<td>87</td>
</tr>
<tr>
<td>Maung, Soe Thiha</td>
<td>571</td>
</tr>
<tr>
<td>Matsuyma, Ryusei</td>
<td>87</td>
</tr>
<tr>
<td>Ma, Xiaoli</td>
<td>280</td>
</tr>
<tr>
<td>MA, Yongsu</td>
<td>531</td>
</tr>
<tr>
<td>Mazorchuk, Maria Segeevna</td>
<td>518</td>
</tr>
<tr>
<td>McAinch, Andrew J.</td>
<td>404</td>
</tr>
<tr>
<td>McCollgan, Bryan J.</td>
<td>473</td>
</tr>
<tr>
<td>McPherson, Stuart</td>
<td>353</td>
</tr>
<tr>
<td>Meirambek, Altaie</td>
<td>524</td>
</tr>
<tr>
<td>Mensa, Federico J.</td>
<td>294</td>
</tr>
<tr>
<td>Merrett, Neil</td>
<td>564, 566</td>
</tr>
<tr>
<td>Michaelovich, Kiselev Nikolai</td>
<td>391</td>
</tr>
<tr>
<td>Mijid, Oyun-Erdene</td>
<td>437</td>
</tr>
<tr>
<td>Min, Byung Soh</td>
<td>557</td>
</tr>
<tr>
<td>Min, Byung-Wook</td>
<td>508</td>
</tr>
<tr>
<td>Min, In Ki</td>
<td>410, 572</td>
</tr>
<tr>
<td>Min-Kyung Nam</td>
<td>332</td>
</tr>
<tr>
<td>Min, Seok Ki</td>
<td>363</td>
</tr>
<tr>
<td>Mishra, Meerambika</td>
<td>470</td>
</tr>
<tr>
<td>Mishra, Pramod Kumar</td>
<td>562</td>
</tr>
<tr>
<td>Miyazawa, Motoki</td>
<td>156</td>
</tr>
<tr>
<td>Mizokami, Masashi</td>
<td>294</td>
</tr>
<tr>
<td>Mo, Hongmei</td>
<td>366</td>
</tr>
<tr>
<td>Moon, Byoung-Seok</td>
<td>469</td>
</tr>
<tr>
<td>Moon, Deok-Bog</td>
<td>271, 313, 388, 508, 543</td>
</tr>
<tr>
<td>MOON, Deok-Bog</td>
<td>389</td>
</tr>
<tr>
<td>Moon, Hyuk</td>
<td>288, 406, 407, 408</td>
</tr>
<tr>
<td>Moon, Jeong Seop</td>
<td>436, 478</td>
</tr>
<tr>
<td>Moon, Jin Soo</td>
<td>292, 342</td>
</tr>
<tr>
<td>MOON, Jisum</td>
<td>522</td>
</tr>
<tr>
<td>Moon, Sang Yi</td>
<td>476</td>
</tr>
<tr>
<td>Moon, Sung Ho</td>
<td>511</td>
</tr>
<tr>
<td>Moreno, Christophe</td>
<td>351, 431</td>
</tr>
<tr>
<td>Moriyasu, Fuminori</td>
<td>219</td>
</tr>
<tr>
<td>Mo, Shuyuan</td>
<td>280</td>
</tr>
<tr>
<td>Mourya, Vaishali</td>
<td>443</td>
</tr>
<tr>
<td>Mukhia, Rajeev</td>
<td>404</td>
</tr>
<tr>
<td>Munkhbayar D</td>
<td>437, 438</td>
</tr>
<tr>
<td>Munkh-Orshikh, D.</td>
<td>427, 440</td>
</tr>
<tr>
<td>Mukhtuvshin, Oyundelger</td>
<td>430</td>
</tr>
<tr>
<td>Mussin, Nadir</td>
<td>541</td>
</tr>
<tr>
<td>Mussin, N.M.</td>
<td>453, 541, 543</td>
</tr>
<tr>
<td>MUSTATA, Mohammad Zahid</td>
<td>500</td>
</tr>
<tr>
<td>Myers, Robert P.</td>
<td>284, 473</td>
</tr>
<tr>
<td>Myint, Yan Lynn</td>
<td>451</td>
</tr>
<tr>
<td>Mytlykbai, Rysmakhanov</td>
<td>553</td>
</tr>
<tr>
<td>Mytlykbay, Rysmakhanov</td>
<td>535</td>
</tr>
<tr>
<td>Myrzabayeva, Aliya</td>
<td>561</td>
</tr>
<tr>
<td>Myung, Jisun</td>
<td>280, 354</td>
</tr>
<tr>
<td>NA, Byeong-Gon</td>
<td>539</td>
</tr>
<tr>
<td>Nadiar, Mussin</td>
<td>553</td>
</tr>
<tr>
<td>NA, Gun Hyung</td>
<td>539</td>
</tr>
<tr>
<td>Nahm, Ji Hae</td>
<td>477</td>
</tr>
<tr>
<td>Nah, Yang Won</td>
<td>556</td>
</tr>
<tr>
<td>Na, Jieun</td>
<td>372</td>
</tr>
<tr>
<td>Nakajima, Keiko</td>
<td>300</td>
</tr>
<tr>
<td>Nam, Chang Mo</td>
<td>328</td>
</tr>
<tr>
<td>Nam, Eun Woo</td>
<td>401</td>
</tr>
<tr>
<td>Nam, Hee Chul</td>
<td>282, 283, 316, 317, 327, 334, 344, 357, 359, 375, 379, 383, 397, 446, 486</td>
</tr>
<tr>
<td>Nam, Hoang Duct</td>
<td>517</td>
</tr>
<tr>
<td>Nam, Hyo Suk</td>
<td>471</td>
</tr>
<tr>
<td>Na, Min Jung</td>
<td>486</td>
</tr>
<tr>
<td>Nam, Joon Yeu</td>
<td>318, 480</td>
</tr>
<tr>
<td>Nam, Jun Yeo</td>
<td>298</td>
</tr>
<tr>
<td>Nam, Seong Woo</td>
<td>322, 380, 444, 455</td>
</tr>
<tr>
<td>Nam, Soon Woo</td>
<td>316, 317, 325, 366, 494, 497</td>
</tr>
<tr>
<td>Nam, Suk Woo</td>
<td>486</td>
</tr>
<tr>
<td>Narantuya, Shinebayar</td>
<td>415, 443</td>
</tr>
<tr>
<td>Naranzul N</td>
<td>437</td>
</tr>
<tr>
<td>Author</td>
<td>Page</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Naranzul, N.</td>
<td>438</td>
</tr>
<tr>
<td>Navarro, Jonathan</td>
<td>457</td>
</tr>
<tr>
<td>NAVARRO, Jonathan</td>
<td>533</td>
</tr>
<tr>
<td>Nawara, Hend M</td>
<td>491</td>
</tr>
<tr>
<td>Na, Young Sun</td>
<td>478</td>
</tr>
<tr>
<td>Nazerke, Seidakhetova</td>
<td>535</td>
</tr>
<tr>
<td>Neff, Guy</td>
<td>473</td>
</tr>
<tr>
<td>Negi, Pooja</td>
<td>317</td>
</tr>
<tr>
<td>Nepal, Gaurav</td>
<td>519</td>
</tr>
<tr>
<td>Neupane, Mani</td>
<td>414,575</td>
</tr>
<tr>
<td>NGHIEM, Ha</td>
<td>306</td>
</tr>
<tr>
<td>Ng, Irene Oi-Lin</td>
<td>271</td>
</tr>
<tr>
<td>NGO, Trung Tat</td>
<td>410</td>
</tr>
<tr>
<td>Ng, Teresa I</td>
<td>429</td>
</tr>
<tr>
<td>Nguyen, Cong Long</td>
<td>494</td>
</tr>
<tr>
<td>NGUYEN, Giang</td>
<td>306</td>
</tr>
<tr>
<td>NGUYEN, Hung</td>
<td>306</td>
</tr>
<tr>
<td>NGUYEN, Lam Ngoc Dai</td>
<td>410</td>
</tr>
<tr>
<td>Nguyen, Mindie H.</td>
<td>315</td>
</tr>
<tr>
<td>Nguyen, Nghe Tinh</td>
<td>494</td>
</tr>
<tr>
<td>Nguyen, Thanh Nam</td>
<td>494</td>
</tr>
<tr>
<td>NGUYEN, Thinh Tien</td>
<td>410</td>
</tr>
<tr>
<td>Nguyen, Tuan</td>
<td>284,473</td>
</tr>
<tr>
<td>Nimisha</td>
<td>406</td>
</tr>
<tr>
<td>NIMJE, Rohit</td>
<td>364</td>
</tr>
<tr>
<td>Ni, Nwe</td>
<td>451</td>
</tr>
<tr>
<td>Nirala, Satendra Kumar</td>
<td>403</td>
</tr>
<tr>
<td>Ni, Xiaoqian</td>
<td>531</td>
</tr>
<tr>
<td>Ni, Xiaoling</td>
<td>531</td>
</tr>
<tr>
<td>Noh, Choong Kyun</td>
<td>319</td>
</tr>
<tr>
<td>Noh, Hyojin</td>
<td>290,376</td>
</tr>
<tr>
<td>North, John</td>
<td>568</td>
</tr>
<tr>
<td>Nurbulat, Uteulin</td>
<td>525</td>
</tr>
<tr>
<td>Nurlan, Mamashev</td>
<td>505,506</td>
</tr>
<tr>
<td>Nurmagambetov, Azamat</td>
<td>481</td>
</tr>
<tr>
<td>Nurmukhametova, Elena</td>
<td>280</td>
</tr>
<tr>
<td>Nyamaa, Bayarmaa</td>
<td>415,430,434,443</td>
</tr>
</tbody>
</table>

**O**

<table>
<thead>
<tr>
<th>Author</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ochiya, Takahiro</td>
<td>124</td>
</tr>
<tr>
<td>Odgerel Ts</td>
<td>437</td>
</tr>
<tr>
<td>Oh, Cheong-Hae</td>
<td>492</td>
</tr>
<tr>
<td>Ohdan, Hideki</td>
<td>488,553</td>
</tr>
<tr>
<td>Oh, Dong Kyu</td>
<td>541</td>
</tr>
<tr>
<td>Oh, Eun Ju</td>
<td>288</td>
</tr>
<tr>
<td>Oh, Hyunwoo</td>
<td>315,376</td>
</tr>
<tr>
<td>Oh, Hyun-Woo</td>
<td>421,424</td>
</tr>
<tr>
<td>Oh, In-Hwan</td>
<td>280,354</td>
</tr>
<tr>
<td>Ohira, Masahiro</td>
<td>553</td>
</tr>
<tr>
<td>Oh, Ji-Hye</td>
<td>301</td>
</tr>
<tr>
<td>Oh, Jin-Kyoung</td>
<td>414</td>
</tr>
<tr>
<td>Oh, Jongwook</td>
<td>388</td>
</tr>
<tr>
<td>Oh, Joo Hyun</td>
<td>311,472</td>
</tr>
<tr>
<td>Oh, Seok Hee</td>
<td>292</td>
</tr>
<tr>
<td>Oh, Seung Cheol</td>
<td>541</td>
</tr>
<tr>
<td>Oh, Sohee</td>
<td>347</td>
</tr>
<tr>
<td>Oh, Sooyeon</td>
<td>308</td>
</tr>
<tr>
<td>Ohtsuka, Masayuki</td>
<td>168</td>
</tr>
<tr>
<td>Oidov, Tsogzolmaa</td>
<td>498</td>
</tr>
<tr>
<td>Okada, Kenichi</td>
<td>156</td>
</tr>
<tr>
<td>Okanoue, T</td>
<td>284</td>
</tr>
<tr>
<td>Okanoue, Takeshi</td>
<td>473</td>
</tr>
<tr>
<td>Ok, Baek Geum</td>
<td>289,384</td>
</tr>
<tr>
<td>Orazbaeva D.R.</td>
<td>562</td>
</tr>
<tr>
<td>Osinus, Anu</td>
<td>294,431</td>
</tr>
<tr>
<td>Osinus, Anu O.</td>
<td>351</td>
</tr>
<tr>
<td>Osman, Amira M</td>
<td>491</td>
</tr>
<tr>
<td>Ospanova, Arailym</td>
<td>546</td>
</tr>
<tr>
<td>Ospanov, Shahrarat</td>
<td>482</td>
</tr>
<tr>
<td>Otohnbayar, O.</td>
<td>440</td>
</tr>
</tbody>
</table>

**P**

<table>
<thead>
<tr>
<th>Author</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAIK, Kwang Yeol</td>
<td>363</td>
</tr>
<tr>
<td>Paik, Yong-Han</td>
<td>173,274,282,378,420,493,495</td>
</tr>
<tr>
<td>Paik, Young-Ki</td>
<td>556</td>
</tr>
<tr>
<td>Pakkirisamy, Umamaheswari</td>
<td>405</td>
</tr>
<tr>
<td>PALLONI, Andrea</td>
<td>500</td>
</tr>
<tr>
<td>PALMISANO, Angela</td>
<td>504</td>
</tr>
<tr>
<td>Pan, Calvin Q.</td>
<td>345</td>
</tr>
<tr>
<td>Parasar, Kunal</td>
<td>562</td>
</tr>
<tr>
<td>Parhy, Bandita</td>
<td>366</td>
</tr>
<tr>
<td>Park, Bo Ryung</td>
<td>367,418</td>
</tr>
<tr>
<td>PARK, Boyoung</td>
<td>543</td>
</tr>
<tr>
<td>Park, Chang Hwan</td>
<td>398</td>
</tr>
<tr>
<td>Park, Cheon Soo</td>
<td>509,526</td>
</tr>
<tr>
<td>Park, Choong Kee</td>
<td>433,445</td>
</tr>
<tr>
<td>PARK, Dae Joon</td>
<td>363</td>
</tr>
<tr>
<td>Park, Dong Jun</td>
<td>291,344,346,427,469</td>
</tr>
<tr>
<td>Park, Dong Kyun</td>
<td>339,373</td>
</tr>
<tr>
<td>Park, DoYeun</td>
<td>75</td>
</tr>
<tr>
<td>Park, Eun Ji</td>
<td>367,418</td>
</tr>
<tr>
<td>PARK, Eunkyu</td>
<td>523</td>
</tr>
<tr>
<td>Park, Eun Taek</td>
<td>435</td>
</tr>
<tr>
<td>Park Gil-Chun</td>
<td>313</td>
</tr>
<tr>
<td>Park, Gil-Chun</td>
<td>271,388,389,484,543</td>
</tr>
<tr>
<td>Park, Hana</td>
<td>292,382</td>
</tr>
<tr>
<td>Park, Han Seul</td>
<td>291</td>
</tr>
<tr>
<td>Park, Hee Hyun</td>
<td>512</td>
</tr>
<tr>
<td>Park, Hee Sun</td>
<td>285</td>
</tr>
<tr>
<td>PARK, Hwon Kyun</td>
<td>543</td>
</tr>
<tr>
<td>Park, Hye Jung</td>
<td>277,353,406</td>
</tr>
<tr>
<td>Park, Hye Kyong</td>
<td>493</td>
</tr>
<tr>
<td>Park, Hyun-Jin</td>
<td>411</td>
</tr>
<tr>
<td>Park, Jae Berm</td>
<td>420</td>
</tr>
<tr>
<td>Park, Jae Ho</td>
<td>367</td>
</tr>
<tr>
<td>Park, Jeong-Ik</td>
<td>558</td>
</tr>
<tr>
<td>Name</td>
<td>Pages</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>RON, Yefei</td>
<td>528</td>
</tr>
<tr>
<td>Ro, Simon W.</td>
<td>288,375,406,407,408,480</td>
</tr>
<tr>
<td>Rou, Woo Sun</td>
<td>328,346,377,410,423,439,572</td>
</tr>
<tr>
<td>Ro, Weonsang</td>
<td>11</td>
</tr>
<tr>
<td>Ryoo, Baek-Yeol</td>
<td>136</td>
</tr>
<tr>
<td>Rysmakhanov, M.S.</td>
<td>453,541,543</td>
</tr>
<tr>
<td>Rysmakhanov, Mytykby</td>
<td>546</td>
</tr>
<tr>
<td>Ryspanbetov, Zh.</td>
<td>488</td>
</tr>
<tr>
<td>Ryu, Dong Hee</td>
<td>521</td>
</tr>
<tr>
<td>Ryu, Hwaseong</td>
<td>448</td>
</tr>
<tr>
<td>Ryu, Seongho</td>
<td>291</td>
</tr>
<tr>
<td>Ryu, Seungho</td>
<td>372</td>
</tr>
<tr>
<td>Ryu, Seung Yeon</td>
<td>359</td>
</tr>
<tr>
<td>Ryu, Shin-Young</td>
<td>469</td>
</tr>
<tr>
<td>Ryu, Soo Hyung</td>
<td>436,478</td>
</tr>
<tr>
<td>Ryu, Sungwoo</td>
<td>475</td>
</tr>
<tr>
<td>Ryu, Tom</td>
<td>291,338,398</td>
</tr>
<tr>
<td>Saeed, Waqar Khalid</td>
<td>406,465</td>
</tr>
<tr>
<td>Sah, Ashok Kumar</td>
<td>458</td>
</tr>
<tr>
<td>SAINT cohort study group</td>
<td>421</td>
</tr>
<tr>
<td>SAINT Study Group</td>
<td>424</td>
</tr>
<tr>
<td>Sakamoto, Naoya</td>
<td>142</td>
</tr>
<tr>
<td>Saluja, Sundeep Singh</td>
<td>406,562</td>
</tr>
<tr>
<td>SAN, Aye Min</td>
<td>534</td>
</tr>
<tr>
<td>Sanduivaj, R.</td>
<td>498</td>
</tr>
<tr>
<td>Santos, Ana Gabriela Pires dos</td>
<td>353</td>
</tr>
<tr>
<td>Sapkota, Srijana</td>
<td>458</td>
</tr>
<tr>
<td>Sarangua, G</td>
<td>573</td>
</tr>
<tr>
<td>Sarin, Shiv</td>
<td>284,473</td>
</tr>
<tr>
<td>Sarin, Shiv Kumar</td>
<td>317</td>
</tr>
<tr>
<td>Sarkitovich, Setaev Saken</td>
<td>546</td>
</tr>
<tr>
<td>Saruul, B.</td>
<td>437</td>
</tr>
<tr>
<td>Sato, Koki</td>
<td>553</td>
</tr>
<tr>
<td>Savilov, Eugeny</td>
<td>498</td>
</tr>
<tr>
<td>Saxena, Dhiraj</td>
<td>568</td>
</tr>
<tr>
<td>Schnell, Gretja</td>
<td>294</td>
</tr>
<tr>
<td>Schwabe, Christian</td>
<td>351</td>
</tr>
<tr>
<td>Segev, Dorry L.</td>
<td>204</td>
</tr>
<tr>
<td>Seidakhetmetov, Akhmet</td>
<td>553</td>
</tr>
<tr>
<td>Seitova, Aizhan</td>
<td>547</td>
</tr>
<tr>
<td>Seitzhanov, Askhat</td>
<td>456</td>
</tr>
<tr>
<td>SELVAKUMAR, Naganathan</td>
<td>390</td>
</tr>
<tr>
<td>Seno, Akimasa</td>
<td>491</td>
</tr>
<tr>
<td>Seno, Masaharu</td>
<td>491</td>
</tr>
<tr>
<td>S. Chul Won</td>
<td>289,384,493</td>
</tr>
<tr>
<td>Seo, Chung Gyo</td>
<td>507</td>
</tr>
<tr>
<td>Seo, Hye-Young</td>
<td>333</td>
</tr>
<tr>
<td>Seo, Jae Kyoung</td>
<td>377</td>
</tr>
<tr>
<td>Seo, Jongwon</td>
<td>377</td>
</tr>
<tr>
<td>Seok, Jin-I</td>
<td>391,567</td>
</tr>
<tr>
<td>Seo, Kwang II</td>
<td>295</td>
</tr>
<tr>
<td>Seo, Kwang II</td>
<td>435</td>
</tr>
<tr>
<td>Seong, Gyeol</td>
<td>282</td>
</tr>
<tr>
<td>Seong, In-Ock</td>
<td>492</td>
</tr>
<tr>
<td>Seong, Jinsil</td>
<td>299,387</td>
</tr>
<tr>
<td>Seong, Moon-Woo</td>
<td>342</td>
</tr>
<tr>
<td>Seo, Seung Young</td>
<td>348,359</td>
</tr>
<tr>
<td>Seo, Sooin</td>
<td>541</td>
</tr>
<tr>
<td>Seo, Wonhyo</td>
<td>338</td>
</tr>
<tr>
<td>Seo, Won Woo</td>
<td>293,369,409</td>
</tr>
<tr>
<td>Seo, Won Wu</td>
<td>343</td>
</tr>
<tr>
<td>Seo, Yeon Seok</td>
<td>96,289,310,314,321,324,331,346,349,350,368,370,374,380,385,415,416,478,496,507,515,516</td>
</tr>
<tr>
<td>Seo, Yeon Suk</td>
<td>421</td>
</tr>
<tr>
<td>Seo, Youn Seok</td>
<td>344</td>
</tr>
<tr>
<td>Sergelen, Bolortsetseg</td>
<td>459</td>
</tr>
<tr>
<td>Serikbayev, Yerbulan</td>
<td>544</td>
</tr>
<tr>
<td>Serik, Zharikov</td>
<td>535</td>
</tr>
<tr>
<td>Serkulov, Alibek</td>
<td>534</td>
</tr>
<tr>
<td>Seto, Wai Kay Walter</td>
<td>280,345</td>
</tr>
<tr>
<td>Shafran, Stephen David</td>
<td>351</td>
</tr>
<tr>
<td>Shalimar</td>
<td>345</td>
</tr>
<tr>
<td>Sharav, Bold</td>
<td>437</td>
</tr>
<tr>
<td>Sharma, Abhay Kumar</td>
<td>406</td>
</tr>
<tr>
<td>Sharma, Bhoopendra</td>
<td>458</td>
</tr>
<tr>
<td>Sharma, Bimala</td>
<td>401,414</td>
</tr>
<tr>
<td>SHARMA, Gopal</td>
<td>364</td>
</tr>
<tr>
<td>Sharma, Rohit</td>
<td>405</td>
</tr>
<tr>
<td>Sharma, SB</td>
<td>402</td>
</tr>
<tr>
<td>Sharma, Sujan</td>
<td>458</td>
</tr>
<tr>
<td>SHARMA, Vishal</td>
<td>364</td>
</tr>
<tr>
<td>Sharmenov, Abuyaikhan</td>
<td>547,548</td>
</tr>
<tr>
<td>Shasthrty, SM</td>
<td>20</td>
</tr>
<tr>
<td>Sheen, I-Shyan</td>
<td>429</td>
</tr>
<tr>
<td>SHEHTA, Ahmed</td>
<td>390</td>
</tr>
<tr>
<td>Sheikh, Aasim</td>
<td>473</td>
</tr>
<tr>
<td>SHEN, Feng</td>
<td>330,387,489,503,527</td>
</tr>
<tr>
<td>SHEN, Sheng</td>
<td>531</td>
</tr>
<tr>
<td>SHENVI, Sunil</td>
<td>364</td>
</tr>
<tr>
<td>Shen, Xue-Yin</td>
<td>306</td>
</tr>
<tr>
<td>SHEN, Xue-Yin</td>
<td>539</td>
</tr>
<tr>
<td>Shiffman, Mitchell L.</td>
<td>284,473</td>
</tr>
<tr>
<td>Shiina, Shuichiro</td>
<td>199,236</td>
</tr>
<tr>
<td>Shim, Jae Jun</td>
<td>433</td>
</tr>
<tr>
<td>Shim, Ja-Jun</td>
<td>270,280,354,421,424,491</td>
</tr>
<tr>
<td>Shim, Ju Hyun</td>
<td>46,298,301,320,385,496</td>
</tr>
<tr>
<td>Shim, Young-Ri</td>
<td>338,398</td>
</tr>
<tr>
<td>SHIN, Aesun</td>
<td>312</td>
</tr>
<tr>
<td>Shin, Dong Wook</td>
<td>334</td>
</tr>
<tr>
<td>Shin, Eui-Cheol</td>
<td>8,277,344</td>
</tr>
<tr>
<td>Shin, Hyun Phil</td>
<td>439</td>
</tr>
<tr>
<td>Shin, In Sik</td>
<td>502,549</td>
</tr>
<tr>
<td>Shin, Ji-Hyun</td>
<td>289</td>
</tr>
<tr>
<td>Shin, Jongbeom</td>
<td>371,497</td>
</tr>
<tr>
<td>Shin, Jung</td>
<td>380,444</td>
</tr>
<tr>
<td>Name</td>
<td>Page</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Shin, Jung Woo</td>
<td>367,418</td>
</tr>
<tr>
<td>Shin, Min Jea</td>
<td>309,338,465,466,467</td>
</tr>
<tr>
<td>Shin, Min Young</td>
<td>410,423,439,572</td>
</tr>
<tr>
<td>Shin, Seung Kak</td>
<td>55,339,373,422</td>
</tr>
<tr>
<td>Shin, Soonyeong</td>
<td>407</td>
</tr>
<tr>
<td>Shin, Soonyoung</td>
<td>288,408</td>
</tr>
<tr>
<td>SHIN, Yong Chan</td>
<td>522</td>
</tr>
<tr>
<td>Shin, Yun Jae</td>
<td>436,478</td>
</tr>
<tr>
<td>Shin, Yu Ri</td>
<td>325</td>
</tr>
<tr>
<td>Shrestha, Abhishek</td>
<td>408</td>
</tr>
<tr>
<td>Shrestha, Manisha</td>
<td>458</td>
</tr>
<tr>
<td>Shrestha, Nirajan</td>
<td>404</td>
</tr>
<tr>
<td>Shrestha, Rojeet</td>
<td>464,573</td>
</tr>
<tr>
<td>Shridhar, Patil</td>
<td>455</td>
</tr>
<tr>
<td>Shukla, Pramod Shankar</td>
<td>573</td>
</tr>
<tr>
<td>SIDDIQUI, Hafiz Abdul Basit</td>
<td>402</td>
</tr>
<tr>
<td>SIDOROV, Dmitry</td>
<td>504,505</td>
</tr>
<tr>
<td>Sigdel, Manoj</td>
<td>574</td>
</tr>
<tr>
<td>Singh, Deepika</td>
<td>451</td>
</tr>
<tr>
<td>Singh, Dharmender</td>
<td>485</td>
</tr>
<tr>
<td>SINGH, Harjeet</td>
<td>364</td>
</tr>
<tr>
<td>Singh, Manvendra</td>
<td>451</td>
</tr>
<tr>
<td>Singh, Narendra K.</td>
<td>291</td>
</tr>
<tr>
<td>Singh, Ranbir</td>
<td>485</td>
</tr>
<tr>
<td>Sinha, Sukrat</td>
<td>461</td>
</tr>
<tr>
<td>Sinn, Dong Hyun</td>
<td>270,274,282,311,318,322,344,372,420,454,472,493,499</td>
</tr>
<tr>
<td>Sinn, Dong-Hyun</td>
<td>298,378,420,495</td>
</tr>
<tr>
<td>Sise, Meghan</td>
<td>431</td>
</tr>
<tr>
<td>Skelly, Deanne</td>
<td>404</td>
</tr>
<tr>
<td>Smagulov, A.</td>
<td>482</td>
</tr>
<tr>
<td>Smith, Nate</td>
<td>293</td>
</tr>
<tr>
<td>Sochnieva, Anastasiia Luvna</td>
<td>518</td>
</tr>
<tr>
<td>SOE, Myat Su Mon</td>
<td>534</td>
</tr>
<tr>
<td>Sohn, Jenny</td>
<td>564,566</td>
</tr>
<tr>
<td>Sohn, Joo Hyun</td>
<td>228,322,455</td>
</tr>
<tr>
<td>Sohn, Kyung Min</td>
<td>459</td>
</tr>
<tr>
<td>Sohn, Won</td>
<td>370,421</td>
</tr>
<tr>
<td>Sokal, Etienne</td>
<td>429</td>
</tr>
<tr>
<td>Soloveva N. A</td>
<td>411</td>
</tr>
<tr>
<td>Soloveva Y. A.</td>
<td>411</td>
</tr>
<tr>
<td>Song, Bo-Hye</td>
<td>379</td>
</tr>
<tr>
<td>Song, Dong Woo</td>
<td>342</td>
</tr>
<tr>
<td>Song, Do Seon</td>
<td>322,349,371,383,454,494,497</td>
</tr>
<tr>
<td>Song, Gi-Won</td>
<td>271,298,375,388,484,508,543</td>
</tr>
<tr>
<td>SONG, Gi Won</td>
<td>389</td>
</tr>
<tr>
<td>SONG, Gi-Won</td>
<td>313</td>
</tr>
<tr>
<td>Song, Il Han</td>
<td>435</td>
</tr>
<tr>
<td>Song, In-Sang</td>
<td>492</td>
</tr>
<tr>
<td>Song, Jeong Eun</td>
<td>254,314,371</td>
</tr>
<tr>
<td>Song, Ki Byung</td>
<td>558</td>
</tr>
<tr>
<td>Song, Mi Kyoung</td>
<td>356</td>
</tr>
<tr>
<td>Song, Myeong Jun</td>
<td>296,383</td>
</tr>
<tr>
<td>SONG, Sanghwa</td>
<td>521</td>
</tr>
<tr>
<td>Song, Young Bin</td>
<td>372</td>
</tr>
<tr>
<td>Song, Young Rim</td>
<td>445</td>
</tr>
<tr>
<td>Son, MiJu</td>
<td>328</td>
</tr>
<tr>
<td>Sputayev, Zhanat</td>
<td>548</td>
</tr>
<tr>
<td>Spaulding, Anne</td>
<td>431</td>
</tr>
<tr>
<td>Squires, Robert H</td>
<td>429</td>
</tr>
<tr>
<td>Stepanova, Maria</td>
<td>284</td>
</tr>
<tr>
<td>Stepanova, Tatjana</td>
<td>345</td>
</tr>
<tr>
<td>Strasser, Simone</td>
<td>473</td>
</tr>
<tr>
<td>Strasser, Simone L.</td>
<td>351</td>
</tr>
<tr>
<td>Streinu-Cercel, Adrian</td>
<td>280</td>
</tr>
<tr>
<td>Strokov, Tatsiana</td>
<td>429</td>
</tr>
<tr>
<td>Subedi, Nuwadatta</td>
<td>399</td>
</tr>
<tr>
<td>Subramanian, G. Mani</td>
<td>284,473</td>
</tr>
<tr>
<td>Subramanian, Senthil Kumar</td>
<td>405</td>
</tr>
<tr>
<td>Sudiarso, Hilmi Ardian</td>
<td>468</td>
</tr>
<tr>
<td>Suh, Chul Won</td>
<td>308,319</td>
</tr>
<tr>
<td>Suh, Dong Jin</td>
<td>496</td>
</tr>
<tr>
<td>Suh, Jeong II</td>
<td>322,432,455</td>
</tr>
<tr>
<td>Suh, Kyung-Suk</td>
<td>304,318,319,330,412,535,541,557</td>
</tr>
<tr>
<td>Suh, Kyung-Suk</td>
<td>312,388,390,537,538</td>
</tr>
<tr>
<td>Suh, Sang Jun</td>
<td>310,314,331,344,346,349,350,368,370,374,380,385,421,422,478,496,507</td>
</tr>
<tr>
<td>Suk, Ki Tae</td>
<td>158,309,314,322,324,338,371,433,454,465,466,467</td>
</tr>
<tr>
<td>Sulaberidze, Gela</td>
<td>470</td>
</tr>
<tr>
<td>Sultangereyev, E.B.</td>
<td>543</td>
</tr>
<tr>
<td>Sung, Chang Ohk</td>
<td>301</td>
</tr>
<tr>
<td>Sung, Min Je</td>
<td>357,472,479</td>
</tr>
<tr>
<td>Sung, Pil Soo</td>
<td>283,316,325,327,334,344,346,359,375,379,383,397,427,446,486,494,497</td>
</tr>
<tr>
<td>SUN, Hai-Ying</td>
<td>527</td>
</tr>
<tr>
<td>SUO, Tao</td>
<td>531</td>
</tr>
<tr>
<td>Suri, Vithika</td>
<td>280,345</td>
</tr>
<tr>
<td>Surova, Rokiya</td>
<td>457</td>
</tr>
<tr>
<td>Su, Wei-Wen</td>
<td>431</td>
</tr>
<tr>
<td>Sydykova L. A.</td>
<td>411</td>
</tr>
<tr>
<td>SYRULBAV, Dariga</td>
<td>529</td>
</tr>
<tr>
<td>Sze, Karen Man-Fong</td>
<td>271</td>
</tr>
<tr>
<td>T</td>
<td></td>
</tr>
<tr>
<td>Tabak, Fehmi</td>
<td>280</td>
</tr>
<tr>
<td>Tahara, Hiroyuki</td>
<td>553</td>
</tr>
<tr>
<td>Takano, Shigetsugu</td>
<td>168</td>
</tr>
<tr>
<td>Takayashiki, Tsukasa</td>
<td>168</td>
</tr>
<tr>
<td>Tak, Eun Young</td>
<td>484</td>
</tr>
<tr>
<td>Tak, Kwon Yong</td>
<td>325,334,359,379,383,397,446</td>
</tr>
<tr>
<td>Tak, Won Young</td>
<td>131,281,340,344,345,346,377,378,381,415,429,432</td>
</tr>
<tr>
<td>Tamada, Ryohei</td>
<td>573</td>
</tr>
<tr>
<td>Author</td>
<td>Page</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Tanaka, Atsushi</td>
<td>146</td>
</tr>
<tr>
<td>Tanaka, Yasuhiro</td>
<td>33</td>
</tr>
<tr>
<td>Tanaka, Yuka</td>
<td>488</td>
</tr>
<tr>
<td>Taneja, BK</td>
<td>404</td>
</tr>
<tr>
<td>TAN, Luc DAO</td>
<td>564</td>
</tr>
<tr>
<td>TANVEER, Zunera</td>
<td>500</td>
</tr>
<tr>
<td>TAVOLARI1, Simona</td>
<td>500</td>
</tr>
<tr>
<td>Terai, Shuji</td>
<td>150</td>
</tr>
<tr>
<td>Thai, Nguyen Van</td>
<td>426</td>
</tr>
<tr>
<td>Thant, Khine Nwe</td>
<td>571</td>
</tr>
<tr>
<td>The Korean Study Group of Portal Hypertension</td>
<td>324</td>
</tr>
<tr>
<td>The Korean TACE Study Group</td>
<td>378,381</td>
</tr>
<tr>
<td>THU, Myo Myat</td>
<td>534</td>
</tr>
<tr>
<td>Thuy, Tran Ngoc</td>
<td>447,516</td>
</tr>
<tr>
<td>TIAN, Xiaodong</td>
<td>364,530,531</td>
</tr>
<tr>
<td>Tilek, Umetaliev</td>
<td>506,554,555,559,560</td>
</tr>
<tr>
<td>Tiwari, Bishnu Raj</td>
<td>401,414,575</td>
</tr>
<tr>
<td>Tleulev, Bolat</td>
<td>482</td>
</tr>
<tr>
<td>TOMMASO, Luca Di</td>
<td>504</td>
</tr>
<tr>
<td>Toolubbek, Sakamamakov</td>
<td>560</td>
</tr>
<tr>
<td>Toolubbek, Sakamamtol</td>
<td>559</td>
</tr>
<tr>
<td>Toremuratov, Bekzat</td>
<td>554</td>
</tr>
<tr>
<td>TORZILLI, Guido</td>
<td>504</td>
</tr>
<tr>
<td>TOVOLI, Francesco</td>
<td>500</td>
</tr>
<tr>
<td>TOVUU, Lkhagva-Ochir</td>
<td>461</td>
</tr>
<tr>
<td>Trauner, Michael</td>
<td>284,473</td>
</tr>
<tr>
<td>Trehanpati, Nirupma</td>
<td>317</td>
</tr>
<tr>
<td>Trinh, Roger</td>
<td>294,353</td>
</tr>
<tr>
<td>TRUNG, Hieu LE</td>
<td>564</td>
</tr>
<tr>
<td>TSAI, Chun-Yi</td>
<td>501</td>
</tr>
<tr>
<td>Tsang, Owen</td>
<td>345</td>
</tr>
<tr>
<td>Tseng, Kuo-Chih</td>
<td>352</td>
</tr>
<tr>
<td>Tserendagva D</td>
<td>437</td>
</tr>
<tr>
<td>Tserendeijd Ts</td>
<td>437,438</td>
</tr>
<tr>
<td>Tsevelmaa, Munkhchuluun</td>
<td>438</td>
</tr>
<tr>
<td>Tsevelmaa, O.</td>
<td>441</td>
</tr>
<tr>
<td>Tse, Yee-Kit</td>
<td>316</td>
</tr>
<tr>
<td>Tsui, Yu-Man</td>
<td>271</td>
</tr>
<tr>
<td>Tuan, Le Quoc</td>
<td>369</td>
</tr>
<tr>
<td>TUAN, LE QUOC</td>
<td>518</td>
</tr>
<tr>
<td>Tugsila, Yuporn</td>
<td>569,572</td>
</tr>
<tr>
<td>Tukennova, A.</td>
<td>541</td>
</tr>
<tr>
<td>Tun, Yarzar</td>
<td>451</td>
</tr>
<tr>
<td>Tuvshinbayar</td>
<td>437</td>
</tr>
<tr>
<td>Uemura, Kenichiro</td>
<td>553</td>
</tr>
<tr>
<td>Ueno, Masaki</td>
<td>156</td>
</tr>
<tr>
<td>Ueshima, Kazuomi</td>
<td>130</td>
</tr>
<tr>
<td>Ulzmaa, G.</td>
<td>427,437</td>
</tr>
<tr>
<td>Umirbekov, Yerlan</td>
<td>460</td>
</tr>
<tr>
<td>Um, Kang Hyun</td>
<td>421</td>
</tr>
<tr>
<td>Um, Soon Ho</td>
<td>289,310,314,324,331,344,346,349,350,368,370,380,415,478,496,507,515,516</td>
</tr>
<tr>
<td>Um, Sun Ho</td>
<td>421</td>
</tr>
<tr>
<td>Uugantssetseg G</td>
<td>437</td>
</tr>
</tbody>
</table>
Vaishnav, Jayesh  443
VALLEE, Jean Charles DUCLOS  500
Valle-Segarra, Antonio del  429
VAN, Linh HO  564
VAN, Loi LE  564
VAN, Quang VU  564
VAN, Thanh LE  564
Varshney, Vaibhav Kumar  562
Vasavada, Bhavin  532,563
VASAVADA, Bhavin  400
VASURI, Francesco  500
VASWANI, Prateek  364
Verma, Sagar  520
Viktorovic, Bobrov Nikolay  391
Vogel, Arndt  134
Vu, Manh Duy  494
Vuppalanchi, Raj  284
Vu, Quang Van  410,553
Vu, Truong Khanh  494
Vyas, Ashish Kumar  317
Wai, Thazin Soe  552
WANG, Bo  531
Wang, Chen-Yu  294
WANG, Dansong  528
WANG, Gang  529
Wang, Hee-Jung  306,319,539
WANG, Hong  330,387,489
Wang, Horng-Yuan  429
WANG, Jiwen  531
Wang, Lei  417
WANG, Ming-Da  387,503,527
WANG, Qi  364
Wang, Shang Yu  161
WANG, Shang-Yu  501
Wang, Stanley  294
WANG, Xu'an  301
WANG, Xuefeng  301
WANG, Yazhou  364,530
Wei, Lai  294
Wenchuan W  528
WENG, Hao  301
Win, Khin Maung  571
Win, Si Thu Sein  571
Wong, Carmen Chak-Lui  271
Wong, Gabriel  293
Wong, Grace Lai-Hung  286,316
Wong, Vincent  22,114
Wong, Vincent Wai-Sun  284,286,316,473
Won, Kyoong Sook  519
Won, Yong Kyun  294,353,429

Won, Yoo Dong  536
Woo, Eun Jung  308
Woo, Sang Myung  511
Wu, Bin  417
WU, Han  387,489
WU, Meng-Chao  387
WU, Wenchuan  528,531
WU, Wenguang  301
WU, Zichen  528

Xie, Qing  294
XING, Hao  387,489,527
Xue, Zhenyi  353
XU, Xin-Fei  527
XU, Xuefeng  528
XU, Yaolin  528

Yabushita, Yasuhiro  87
Yadav, Dhananjay  470
Yadav, Ekta  481
Yadav, Naval Kishor  573,574
Yadav, Nutan  474
Yadav, Pankajkumar  442
Yadav, Satya Narayan  456
Yamaue, Hiroki  156
Yang, Gyung-deck  438
Yang, Hee Chan  348,359
Yang, Hee Doo  486
Yang, Hye Yeon  275
Yang, Hyun  325,334,359,379,446
YANG, Jae Do  510,522
Yang, Jin Mo  322,371,383,455,494,497
Yang, Keungmo  325,338,398,427
Yang, Seok-hun  340
Yang, Seok Jeong  313,542
YANG, Tian  330,387,489,503,527
Yang, Yida  417
YANG, Yinmo  364,530,531
Yatsushashi, Hiroshi  345
YEH, Chun-Nan  501
Yeh, Ming-Lun  430
YEH, Ta-Sen  501
Yelchibayev, Berdibek  534
Yelemessov, A.A.  543
Yelemessov, Asset  460
Yelbeyev, Albat  545
Yen, Le Thi Hoang  444
Yeo, Ji Hyun  293,343,369,409
Yeo, Min-Kyung  492
Yeong, Jong Eun  285,310,331,349,350,368,370,374,385,421,422,478,496,516
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yemiyanov, N.</td>
<td>550</td>
<td>2012</td>
</tr>
<tr>
<td>Yim, Sung Kyun</td>
<td>348, 359</td>
<td>2012</td>
</tr>
<tr>
<td>Yim, Sun Young</td>
<td>289, 310, 314, 331, 344, 346, 349, 350, 370, 380, 421, 496, 507</td>
<td>2012</td>
</tr>
<tr>
<td>Yi, Nam-Joon</td>
<td>304, 312, 318, 329, 330, 389, 412, 535, 537, 538, 541, 557</td>
<td>2012</td>
</tr>
<tr>
<td>YIN, Hanlin</td>
<td>531</td>
<td>2012</td>
</tr>
<tr>
<td>Yip, Terry Cheuk-Fung</td>
<td>316</td>
<td>2012</td>
</tr>
<tr>
<td>Yi, Woo Jin</td>
<td>434</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, and Kwon</td>
<td>286</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, Jae Eun</td>
<td>324, 351, 356</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, Jeong-Ju</td>
<td>291, 310, 314, 324, 326, 335, 346, 355, 356, 373</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, Kideok</td>
<td>457</td>
<td>2012</td>
</tr>
<tr>
<td>Yook, Jong In</td>
<td>406</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, Kwon</td>
<td>318, 378, 480</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Byung Cheol</td>
<td>435</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Byung Chul</td>
<td>293, 343, 369, 409</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Dong Sup</td>
<td>363, 390, 520</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Eileen</td>
<td>371</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Eileen L</td>
<td>50, 322, 349, 421, 424, 454</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Jae Hyeon</td>
<td>371, 432, 449</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Jai Hoon</td>
<td>293, 343, 369, 409</td>
<td>2012</td>
</tr>
<tr>
<td>YOON, Junghyun</td>
<td>543</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Jun Sik</td>
<td>298, 356</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Ki Tae</td>
<td>180, 295, 321, 366, 378, 381, 416, 448</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Kyung Chul</td>
<td>305, 312, 391, 541, 567</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Kyung-Chul</td>
<td>362, 510</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Sang Jun</td>
<td>309, 338, 465, 466, 467</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Sang Min</td>
<td>205, 512</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, So Young</td>
<td>319</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Yoo-Seok</td>
<td>307, 362, 363, 526</td>
<td>2012</td>
</tr>
<tr>
<td>Yoon, Young In</td>
<td>313, 388, 389, 510, 537, 543, 556, 567</td>
<td>2012</td>
</tr>
<tr>
<td>Yoo, Sun Hong</td>
<td>316, 317, 325, 366, 383, 494, 497</td>
<td>2012</td>
</tr>
<tr>
<td>Yoshitomi, Hideyuki</td>
<td>168</td>
<td>2012</td>
</tr>
<tr>
<td>Younes, Ziad</td>
<td>284, 473</td>
<td>2012</td>
</tr>
<tr>
<td>Youn, Gi Soo</td>
<td>309, 338, 465, 466, 467</td>
<td>2012</td>
</tr>
<tr>
<td>Youn, Jin</td>
<td>294, 351, 431, 432</td>
<td>2012</td>
</tr>
<tr>
<td>Younossi, Zobair M.</td>
<td>284, 473</td>
<td>2012</td>
</tr>
<tr>
<td>Youn, Woo Young</td>
<td>558</td>
<td>2012</td>
</tr>
<tr>
<td>You, Young Kyoung</td>
<td>312, 361, 379, 539</td>
<td>2012</td>
</tr>
<tr>
<td>YUAN, Peng</td>
<td>528</td>
<td>2012</td>
</tr>
<tr>
<td>Yu, Han Jong</td>
<td>227</td>
<td>2012</td>
</tr>
<tr>
<td>YU, Hee Chul</td>
<td>510</td>
<td>2012</td>
</tr>
<tr>
<td>YU, Jiong-Jie</td>
<td>387, 489, 503, 527</td>
<td>2012</td>
</tr>
<tr>
<td>Yu, Jung Hwan</td>
<td>296, 314, 344, 346, 371, 379, 497</td>
<td>2012</td>
</tr>
<tr>
<td>Yu, Ming-Lung</td>
<td>143, 429, 430</td>
<td>2012</td>
</tr>
<tr>
<td>Yun, Sung Ho</td>
<td>375</td>
<td>2012</td>
</tr>
<tr>
<td>YUN, Sung-Su</td>
<td>517</td>
<td>2012</td>
</tr>
<tr>
<td>YU, Yong</td>
<td>531</td>
<td>2012</td>
</tr>
<tr>
<td>Yu, Young-Dong</td>
<td>305, 362, 510</td>
<td>2012</td>
</tr>
<tr>
<td>ZA, Maram H</td>
<td>491</td>
<td>2012</td>
</tr>
<tr>
<td>ZAKRIA, Muhammad</td>
<td>462</td>
<td>2012</td>
</tr>
<tr>
<td>ZENG, Yong-Yi</td>
<td>489, 503</td>
<td>2012</td>
</tr>
<tr>
<td>Zeng, Zhao Chong</td>
<td>299</td>
<td>2012</td>
</tr>
<tr>
<td>Zeuzem, Stefan</td>
<td>351, 353</td>
<td>2012</td>
</tr>
<tr>
<td>Zhakiev, Bazybek</td>
<td>526</td>
<td>2012</td>
</tr>
<tr>
<td>Zhakiev, Bazybek</td>
<td>548</td>
<td>2012</td>
</tr>
<tr>
<td>Zhakiev, Bazybek</td>
<td>546</td>
<td>2012</td>
</tr>
<tr>
<td>Zhanar, Makhatova</td>
<td>561</td>
<td>2012</td>
</tr>
<tr>
<td>Zhangbaj, Naurygzul</td>
<td>465</td>
<td>2012</td>
</tr>
<tr>
<td>ZHANG, Han</td>
<td>489, 527</td>
<td>2012</td>
</tr>
<tr>
<td>ZHANG, Kai</td>
<td>364</td>
<td>2012</td>
</tr>
<tr>
<td>ZHANG, Wan-Guang</td>
<td>330, 387, 489</td>
<td>2012</td>
</tr>
<tr>
<td>ZHANG, Yao-Ming</td>
<td>387</td>
<td>2012</td>
</tr>
<tr>
<td>ZHANG, Zhengkui</td>
<td>364, 530</td>
<td>2012</td>
</tr>
<tr>
<td>ZHAO, Guochoo</td>
<td>531</td>
<td>2012</td>
</tr>
<tr>
<td>ZHAO, Guo-Dong</td>
<td>392</td>
<td>2012</td>
</tr>
<tr>
<td>ZHAO, Xiaohang</td>
<td>531</td>
<td>2012</td>
</tr>
<tr>
<td>ZHAO, Xudong</td>
<td>531</td>
<td>2012</td>
</tr>
<tr>
<td>Zhapasov, Nurlan</td>
<td>548</td>
<td>2012</td>
</tr>
<tr>
<td>Zharkov, Serik</td>
<td>403, 534</td>
<td>2012</td>
</tr>
<tr>
<td>Zheksenbaev, A.</td>
<td>488</td>
<td>2012</td>
</tr>
<tr>
<td>ZHONG, Qian</td>
<td>503</td>
<td>2012</td>
</tr>
<tr>
<td>Zhong, Yan</td>
<td>432</td>
<td>2012</td>
</tr>
<tr>
<td>ZHOU, Wentao</td>
<td>528</td>
<td>2012</td>
</tr>
<tr>
<td>ZHOU, Xueping</td>
<td>301</td>
<td>2012</td>
</tr>
<tr>
<td>ZHOU, Ya-Hao</td>
<td>330, 387, 489, 503</td>
<td>2012</td>
</tr>
<tr>
<td>Zhuo, Yueran</td>
<td>431</td>
<td>2012</td>
</tr>
<tr>
<td>Zin, Myo</td>
<td>551</td>
<td>2012</td>
</tr>
<tr>
<td>Zorigt, Bat-Erdene</td>
<td>437</td>
<td>2012</td>
</tr>
<tr>
<td>Zulkharnay, Aidar</td>
<td>403</td>
<td>2012</td>
</tr>
</tbody>
</table>
The Liver Week 2019

President: Jin Mo Yang, M.D.
Editor-in-Chief: Yoon Jun Kim, M.D.

Published by
The Korean Association for the Study of the Liver
Room A1210, Mapo Trapalace,
53 Mapo-daero, Mapo-gu, Seoul 04158,
South Korea

Printed by
J PLUS CO.
12, Pildong-ro, Jung-gu, Seoul 04625,
South Korea