New Horizons

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Program & Abstracts

for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics

Single Topic Conference

APASL

2025 Tokyo

Term
October 2-3, 2025

Venue
Toshi Center Hotel
Tokyo, Japan

Chairperson of the Organizing Committee:
Kenichi Ikejima, MD., PhD.
Professor of Medicine
Department of Gastroenterology
Juntendo University Graduate School of Medicine

www.apasl-stc2025tokyo.org

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

October 2-3, 2025

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Welcome Message

Dear Colleagues,

On behalf of the Organizing Committee, it gives us great pleasure to invite you to Asian Pacific Association for the Study of the Liver APASL STC 2025 Tokyo, which will be held on October 2-3 2025 in Tokyo, Japan. We are delighted to welcome you to the attractive city of Tokyo.

The scientific program will consist of invited lectures, plenary sessions, symposia, and free papers on significant developments on the theme of "New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics". The program will also provide the latest information and fresh ideas for hepatologists.

The delegates of experts from all over the world are expected to attend this conference. We are sure that this will provide an excellent opportunity for those of us in the Asian Pacific region to share the latest views, values, experience and practice, and greatly contribute to this field.

The conference has called the submission of free papers for oral and poster presentations and have received more than 250 free papers. We would appreciate the large number of submission and anticipate those to stimulate our active discussions.

We look forward to welcoming you to Tokyo, a truly exotic and fascinating metropolis.

With warmest regards,

Kenichi Ikejima, MD. PhD.
FACP, AGAF, FAASLD,
President of APASL STC 2025 Tokyo
Professor of Medicine,
Department of Gastroenterology,
Juntendo University Graduate School of Medicine, Japan

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In alphabetical order

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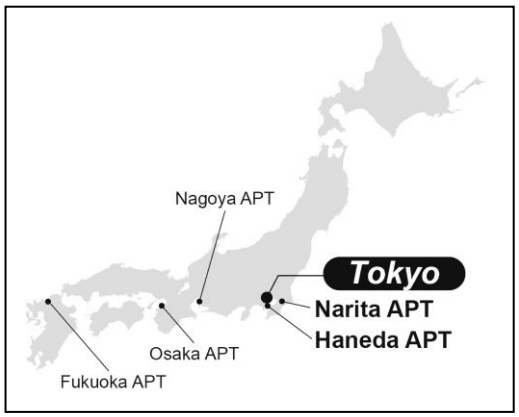

Toshi Center Hotel Tokyo

Address 2-4-1 Hirakawa-cho, Chiyoda-ku, Tokyo 102-0093, Japan
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URL: https://www.rihga.com/toshicenter_tokyo/

Access

From Narita International Airport

By train About 85 minutes

1. Take JR Narita Express for TOKYO Station
2. Transfer to the JR Yamanote Line at TOKYO Station to Yurakucho Station
3. From Yurakucho Station transfer to Tokyo Metro Yurakucho Line
4. Get off at Nagatacho Station

By bus About 120 minutes

Limousine bus to TOKYO GARDEN TERRACE KIOICHO

From Tokyo International Airport (Haneda)

By train About 40 minutes

1. Take Tokyo Monorail at Haneda Airport Station for Hamamatsucho Station
2. Transfer to the JR Yamanote Line at Hamamatsucho Station to Yurakucho Station
3. From Yurakucho Station transfer to Tokyo Metro Yurakucho Line
4. On the Tokyo Metro Yurakucho Line get off at Nagatacho Station

By bus About 70 minutes

Limousine bus to TOKYO GARDEN TERRACE KIOICHO

From Tokyo Station

By train About 20 minutes

1. Take JR Yamanote Line from Tokyo Station to Yurakucho Station
2. From Yurakucho Station transfer to Tokyo Metro Yurakucho Line
3. Get off at Nagatacho Stationat on Tokyo Metro Yurakucho Line

By Taxi About 15 minutes

From Nearby Station

From Nagatacho Station (Subway Yurakucho Line, Hanzomon Line, Nanboku Line)

On foot About 3 minutes, walk from Exit 9a

From Kojimachi Station (Subway Yurakucho Line)

On foot About 4 minutes, walk from Exit 1

From Akasaka-mitsuke Station (Subway Marunouchi Line, Ginza Line)

On foot About 8 minutes, walk from Exit D

Conference Information

Registration Fee and Category

Category \ Term	Early Bird until July 31, 2025	Pre-Registration September 26, 2025	On Site
APASL Member	JPY 20,000	JPY 25,000	JPY 30,000
Non-Member	JPY 30,000	JPY 35,000	JPY 40,000
Accepted Abstract Submitter	JPY 25,000	JPY 30,000	JPY 35,000
Trainee / Resident	JPY 15,000	JPY 20,000	JPY 25,000
Medical Student	JPY 3,000	JPY 5,000	JPY 10,000
Accompanying Person	JPY 5,000	JPY 5,000	JPY 5,000

JPY=Japanese Yen
*APASL Members who have paid 2025 Membership Fee can apply for discounted registration fee.

Onsite Registration/PC Pre-view Hours

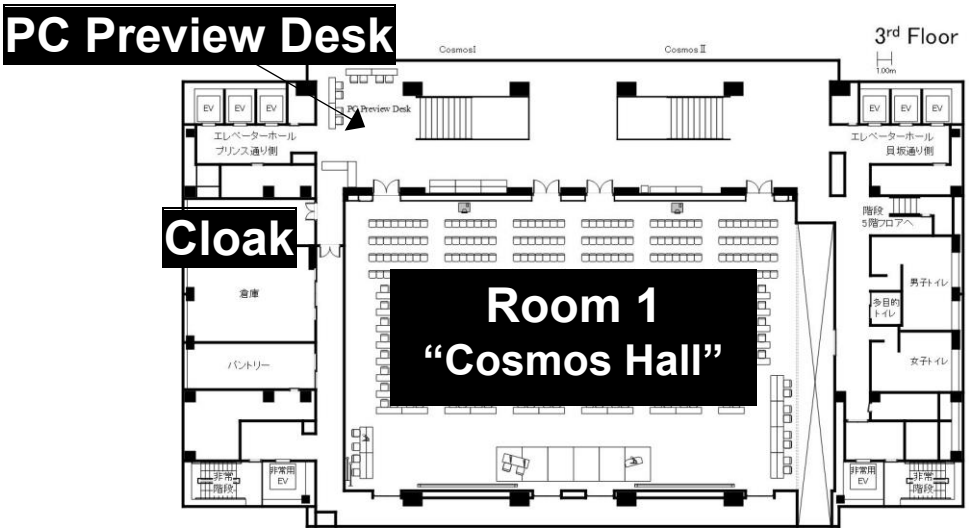
October 2 (Thursday) 8:00-18:00
October 3 (Friday) 7:30-17:00

Floor Plan: Toshi Center Hotel

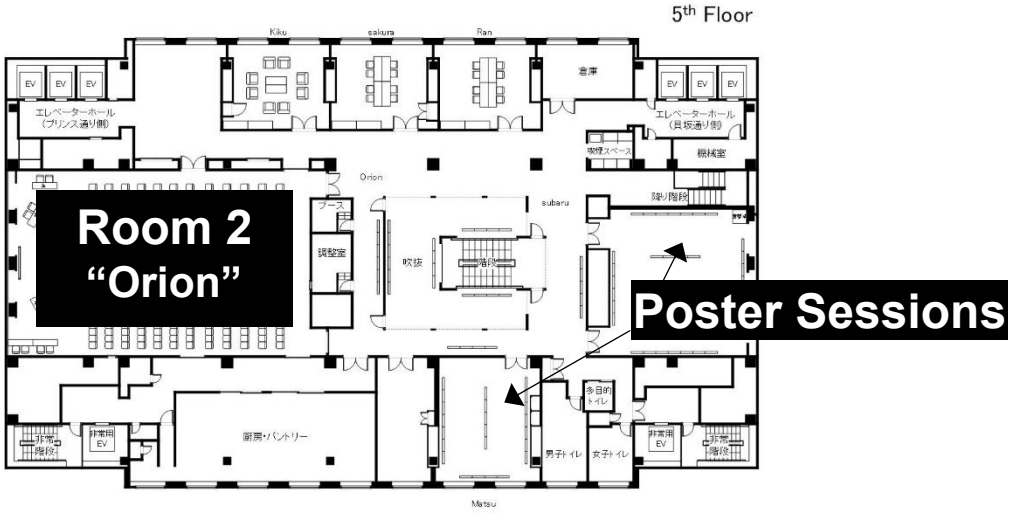
Room 1: “Cosmos Hall”, 3rd Floor
Room 2: “Orion”, 5th Floor
Room 3: “606”, 6th Floor
Welcome Reception: “Cosmos Hall, 3rd Floor
Cloak: Meeting Room, 3rd Floor
Registration: Entrance Hall, 1st Floor
PC Preview Desk: Foyer, 3rd Floor
Poster Sessions: “Subaru” “Matsu” and Foyer, 5th Floor
Speakers/Chairs Ready Room: “Ran””Sakura” 5th Floor, “602”, 6th Floor“
Members Lounge: “605”, 6th Floor
Congress Secretariat Room: “603”, 6th Floor
Scientific Secretariat Room: “604”, 6th Floor

1st Floor, Toshi Center Hotel

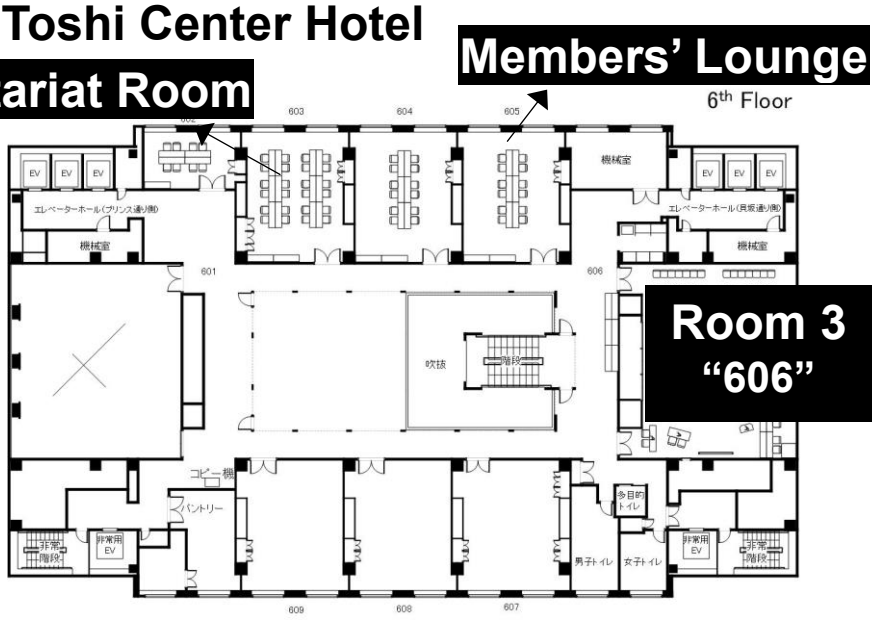
3rd Floor, Toshi Center Hotel



5th Floor, Toshi Center Hotel



6th Floor, Toshi Center Hotel



Instruction for Oral Presentation

- Please complete your registration of presentation data at the Data Pre-View Desk, which will be located at the foyer on the 3rd floor in front of the Room 1 “Cosmos Hall”, until 30 min. before your presentation time.
- The open hours of Data Pre-View Desk are as follows.

October 2 (Thursday)	October 3 (Friday)
8:00-18:00	7:30-17:00

- Please be seated at the “next speaker’s seat” at least 10 minutes before your presentation. The seat will be located near the podium.
- The slides which you have submitted in advance for the presentation are prepared on the computer of the podium.
- Your Presentation Time will be announced individually by E-mail.
- After presentation, the discussion time (a question-and-answer session) will be held according to the moderator’s instructions.
- The PC set at the podium is OS: Windows 11 (PowerPoint: 2024).
- Please bring your data by USB memory stick.
- To avoid garbled characters, please use standard font which is originally installed by OS.
- Please put your name on your data file.
- If you bring your movies by data file, please prepare the file which can be played by standard Windows Media Player.
- Backup data by another media should be kept by presenter.
- The projector’s screen resolution is set at 16:9 FULL HD. Please make your PPT data as such. (4:3 XGA is also projectable with a size smaller, black flamed on both left and right sides).
- Please operate your PPT data by yourself at the podium.
- You can use Presenter View of PPT only if you bring your own PC. It will take a few minutes to set up.

<If you bring your own PC>

- Please make sure that your PC has HDMI terminal for monitor output. (Some compact PC needs another connector. In case of that, please carry your own connector.)
- Macintosh and Key Note are acceptable only if you bring your own PC (Please carry your own connector).
- Please bring battery adapter to avoid battery off. Because sometimes screen saver or power saving system could be a reason of battery off, please set your PC appropriately.

Instruction for Chairs

Please be seated at the “next chair’s seat” at least 10 minutes before the session starts. The seat will be located forward near the stage.
After presentation, the discussion time (a question-and-answer session) will be held according to the moderator’s instructions. The participants will ask questions using the microphone at the conference hall.

Instruction for Poster Presentation

- Presentation time for each poster will be announced individually by email.
- Location: Poster Session will be performed at Room “Subaru”, “Matsu” and Foyer on the 5th Floor.
- Schedule: Poster Presentation is scheduled as follows.

For Presenter on Day 1 October 2 (Thursday)

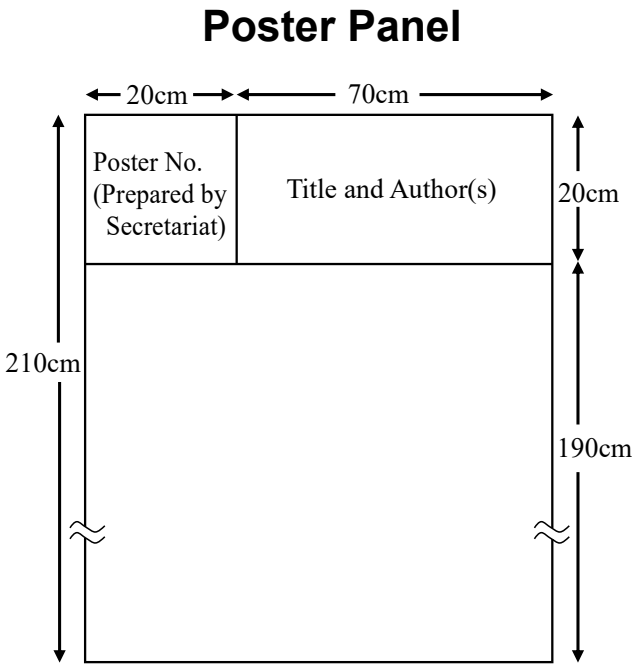
Poster Attachment: 8:00-10:00 on October 2 (Thursday)
Poster Viewing: 10:00-17:30 on October 2 (Thursday)
Poster Session: 17:40-18:40 on October 2 (Thursday)
Awarding Ceremony: 18:45-19:00 on October 2 (Thursday) at Room 1 “Cosmos Hall”
Poster Removal: 19:00-20:30 on October 2 (Thursday)

For Presenter on Day 2 October 3 (Friday)

Poster Attachment: 8:00-9:00 on October 3 (Friday)
Poster Viewing: 9:00-16:30 on October 3 (Friday)
Poster Session: 13:00-14:00 on October 3 (Friday)
Awarding Ceremony: 18:45-19:00 on October 2 (Thursday) at Room 1 “Cosmos Hall”
Poster Removal: 16:30-18:00 on October 3 (Friday)

- For those who have not removed posters until above removal time, please accept that the secretariat will discard any posters that have remained.
- A panel width 90cm×length 210cm will be provided for each poster as the following sample.
- Poster number will be prepared by secretariat.
- Title and author’s name are required to be prepared by each presenter.
- Pins for display will be provided at each poster panel.

<Sample of Poster PaneI>



<Disclosure of COI>

Regarding the disclosure of conflicts of interest, please include one of the conflicts of interest disclosure slides using attached template.

If you have any questions, please contact the secretariat below.

We would like to thank you all for your cooperation.

Contact: APASL STC 2025 Tokyo Congress Secretariat

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Awards

Excellent papers will be awarded as “Presidential Award”, “Investigator Award”, “Travel Award”. The Awardees will be presented at the Awarding Ceremony for all presenters at 18:45-19:00 on October 2 at Room 1 “Cosmos Hall” 3F Toshi Center Hotel.

Presidential Award

“APASL STC 2025 Tokyo Presidential Award” will be awarded to whom performed the most excellent presentation in APASL STC 2025 Tokyo to encourage their research and progress.

Investigator Award

The purpose of the “APASL STC 2025 Tokyo Investigator Award” is to praise outstanding examples of excellence amongst those involved in research training in the early stages of their career.

Travel Award

“APASL STC 2025 Tokyo Travel Award” will be awarded to whom performed the excellent presentation traveling to the onsite venue in APASL STC 2025 Tokyo.

Contact

APASL STC 2025 Tokyo Scientific Secretariat

Department of Gastroenterology,
Juntendo University Graduate School of Medicine, Japan

APASL STC 2025 Tokyo Congress Secretariat

c/o Academia Support Japan
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APASL STC 2025 Tokyo Official Website

URL http://www.apasl-stc2025tokyo.org

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Memo

APASL STC 2025 Tokyo
Program at a Glance Day 1

October 2 (Thursday) 2025

	3F Room 1 "Cosmos Hall"	5F Room 2 "Orion"	6F Room 3 "606"	5F Foyer "Subaru" "Matsu"
08:00	8:00- Registration			
	8:50-9:00 **Opening Remarks**			
09:00	9:00-9:50 **Panel Discussion 1** *Definition and Epidemiology of SLD*	9:00-9:50 **Workshop 1** *Therapeutic Diversity and Metabolic Response in SLD*	9:00-9:30 **Parallel Session 1**	
			9:30-10:00 **Parallel Session 2**	
10:00	9:50-11:10 **Symposium 1** *Recent Advances in the Diagnosis of SLD*	9:50-10:40 **Workshop 2** *Strategies for Managing SLD-Related Hepatocellular Carcinoma*	10:05-10:35 **Parallel Session 3**	Poster Viewing
11:00			10:35-11:05 **Parallel Session 4**	
	11:10-11:55 **State of the Art Lecture 1** *Emerging Therapies for MASH Related Fibrosis*			
12:00	12:00-13:00 **Luncheon Seminar 1** (Gilead Sciences K.K.)	12:00-13:00 **Luncheon Seminar 2** (Boehringer Ingelheim)		
13:00	13:10-14:00 **Panel Discussion 2** *Multidisciplinary Approach for SLD*	13:10-14:00 **Workshop 3** *The Role of Genetic and Environmental Factors in SLD*	13:00-13:30 **Parallel Session 5**	
			13:30-14:10 **Parallel Session 6**	
14:00	14:00-15:20 **Symposium 2** *ALD: Emerging Insights and Unresolved Challenges (ISBRA Joint Session)*		14:10-14:50 **Parallel Session 7**	
		14:20-15:20 **Late Breaking Session**	14:50-15:20 **Parallel Session 8**	
15:00				
16:00	15:40-16:40 **Teatime Seminar 1** (Novo Nordisk Pharma Ltd.)	15:40-16:40 **Teatime Seminar 2** (AbbVie G.K.)		
17:00	16:40-17:10 **Special Lecture 1**	16:40-17:30 **Workshop 4** *Surgical Approaches to SLD*	16:40-17:10 **Parallel Session 9**	
	17:10-17:40 **Special Lecture 2**		17:10-17:40 **Parallel Session 10**	
18:00		17:40-18:30 **Evening Seminar** (Miyarisan Pharmaceutical Co., Ltd.)		17:40-18:40 **Poster Session Day 1**
19:00	18:45-19:00 **Awarding Ceremony** 19:00-21:00 **Welcome Reception**			

APASL STC 2025 Tokyo
Program at a Glance Day 2

October 3 (Friday) 2025

	3F Room 1 "Cosmos Hall"	5F Room 2 "Orion"	5F Foyer "Subaru" "Matsu"
08:00	8:00- 9:00 **Morning Seminar 1** (Gilead Sciences K.K.)	8:00- 9:00 **Morning Seminar 2** (Nobelpharma Co., Ltd.)	
09:00	9:10-10:30 **Symposium 3** ***Novel Insights in SLD pathogenesis (ISHSR Joint Symposium)***	9:10-10:00 **Workshop 5** ***Management of SLD-Related Comorbidities***	**Poster Viewing**
10:00		10:05-10:55 **Workshop 6** ***Exploring Biomarkers for the Diagnosis of SLD***	
11:00	10:30-11:50 **Symposium 4** ***Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)***	11:00-11:50 **Workshop 7** ***Translational Research in SLD***	
12:00	12:00-13:00 **Luncheon Seminar 3** (AbbVie G.K.)	12:00-13:00 **Luncheon Seminar 4** (Meiji Seika Pharma Co., Ltd)	
13:00	13:10-14:10 **Plenary Session**	13:10-13:40 **Parallel Session 11**	13:00-14:00 **Poster Session Day 2**
14:00		13:40-14:10 **Parallel Session 12**	
	14:10-14:55 **State of the Art Lecture 2** ***A Rationale Approach to Drug Discovery in MetALD***		
15:00	14:55-16:15 **Symposium 5** ***Fibrogenesis in SLD***	14:55-16:15 **Symposium 6** ***Practical Management of SLD and Novel Insights***	
16:00	16:15-17:35 **Symposium 7** ***Cancer Development in SLD***	16:15-16:45 **Parallel Session 13**	
17:00		16:45-17:35 **Workshop 8** ***The Role of Gut-liver Axis in SLD***	
	17:40-17:50 **Closing Remarks**		
18:00			

*The program is subject to change.

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The Japan Society of Hepatology
Tokyo Convention & Visitors Bureau

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Scientific Program

APASL STC 2025 Tokyo Scientific Program

Day 1: October 2 (Thursday) 2025

Room 1 "Cosmos Hall" 3rd Floor

08:50-9:00 Opening Ceremony

Opening Remarks: Dr. Kenichi Ikejima, President of APASL STC 2025 Tokyo

09:00-9:50 Panel Discussion 1: Definition and Epidemiology of SLD

Moderators: Dr. Jia-Horng Kao (Taiwan), Dr. Yoshito Itoh (Japan)

PD1-1 Classification and Epidemiology of SLD/FLD in Lean Individuals
Dr. Vincent W. S. Wong (Hong Kong SAR, China)

PD1-2 MAFLD in Lean Individuals: What do We Know?
Dr. Mohammed Eslam (Australia)

PD1-3 Clinical Manifestations of MASLD Based on the New Diagnostic Criteria in Japan
Dr. Tomomi Kogiso (Japan)

PD1-4 Diabetes Connection: A Bidirectional Relationship in Steatotic Liver Disease
Dr. Diana A. Payawal (Philippines)

09:50-11:10 Symposium 1: Recent Advances in the Diagnosis of SLD

Moderators: Dr. Dong Joon Kim (Korea), Dr. Katsutoshi Tokushige (Japan)

S1-1 Keynote Lecture:
The Non-invasive Assessment of Liver Fibrosis in Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) in the Asia Population
Dr. Lai Wei (China)

S1-2 Screening for Patients with MetALD in At-Risk Populations: A Practical Approach to Early Detection
Dr. Suthat Liangpunsakul (USA)

S1-3 The Role of Noninvasive Tests in the Diagnosis and Prognosis Assessment in MASLD
Dr. Seung Up Kim (Korea)

S1-4 Liver MR Fingerprinting: Tissue Characterization and Comparison with Conventional Quantitative MR Imaging
Dr. Katsuhiro Sano (Japan)

S1-5 Pathology of Steatotic Liver Disease
Dr. Kenichi Harada (Japan)

11:10-11:55 State of the Art Lecture 1

Moderator: Dr. Kenichi Ikejima (Japan)

Emerging Therapies for MASH Related Fibrosis
Dr. Rohit Loomba (USA)

12:00-13:00 Luncheon Seminar 1 (Gilead Sciences K.K.)

Moderator: Dr. Shuji Terai (Japan)

LS1-1 Real-World Evidence of Sofosbuvir/Velpatasvir and Post-SVR Strategies for HCC Risk Reduction
Dr. Jia-Horng Kao (Taiwan)

LS1-2 From HCV to SLD: Cutting-edge Research in Liver Disease
Dr. Hayato Nakagawa (Japan)

13:10-14:00 Panel Discussion 2: Multidisciplinary Approach for SLD

Moderators: Dr. Mohammed Eslam (Australia), Dr. Yasuhiro Asahina (Japan)

PD2-1 Multidisciplinary Management of Hepatocellular Carcinoma in Steatotic Liver Disease: A Hepatologist's Perspective
Dr. Kaoru Tsuchiya (Japan)

PD2-2 Innate Immune Receptor Profiles in Steatotic Liver Disease: Sex and Etiology
Dr. Akira Uchiyama (Japan)

PD2-3 Developing New Therapy for SLD-related Cirrhotic Patients Using Extracellular Vesicles from Human iPS-derived Mesenchymal Stem Cell
Dr. Taro Takami (Japan)

PD2-4 Digital Pathology Using Fibrosis Pattern Analysis to Predict Hepatocellular Carcinoma Development in Patients with MASLD
Dr. Hisamitsu Miyaaki (Japan)

14:00-15:20 Symposium 2: ALD: Emerging Insights and Unresolved Challenges (ISBRA Joint Session)

Moderators: Dr. Ina Bergheim (Austria), Dr. Shuji Terai (Japan)

S2-1 Keynote Lecture:
Single Cell RNA Seq Analysis of Inflammation in Alcohol-associated Liver Disease: Identification of Novel Therapeutic Targets
Dr. Bin Gao (USA)

S2-2 Alterations of Alcohol Dehydrogenase (ADH) Activity in MASLD Development: Mechanisms and Implications
Dr. Ina Bergheim (Austria)

S2-3 Liver Inflammation and Injury
Dr. Hua Wang (China)

S2-4 Glutamatergic Metabolic Synapse in ASH
Dr. Won-Il Jeong (Korea)

S2-5 Genetic Variants of Alcohol-metabolizing Enzymes and Their Clinical Relevance to Psychiatry and Hepatology in Asian Populations
Dr. Sachio Matsushita (Japan)

15:20-15:40 Coffee Break

15:40-16:40 Teatime Seminar 1 (Novo Nordisk Pharma Ltd.)

Moderator: Dr. Kenichi Ikejima (Japan)

TS1-1 Proposals for the Management of MASLD/MASH in Japan
Dr. Yoichi Hiasa (Japan)

TS1-2 Management of MASLD/MASH: Current Situation and Challenges
Dr. Hideki Fujii

16:40-17:10 Special Lecture 1

Moderator: Dr. Masao Omata (Japan)

Precision Medicine for Metabolic Dysfunction Associated Fatty Liver Disease (MAFLD)
Dr. Shiv K. Sarin (India)

17:10-17:40 Special Lecture 2

Moderator: Dr. Sumio Watanabe (Japan)

AI Diagnostic Systems can Accurately Diagnose Stage of Liver Fibrosis and Predict HCC Development in MASH
Dr. Takeshi Okanoue (Japan)

18:45-19:00 Awarding Ceremony

19:00-21:00 Welcome Reception

Day 1: October 2 (Thursday) 2025

Room 2 "Orion" 5th Floor

09:00-09:50 Workshop 1: Therapeutic Diversity and Metabolic Response in SLD

Moderators: Dr. Won Kim (Korea), Dr. Keisuke Hino (Japan)

WS1-1 Multi-Omic Deep Learning Model Predicts IVA337 Response in MASLD Patients Using Liver Transcriptomics, Serum Proteomics, and Immune Single-Cell RNA-seq

Dr. Prihantini Prihantini (Indonesia) *Abstract Submission No. 10167

WS1-2 Improvement Effect of Metabolic and Bariatric Surgery on Steatotic Liver Disease and its Mechanism

Dr. Takeshi Naitoh (Japan)

WS1-3 Paradoxical Effects of Fat Accumulation on Immune Checkpoint Inhibitor Efficacy in HCC Treatment

Dr. Takahiro Kodama (Japan)

WS1-4 Inhibitory Effect of Pemafibrate on Fatty Acid-Induced Mitochondrial and Cellular Damage by Induction of Autophagy

Dr. Shunhei Yamashina (Japan)

09:50-10:40 Workshop 2: Strategies for Managing SLD-Related Hepatocellular Carcinoma

Moderators: Dr. Michiie Sakamoto (Japan), Dr. Yoshiyuki Ueno (Japan)

WS2-1 Keynote Lecture:
The Role of SASP in the Liver Tumor Microenvironment:
The Gut-liver Axis-mediated Mechanism

Dr. Naoko Ohtani (Japan)

WS2-2 Surgical Treatment for SLD-related HCC: Trends in Liver Resection and Transplantation

Dr. Takahiro Nishio (Japan)

WS2-3 Spatial Profiling Identifies GPNMB-positive Macrophages as Regulators of Fibrosis and Tumor Growth and as Predictive Biomarkers in Hepatocarcinogenesis

Dr. Kenji Fukumoto (Japan) *Abstract Submission No. 10156

12:00-13:00 Luncheon Seminar 2 (Boehringer Ingelheim)

Moderator: Dr. Atsushi Nakajima (Japan)

LS2-1 MASLD Pathogenesis: Focus on Cellular Stress Responses
Dr. Kanji Yamaguchi (Japan)

LS2-2 MASLD as a Condition Necessitating Decisions on the Management and Risk Reduction of Lifestyle-Related Diseases
Dr. Hirokazu Takahashi (Japan)

13:10-14:00 Workshop 3: The Role of Genetic and Environmental Factors in SLD

Moderators: Dr. Juliane I. Beier (USA), Dr. Hayato Nakagawa (Japan)

WS3-1 Toxic Relationships: When Environmental Exposures Meet Metabolic Liver Disease
Dr. Juliane I. Beier (USA)

WS3-2 Impact of Fatty Acid Desaturase (FADS) 2 Gene Variants on Progression of Hepatic Fibrosis in MASLD
Dr. Shunsuke Ikejima (Japan)

WS3-3 ALDH2 Variants and Liver Disease
Dr. Yanhang Gao (China)

WS3-4 Decoding Cell-State Specific Expression Quantitative Trait Locus Regulation of Fibrosis Progression in Human Metabolic Liver Disease Using Single-Cell Transcriptomic Analysis
Dr. Rini Winarti (Indonesia) *Abstract Submission No. 10171

14:20-15:20 Late Breaking Oral Session

Moderator: Dr. Yasuhito Tanaka (Japan)

LBO-1 #10242
Histologic Improvement and Sustained Benefit Across Hepatic and Metabolic Biomarkers with Pegozafermin Therapy: Results from a 48-week Multi-center, Randomized, Double-blind, Placebo-controlled Phase 2b trial (ENLIVEN)
Dr. Rohit Loomba (USA)

LBO-2 #10243

Insights from Phase 2 Study Results for Survodutide in People with MASH Fibrosis F1-F3

Dr. Ahmad Alhussein (Germany)

LBO-3 #10239

TMBIM5 Attenuates High-fat-mediated Liver Injury by Activating Fundc1-related Mitophagy and Suppressing Drp1-related Fission

Dr. Qi Shen (China)

LBO-4 #10241

The Mechanism of TMBIM5 in Ameliorating Alcohol-related Liver Disease by Regulating Mitochondrial Dynamics

Dr. Qi Shen (China)

LBO-5 #10246

Using a Human Liver-on-a-chip Model to Study Alcohol-associated Liver Disease by Targeting LSEC and ALDH2

Dr. Takashi Tsuchiya (USA)

15:20-15:40 Coffee Break

15:40-16:40 Teatime Seminar 2 (AbbVie G.K.)

Moderator: Dr. Naoya Sakamoto (Japan)

TS2-1 Efficacy of HCV Treatment and Challenges in Disease Progression Following Viral Eradication

Dr. Nobuharu Tamaki (Japan)

TS2-2 Prediction of Hepatocellular Carcinoma by Serum Biomarkers

Dr. Taro Yamashita (Japan)

16:40-17:30 Workshop 4: Surgical Approaches to SLD

Moderators: Dr. Kiyoshi Hasegawa (Japan), Dr. Yuji Iimuro (Japan)

WS4-1 Metabolic and Bariatric Surgery as a Strong Alternative for MASH in Patients with Severe Obesity

Dr. Akira Umemura (Japan)

WS4-2 Preoperative HbA1c Predicts Postoperative Liver Inflammation after Metabolic Bariatric Surgery in Patients with Severe Obesity and Steatotic Liver Disease
Dr. Hiromasa Nanba (Japan)

WS4-3 Liver Transplantation for Steatotic Liver Disease: Current Problems and Future Challenges
Dr. Yoichiro Uchida (Japan)

WS4-4 Conversion Surgery Following Chemotherapy for Advanced Hepatocellular Carcinoma with Underlying SLD
Dr. Hirofumi Ichida (Japan)

17:40-18:30 Evening Seminar (Miyarisan Pharmaceutical Co., Ltd.)

Moderator: Dr. Tetsuo Takehara (Japan)

ES-1 Harnessing the Liver–Brain–Gut Axis: A Novel Vagal Stimulation Strategy for Intestinal Treg Regulation
Dr. Takanori Kanai (Japan)

ES-2 Targeting Goblet Cell Pathways to Prevent Microbial Translocation and Alcohol-Associated Liver Disease
Dr. Bernd Schnabl (USA)

Day 1: October 2 (Thursday) 2025

Room 3 "606" 6th Floor

Parallel Sessions (Oral Free Papers)

9:00-9:30 Parallel Session 1: Epidemiology & Clinical Predictors 1

Moderator: Dr. Mina Nakagawa (Japan)

OF1-1 Gender-Specific Body Composition Phenotypes Predict Advanced Fibrosis in Metabolic Dysfunction-Associated Steatohepatitis: A Cross-Sectional MRI-Based Clustering Analysis
Dr. Jordan Low (Singapore)

OF1-2 Pathological Classification of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) Based on Muscle Fatty Changes and Quantitative Changes Using MRI: A Cluster Analysis Study
Dr. Yoshiko Nakamura (Japan)

OF1-3 Metabolic-associated Fatty Liver Disease: Research Advanced in Epidemiology, Risk Factors, and Precision Prevention and Control Strategies in China
Dr. Liu Jing (China)

9:30-10:00 Parallel Session 2: Epidemiology & Clinical Predictors 2

Moderator: Dr. Takemi Akahane (Japan)

OF2-1 Dynamic Changes in Steatotic Liver Disease Subtypes and Risk of Cardiovascular Disease: A Nationwide Cohort Study
Dr. Seohui Jang (Korea)

OF2-2 The Risk of Heart Failure in Patients with Atrial Fibrillation According to the Steatotic Liver Disease Subtype
Dr. Jeongin Lee (Korea)

OF2-3 Risk Factors for Cardiovascular Disease Among Older Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Nationwide Cohort Study
Dr. Sangwook Cheon (Korea)

10:05-10:35 Parallel Session 3: Epidemiology & Clinical Predictors 3

Moderator: Dr. Nami Mori (Japan)

OF3-1 Association of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) with Angiographic Severity of Coronary Artery Disease in Acute Coronary Syndrome
Dr. Kamal Parvej (Bangladesh)

OF3-2 Potential Targets in Metabolic-Associated Steatohepatitis Based on Bioinformatics Analysis and Machine Learning Strategies
Dr. Tiansu Lv (China)

OF3-3 Gut Microbiota Dysbiosis and Its Role in the Pathogenesis of Metabolic Dysfunction-Associated Steatotic Liver Disease
Dr. Tatia Khachidze (Georgia)

10:35-11:05 Parallel Session 4: Epidemiology & Clinical Predictors 4

Moderator: TBA

OF4-1 Association of Combustible Cigarette and Noncombustible Tobacco Product Use with Mental Health Outcomes in Subtypes of Fatty Liver Disease: A Nationwide Cohort Study from Korea
Dr. Jin Hyeok Choi (Korea)

OF4-2 Handgrip Strength Estimation as a Predictor of Liver-Relate Outcomes in Patients with Steatotic Liver Disease
Dr. Jin-Hyun Park (Korea)

OF4-3 Differential Effects of Antihypertensive Drug Classes on Liver-relater Outcomes in MASLD/MetALD Patients with Hypertension
Dr. Seokjin Kong (Korea)

13:00-13:30 Parallel Session 5: Epidemiology & Clinical Predictors 5

Moderator: Dr. Ayano Inui (Japan)

OF5-1 AI-Integrated Biosensor Wearables for Monitoring Metabolic Dysfunction-Associated Steatotic Liver Disease in Adolescents with Type 1 Diabetes
Dr. Vikas Sharma (India)

OF5-2 The Role of Wearable Technology and Geo-Fencing in Physiological Monitoring and Pre-Transplant Optimization for Adolescents with NAFLD Undergoing Bariatric Surgery
Dr. Vikas Sharma (India)

OF5-3 Sex and Menopausal Differences in the Association between Visceral Adipose Tissue and Metabolic Dysfunction-associated Steatotic Liver Disease: A Cross-sectional and Mendelian Randomization Study
Dr. Yutian Cao (China)

13:30-14:10 Parallel Session 6: Mechanisms & Injury 1

Moderator: Dr. Hirotoshi Ebinuma (Japan)

OF6-1 Neutrophil Elastase Undergoes Endocytosis into Hepatocytes and Contributes to Liver Injury in Alcoholic Hepatitis
Dr. Noriyoshi Ogino (Japan)

OF6-2 IL-1R1 Deficiency Attenuates Hepatic Ischemia-Reperfusion Injury by Coordinating Oxidative Stress Control, Hepatocyte Regeneration, and Immune Rebalancing
Dr. Yichu Kao (Taiwan)

OF6-3 Role of Recombinant Human Cytoglobin against Acetaminophen-induced Liver Injury
Dr. Nguyen Bui Tam Chi (Japan)

OF6-4 Engineering Vesicle-Mediated Metabolic Regulation and Immune Targeting for the Treatment of Autoimmune Hepatitis
Dr. Mengyi Shen (China)

14:10-14:50 Parallel Session 7: Mechanisms & Injury 2

Moderator: TBA

OF7-1 Pharmacological Inhibition of Hepatic DGAT2 Reduces Triglyceride Synthesis and Attenuates MAFLD Progression in Mice
Dr. Balasubramaniyan Vairappan (India)

OF7-2 Deficiency of Hepatic Protein Tyrosine Phosphatase 1B is Protective in a Mouse Model of MASH
Dr. Fawaz Haj (USA)

OF7-3 Development and Characterization of a Murine Model of Anorexia Nervosa-Associated Microvesicular Steatosis
Dr. Michiko Ishii (Japan)

OF7-4 Deregulation of FTO Isoforms in the Progression of Nonalcoholic Fatty Liver Disease to Nonalcoholic Steatohepatitis and its Amelioration with Entacapone
Dr. Sunita Giri (India)

14:50-15:20 Parallel Session 8: Mechanisms & Injury 3

Moderator: Dr. Tomomi Kogiso (Japan)

OF8-1 Xietu Hemu Prescription Suppresses Adipocytogenesis and Alleviates Dysregulation of Lipid Metabolism in Vitro through LEP/AMPK/PPARG Axis
Dr. Zhe Cheng (China)

OF8-2 Myricetin Ameliorates MASLD by Enhancing Mitochondrial Function and Promoting PINK1/Parkin-dependent Mitophagy
Dr. Weilong Xu (China)

OF8-3 A Novel PEX13 Knockout Liver Cell Line Generated Using CRISPR Prime Editing Provides New Insights into Steatotic Liver Disease
Dr. Navia Vinoy (Australia)

16:40-17:10 Parallel Session 9: Fibrosis 1

Moderator: Dr. Kiyoaki Ito (Japan)

OF9-1 A Proof of Concept for Ultrasound Based Artificial Intelligence Quantification of Liver Steatosis and Fibrosis
Dr. Selvakumar Vigneshwaran (Singapore)

OF9-2 A Novel Fibrosis NIT that Uses the Myofibroblast Marker Fibroblast Activation Protein (FAP) and FIB4 in Metabolic Associated Steatotic Liver Disease
Dr. Mark D. Gorrell (Australia)

OF9-3 Development of Overt Hepatic Encephalopathy Increases Mortality in Patients with Cirrhosis: A Multicenter Retrospective Cohort Study
Dr. Taisei Iwasa (Japan)

17:10-17:40 Parallel Session 10: Fibrosis 2

Moderator: Dr. Misako Matsubara (Japan)

OF10-1 Wilms Tumor 1 Induces Hepatic Stellate Cell Invasion that Develops Bridging Fibrosis in Chronic Liver Injury

Dr. Michitaka Matsuda (Japan)

OF10-2 Effects of Hydroxynonenal on Hepatic Macrophages in the Pathogenesis of MASLD

Dr. Masahiro Yanagi (Japan)

OF10-3 DHX9 Loads Hepatocyte-derived Exosomal miR-106b to Activate Hepatic Stellate Cells via Actin Cytoskeleton in MASLD

Dr. Ji Sun (China)

Day 2: October 3 (Friday) 2025

Room 1 "Cosmos Hall" 3rd Floor

08:00-09:00 Morning Seminar 1 (Gilead Sciences K.K.)

Moderator: Dr. Yasuhito Tanaka (Japan)

MS1-1 A New Era in the Management for Hepatitis B: Toward Treatment Optimization Based on Basic Research and Clinical Data

Dr. Takahiro Kodama (Japan)

MS1-2 Cardiometabolic Disease and Chronic Hepatitis B

Dr. Vincent W.S. Wong (Hong Kong SAR, China)

09:10-10:30 Symposium 3: Novel Insights in SLD Pathogenesis (ISHSR Joint Symposium)

Moderators: Dr. Jordi Gracia-Sancho (Spain), Dr. Norifumi Kawada (Japan)

S3-1 Keynote Lecture: Aldehydes Drive the Shared Pathogenesis of Alcohol-Associated and Metabolic Dysfunction-Associated Steatohepatitis (ASH and MASH) by Inducing Mitochondrial Depolarization (mtDepo), Mitophagy, and Release of Profibrotic and Proinflammatory Mitochondrial Damage-Associated Molecular Patterns (mtDAMPs)

Dr. John J. Lemasters (USA)

S3-2 From Degradome to Defense: CAPN4 Modulation as a Novel Therapeutic Strategy for MASH

Dr. Gavin E. Arteel (USA)

S3-3 The Hepatic Lymphatic System in Cholestatic Liver Disease: Mechanisms and Therapeutic Potential

Dr. Yasuko Iwakiri (USA)

S3-4 Novel Insights into LSECs Dedifferentiation in CLD: Role of miRNAs

Dr. Jordi Gracia-Sancho (Spain)

S3-5 Reduced Expression of Fatty Acid Desaturase 2 Exacerbates Diet-induced Steatohepatitis in Mice

Dr. Kazuyoshi Kon (Japan)

10:30-11:50 Symposium 4: Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)

Moderators: Dr. Hidekazu Tsukamoto (USA), Dr. Yoshiyuki Takei (Japan)

S4-1 Key Note Lecture 1: New Pathways in Lipid Metabolism
Dr. Peter Tontonoz (USA)

S4-2 Key Note Lecture 2: Stress Response by Co-creation of Phase-separated p62 Body and Liver Autophagy
Dr. Masaaki Komatsu (Japan)

S4-3 The Liver-Heart Axis in MASLD: Drivers of Cardiometabolic Remodeling
Dr. Debanjan Dhar (USA)

S4-4 Impaired Autophagy in Hepatic Macrophages: A Key Contributor to MASH Progression
Dr. Hayato Hikita (Japan)

12:00-13:00 Luncheon Seminar 3 (AbbVie K.K.)

Moderator: Dr. Masayuki Kurosaki (Japan)

LS3-1 Current Landscape of HCV: Epidemiology, Treatment, and Long-Term Outcomes after HCV Cure
Dr. Eiichi Ogawa (Japan)

LS3-2 A New Era of Liver Care: MASLD and Post-SVR Outcomes
Dr. Takumi Kawaguchi (Japan)

13:10-14:10 Plenary Session

Moderators: Dr. Kuei-Chuan Lee (Taiwan), Dr. Atsushi Tanaka (Japan)

PL-1 Single Cell Fixed RNA-seq Revealed HSCs(LMCD1+) is a Driver of Liver Fibrosis by Modulating AKT-PRAS40-4EBP1
Dr. Minh Duc Pham (Japan) *Abstract Submission No. 10063

PL-2 Mathematical Modeling of Stellate Cell-Macrophage Crosstalk Predicts Fibrotic Transition Dynamics in MASLD Using Patient-Derived Single-Cell Transcriptomic and Epigenomic Data
Dr. Prihantini Prihantini (Indonesia) *Abstract Submission No. 10169

PL-3 Fibrosis Microenvironment of Reduced HBsAg Area Enriches HCC Recurrence Risk Genes in Chronic Hepatitis B Patients
Dr. Michitaka Matsuda (Japan) *Abstract Submission No. 10121

PL-4 Development of a High-Accuracy Machine Learning Model for Predicting Pathological Cirrhosis in Patients with Steatotic Liver Disease
Dr. Kai Oshima (Japan) *Abstract Submission No. 10081

PL-5 Endotoxin-Induced Metabolic Reprogramming in Liver Sinusoidal Endothelial Cells Drive Hepatic Microvascular Dysfunction and Portal Hypertension During Sepsis in Experimental Models of Liver Cirrhosis
Dr. Vaibhav Tiwari (India) *Abstract Submission No. 10228

PL-6 Macrophages and Hepatic Stellate Cells Interactions via Semaphorin 4D-PlexinB2 Axis Promote Liver Fibrosis
Dr. Pham Tuan Anh (Japan) *Abstract Submission No. 10059

14:10-14:55 State of the Art Lecture 2

Moderator: Dr. Nobuhiro Sato (Japan)

A Rationale Approach to Drug Discovery in MetALD
Dr. David A. Brenner (USA)

14:55-16:15 Symposium 5: Fibrogenesis in SLD

Moderators: Dr. Tatiana Kisseleva (USA), Dr. Hitoshi Yoshiji (Japan)

S5-1 Keynote Lecture: Tumor-promoting Lipid Reprogramming by Hepatic Stellate Cells
Dr. Hidekazu Tsukamoto (USA)

S5-2 Multi-Modal Analysis of Human Hepatic Stellate Cells Identifies Novel Therapeutic Targets for MASH and MetALD
Dr. Tatiana Kisseleva (USA)

S5-3 Involvement of Cannabinoid 1 Receptors in Liver Fibrosis
Dr. Kei Ishizuka (Japan)

S5-4 Intercellular Communication between Hepatic Stellate Cells and Myofibroblasts Mediated by Osteopontin and FGF18 Promotes Liver Fibrosis

Dr. Hiroyasu Nakano (Japan)

S5-5 A Single-cell Fixed RNA Profiling Uncovers Key Transcriptional and Signalling Programs in Liver Fibrosis Progression and Regression
Dr. Le Thi Thanh Thuy (Japan)

16:15-17:35 Symposium 7: Cancer Development in SLD

Moderators: Dr. Ning Zhang (China), Dr. Hayato Hikita (Japan)

S7-1 Keynote Lecture: TBA
Dr. Ning Zhang (China)

S7-2 MASLD Drives CRC Liver Metastasis by Remodeling the Fibrotic Tumor Microenvironment
Dr. Yoon Mee Yang (Korea)

S7-3 Study on the Applications of Nanocarrier as Therapeutic Candidates for Liver Fibrosis
Dr. Wonhyo Seo (Korea)

S7-4 Clinical Aspects of Hepatocarcinogenesis in Steatotic Liver Disease
Dr. Makiko Taniai (Japan)

S7-5 The Immune Landscape of Steatotic Hepatocellular Carcinoma
Dr. Carmen Chak-ui Wong (Hong Kong SAR, China)

17:40-17:50 Closing Ceremony

Closing Remarks: Dr. Kenichi Ikeijma, President of APASL STC 2025 Tokyo

Day 2: October 3 (Friday) 2025

Room 2 "Orion" 5th Floor

08:00-09:00 Morning Seminar 2 (Nobelpharma Co., Ltd)

Moderator: Dr. Hitoshi Yoshiji (Japan)

MS2-1 Zinc Supplementation in the Treatment of Liver Cirrhosis
Dr. Nobuhiro Nakamoto (Japan)

MS2-2 The Role of Zinc in the Management of Hepatocellular Carcinoma
Dr. Ryosuke Tateishi (Japan)

09:10-10:00 Workshop 5: Management of SLD-Related Comorbidities

Moderators: Dr. Yasunari Nakamoto (Japan), Dr. Motoyuki Otsuka (Japan)

WS5-1 Management of MASLD-Related Comorbidities
Dr. Yoshio Sumida (Japan)

WS5-2 Metabolic Dysfunction-Associated Steatotic Liver Disease as a Cardiovascular Risk Equivalent
Dr. Won Kim (Korea)

WS5-3 Predicting HCC Risk in MASLD Using NILDA and Clinical Background Factors
Dr. Miwa Kawanaka (Japan)

10:05-10:55 Workshop 6: Exploring Biomarkers for the Diagnosis of SLD

Moderators: Dr. Yoichi Hiasa (Japan), Dr. Masao Honda (Japan)

WS6-1 Screening Strategies for High-Risk MASLD Populations in Health Check-Up Programs
Dr. Dae Won Jun (Korea)

WS6-2 Non-Invasive Testing Strategies for Managing MASLD on Patient Referral
Dr. Yoshihiro Kamada (Japan)

WS6-3 Exploring Biomarkers for the Diagnosis of SLD-Related Complication
Dr. Akiko Eguchi (Japan)

WS6-4 The Effectiveness of %CDT and γ GT-CDT in the Diagnosis of MetALD and ALD

Dr. Maki Morinaga (Japan)

11:00-11:50 Workshop 7: Translational Research in SLD

Moderators: Dr. Won-Il Jeong (Korea), Dr. Hiroshi Yotsuyanagi (Japan)

WS7-1 Translational Research in Cirrhosis

Dr. Atsunori Tsuchiya (Japan)

WS7-2 Adverse Reactions in Lenvatinib Treatment for Hepatocellular Carcinoma Focusing on Carnitine Changes including the Potential of L-carnitine Supplementation

Dr. Hironao Okubo (Japan)

WS7-3 Single-cell Proteomics and Spatial Proteomics Revealing Creative Pathogenesis of Metabolic Dysfunction-Associated Steatotic Liver Disease

Dr. Tiansu Lv (China) *Abstract Submission No. 10011

WS7-4 Metabolic Inflammation in MASLD Drives Memory CD8+T Cell Differentiation by Downregulating Lnk/Sh2b3, Thereby Activating the IL-15-Jak-STAT Pathway and Exacerbating Hepatic Inflammation and Fibrosis

Dr. Sachiyo Yoshio (Japan) *Abstract Submission No. 10021

12:00-13:00 Luncheon Seminar 4 (Meiji Seika Pharma Co., Ltd.)

Moderator: Dr. Satoshi Mochida (Japan)

LS4-1 Validating the JSH Cirrhosis Guidelines from Real-world Clinical Data in Japan

Dr. Masanori Atsukawa (Japan)

LS4-2 Nutritional Therapy for Cirrhosis – Effects of BCAA on Prevention of Liver Failure –

Dr. Masahito Shimizu (Japan)

13:10-13:40 Parallel Session 11: Fibrosis 3

Moderator: Dr. Wonhyo Seo (Korea)

OF11-1 Mechanism of TRPML1 in MAFLD: AMPK-Mediated Regulation of Autophagy and Lipid Metabolism
Dr. Jiaying Wang (China)

OF11-2 Noninvasive Initiation and Monitoring of the Therapy with TNR-beta Agonist Resmetirom (RT) Using LIVERFASt (LFAST), FIB-4 and Vibration-controlled Transient Elastography (VCTE, Fibroscan) in Patients with MASH
Dr. Mona Munteanu (USA)

OF11-3 Non-targeted Metabolomics Sequencing Combined with 101 Machine Learning Algorithms to Analyse Key Metabolites in Varying Degrees of Non-alcoholic Fatty Liver Disease
Dr. Lin Guan (China)

13:40-14:10 Parallel Session 12: Carcinogenesis 1

Moderator: Dr. Shuntaro Obi (Japan)

OF12-1 Natural Killer Activating Receptor Ligands are Promising Biomarkers to Predict the Pathogenesis of At-risk MASH
Dr. Jun Arai (Japan)

OF12-2 Understanding the Microenvironment and Progression of Liver Fibrosis to Cancer for Developing Novel Precision Therapy
Dr. Hongping Xia (China)

OF12-3 Single Nuclei RNA Sequencing Shows the Engagement of PPARD Target Genes Primarily in Hepatocytes and Cholangiocytes by the Selective PPAR-delta Agonist Seladelpar
Dr. Tomoo Yamazaki (USA)

14:55-16:15 Symposium 6: Practical Management of SLD and Novel Insights

Moderators: Dr. Jacob George (Australia), Dr. Goshi Shiota (Japan)

S6-1 Keynote Lecture:
The Dawn of the Age of Pharmacotherapies for MASH
Dr. Jacob George (Australia)

S6-2 **Epidemiology and Treatment of MASLD in Japanese Real-world Setting**
Dr. Norio Akuta (Japan)

S6-3 **Beyond Glycemic Control: Hepatic and Oncologic Potentials of SGLT2 Inhibitors**
Dr. Takumi Kawaguchi (Japan)

S6-4 **Ferroptosis in MASLD -from Mechanism to Development of New Drugs-**
Dr. Koichi Miura (Japan)

S6-5 **The Role of Bile Acid in Metabolic Dysfunction Steatotic Liver Disease & Its Treatment Implication**
Dr. C. Rinaldi A. Lesmana (Indonesia)

16:15-16:45 Parallel Session 13: Carcinogenesis 2

Moderator: Dr. Naoki Morimoto (Japan)

OF13-1 **Clinical Significance of Leptin Receptors and Promoting Roles of Leptin in Hepatocellular Carcinoma**
Dr. Jirayu Sriphaiboon (Thailand)

OF13-2 **The Risk of Decompensation in Steatotic Liver Disease-related Hepatocellular Carcinoma after Curative Treatment**
Dr. Yuki Matsushita (Japan)

OF13-3 **Micro-RNA Gene Polymorphisms and Development of Hepatocellular Carcinoma in Egyptian Patients with Chronic Viral Hepatitis**
Dr. Mohamed Abdel-Samiee (Egypt)

16:45-17:35 Workshop 8: The Role of Gut-liver Axis in SLD

Moderators: Dr. Bernd Schnabl (USA), Dr. Tatehiro Kagawa (Japan)

WS8-1 **Keynote Lecture:**
Why does the Microbiome Produce Alcohol in Patients with Auto-Brewery Syndrome?
Dr. Bernd Schnabl (USA)

WS8-2 Gut Microbial Therapy in Advanced Chronic Liver Disease

Dr. Kuei-Chuan Lee (Taiwan)

WS8-3 Is There Any Role of Gut Microbiome in Fatty Liver Pathogenesis and Treatment?

Dr. Necati Örmeci (Turkey)

WS8-4 Gut Barrier and Immunotherapy

Dr. Li Zuo (China)

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Poster Session Program

APASL STC 2025 Tokyo Scientific Program

Day 1: October 2 (Thursday) 2025
"Matsu", "Subaru" and Foyer, 5th Floor

17:40 - 18:10 Poster Session 1: Late-Breaking

Moderator: Dr. Yoshihiro Kamada (Japan)

PF1-1 **#10236**
Drug Induced Liver Injury Secondary to Anabolic Steroid Use in a Young Filipino Male: A Case Report and Therapeutic Challenge
Dr. Kaye Bernice T. Siao (Philippines)

PF1-2 **#10237**
Acute Liver Failure Due to Anti-Tuberculosis Drug-Induced Liver Injury: A Case Report from Indonesia
Dr. Fahmi Fauzi Sugandi (Indonesia)

PF1-3 **#10238**
Zonal Differences in Hepatocellular Mitochondrial Depolarization, Mitophagy, and Respiration after Acute Ethanol
Dr. Kenji Takemoto (USA)

PF1-4 **#10240**
Once-Monthly Efimosfermin Alfa (BOS-580) in Metabolic Dysfunction-Associated Steatohepatitis with F2/F3 Fibrosis: Results from A 24 Week, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Trial
Dr. Matthew Bryant (USA)

PF1-5 **#10244**
Therapeutic Evaluation of Resmetirom and Semaglutide in the STAM Mouse Model: Bridging Surrogate and Clinical Outcomes
Dr. Taishi Hashiguchi (Japan)

18:10 - 18:40 Poster Session 2: Other Liver Disease-Clinical/Other Liver Disease-Experimental

Moderator: Dr. Keiko Iwaisako (Japan)

PF2-1 **#10154**

The Impact of Branch-Chained Amino Acid plus Ringer's Acetate Infusion in the Management of Dengue-Related Hepatitis
Dr. Eduward Thendiono (Indonesia)

PF2-2 #10194
Understanding of the Involvement of Cxcl1-associated Neutrophil Infiltration in APAP-Induced Liver Injury
Dr. Ga-Young Kim (Korea)

PF2-3 #10191
Escherichia Coli Expressing the kpsM Gene Exacerbates Drug-induced Liver Injury
Dr. Wenkang Gao (China)

PF2-4 #10105
Elucidating the Role of Ferroptosis in Acute Liver Injury Models
Dr. Oyunjargal Baterdene (Japan)

PF2-5 #10208
Plastic Diets and Liver Dilemmas: Uncovering the Hepatotoxic Divide between Synthetic and Bioplastics
Dr. Rimsha N. A. (Pakistan)

17:40 - 18:10 Poster Session 3: MASLD-Experimental

Moderator: Dr. Debanjan Dhar (USA)

PF3-1 #10064
Enhanced Expression of the FTO Gene in the Liver Correlates with the Progression of Metabolic Dysfunction Associated Steatotic Liver Disease
Dr. Sunita Giri (India)

PF3-2 #10116
Using Non-nutritive Sweeteners in a Fasting Period did not Disturb the Metabolic Benefits and Might Improve Gut Microbiota in Obese Mice Practicing Intermittent Fasting
Dr. Charupong Saengboonmee (Thailand)

PF3-3 #10103
Non Alcoholic Fatty Liver Disease NAFLD: The Estrogen Gut Liver Axis and the Emerging Role of Endometriosis

Dr. Humaira Shah (Malaysia)

PF3-4 #10233
Metabolic Dysfunction-associated Steatohepatitis Exacerbates LPS-induced Liver Injury and Mortality in Obese KK-Ay Mice
Dr. Satoshi Sakuma (Japan)

PF3-5 #10145
Oral Ethanol Administration Induces Hepatitis in Mice with Combining Maternal Id-like Molecule and Melanocortin-4 Receptor Gene Deletions
Dr. Akira Sakamaki (Japan)

18:10 - 18:40 Poster Session 4: MASLD-Clinical

Moderator: Dr. Hideki Fujii (Japan)

PF4-1 #10232
Impact of Dapagliflozin on Liver Function and Body Composition in MASLD with T2DM: A Randomized Controlled Trial
Dr. Hiroo Fukada (Japan)

PF4-2 #10001
Validation of CASLI, Fibroscan-AST (FAST), and Agile3+ in a Russian Cohort of Patients with Metabolic Dysfunction-associated Steatotic Liver Disease
Dr. Veronika Gomonova (Russia)

PF4-3 #10005
Identification of Biomarkers for Progression from NAFL to NASH by Bioinformatics and Mendelian Randomization
Dr. Xinhe Zhang (China)

PF4-4 #10018
Impact of SGLT2 Inhibitors on Liver Imaging Screening and Fibrosis in Diabetes Patients with MASLD
Dr. Tomohide Kurahashi (Japan)

PF4-5 #10024
Efficacy of Imeglimin Hydrochloride in Diabetic Steatotic Liver Disease: A Retrospective Analysis
Dr. Tomohide Kurahashi (Japan)

17:40 - 18:10 Poster Session 5: ALD-Clinical/ALD-Experimental

Moderator: Dr. Koichi Shiraishi (Japan)

PF5-1 **#10047**

Efficacy and Safety of Nalmefene in Alcohol-Related Liver Disease

Dr. Junichi Hanatani (Japan)

PF5-2 **#10164**

A Retrospective Study on the Prognosis of Patients with Alcoholic Liver Cirrhosis

Dr. Yasuka Eriksson (Japan)

PF5-3 **#10173**

Outcomes of Alcoholic Liver Disease in Liver Transplantation: A Systematic Review and Meta-analysis

Dr. Mirudhula Gnanavelou (Singapore)

PF5-4 **#10097**

How Sex and Age Modify the Influence of BMI, CMRFs, and Alcohol on SLD Diagnosis

Dr. Hideki Fujii (Japan)

PF5-5 **#10245**

Drinking Patterns and the Risk of Alcoholic Liver Disease

Dr. Tian Jiao Chen (China)

18:10 - 18:40 Poster Session 6: ALD-Experimental/Fibrosis-Experimental/ MASLD-Clinical

Moderator: Dr. Tiansu Lv (China)

PF6-1 **#10020**

Novel Serum Marker Proteins for Alcohol Abuse Identified through Proteomic Analysis

Dr. Yoshino Sakuma (Japan)

PF6-2 **#10150**

Comparative Liver Fibrosis Severity in Alcohol-Related Liver Disease and Chronic Viral Hepatitis Using Transient Elastography

Dr. Hien T. T. L. (Viet Nam)

PF6-3 **#10200**

Skeletal Muscle Loss and Elevated Phase Angle are Linked to Metabolic Dysfunction-associated Steatotic Liver Disease in Japanese Males

Dr. Satoko Tajirika (Japan)

PF6-4 **#10214**

A 50% Relative Decline in MRI-PDFF Predicts Fibrosis Improvement in Metabolic Dysfunction-associated Steatohepatitis

Dr. Peter Chen-Yang Nikhil Daniel (Singapore)

PF6-5 **#10217**

Narina Sargsyants Armenia Role of Coffee Consumption among Patients with Steatotic Liver Diseases in Armenia

17:40 - 18:10 Poster 7: MASLD-Clinical

Moderator: Dr. Takuya Genda (Japan)

PF7-1 **#10218**

Risk of Liver-Related Events in MASLD: Impact of Cardiometabolic Risk Factor Count and Its Longitudinal Changes

Dr. Han Ah Lee (Korea)

PF7-2 **#10224**

The Interplay of Hepatic Steatosis and Fibrosis in MASLD: Insights from a Clinical Scoring Approach

Dr. Fardah Akil (Indonesia)

PF7-3 **#10212**

Halalopathy in Metabolic Dysfunction-Related Steatotic Liver Disease/MASLD Management: A Holistic Approach to Enhancing Quality of Life for Muslim Patients

Dr. Andi Nursanti (Indonesia)

PF7-4 **#10066**

Liver-related Event Risk in Steatotic Liver Disease According to Smoking Transitions and Subsequent Use of Nicotine Alternatives

Dr. Eun Seok Kang (Korea)

PF7-5 **#10067**

Elevated M2BPGi is Associated with Increased White Matter Hyperintensities, Cognitive Impairment, and Slower Gait Speed in Older Adults with MASLD
Dr. Katsuya Nagaoka (Japan)

18:10 - 18:40 Poster Session 8: ALD-Experimental/MASLD-Clinical

Moderator: Dr. Michitaka Matsuda (Japan)

PF8-1 #10015
Elafibranor Ameliorates Liver Fibrosis Development and Repairs Gut Barrier Function in a Mouse Alcohol-associated Liver Disease Model
Dr. Kosuke Kaji (Japan)

PF8-2 #10060
Hepatoprotective Potential of Phloretin in Alcohol-Induced Liver Disease (ALD) Rat Model: Biochemical and Molecular Evidence
Dr. Dharmendra K. Khatri (India)

PF8-3 #10179
Association between Metabolic Dysfunction-associated Steatotic Liver Disease and Young-onset Thyroid Cancer Risk in Men and Women: A Nationwide Cohort Study of Adults Aged 20-39 Years
Dr. Joo-Hyun Park (Korea)

PF8-4 #10190
Serum Zinc Deficiency Reflects Nutritional Impairment Rather Than Fibrosis Severity in MASLD: A Biopsy-Based Study of 193 Cases
Dr. Naruyasu Kakita (Japan)

PF8-5 #10140
Unraveling the Role of Hepatocyte-Specific DDIT4 in Alcohol-Induced Hepatic Injury
Dr. Taek-Kyong Kim (Korea)

17:40 - 18:10 Poster Session 9: ALD-Clinical/Liver Fibrosis-Experimental/Liver Tumor-Clinical/MASLD-Clinical

Moderator: Dr. Tadashi Namisaki (Japan)

PF9-1 #10210
Culture vs Health: How Traditional Drink Tuak Be a Risk Factor Enhance Liver Disease?

Dr. Jumriani Jumriani (Indonesia)

PF9-2 #10023
Involvement of the ADAMTS13/von Willebrand Factor Axis in Acute Kidney Injury in Mice with Advanced Fibrotic Liver
Dr. Masayoshi Takami (Japan)

PF9-3 #10092
A Case of Esophago-Tracheal Fistula during Atezolizumab plus Bevacizumab after Endoscopic Submucosal Dissection of the Esophagus
Dr. Yoshie Kadota (Japan)

FP9-4 #10109
Dynamic Status of Metabolic Syndrome and Hepatocellular Carcinogenesis: A Big Data Analysis from Japan
Dr. Yutaka Yata (Japan)

PF9-5 #10072
Predictive Utility of Polygenic Risk Scores for Metabolic Dysfunction-Associated Fatty Liver Disease
Dr. Jong-Ho Park (Korea)

18:10 - 18:40 Poster Session 10: MASLD-Clinical

Moderator: Dr. Nobuharu Tamaki (Japan)

PF10-1 #10038
Effects of Probiotics on Gut Microbiota in Patients with Type 2 Diabetes
Dr. Yijing Wu (China)

PF10-2 #10046
Misclassification of Alcohol Use Disorder in MASLD and MetALD: Prevalence, Clinical Characteristics, and Outcomes
Dr. Dae Won Jun (Korea)

PF10-3 #10093
Features of the Course of Metabolically Associated Fatty Liver Disease in Lean Elderly Residents of mid-altitude Areas
Dr. Nurgul Toktogulova (Kyrgyz)

PF10-4 #10114

Screening for Metabolic-associated Fatty Liver Disease in Type 2 Diabetes Patients Using Non-invasive Scores and Ultrasound: a Cross-sectional Study in Egypt
Dr. Atteyat A. Semeya (Egypt)

PF10-5 **#10229**
Noninvasive NASH-FibroTest in Armenian Patients with Steatotic Liver
Dr. Narina Sargsyants (Armenia)

17:40 - 18:10 Poster Session 11: Fibrosis-Experimental
Moderator: Dr. Le Thi Thanh Thuy (Japan)

PF11-1 **#10026**
Aging Increased the Susceptibility of Liver Fibrosis through Enhancing NAT10-mediated ac4C Modification of TGF beta1 mRNA
Dr. Weicheng Liang (China)

PF11-2 **#10082**
Dietary Fermented Rice Bran Inhibit Liver Fibrosis and Hepatic Stellate Cells Activation in Mice
Dr. Yi-Jen Liao (Taiwan)

PF11-3 **#10183**
A Bioinformatics Dissection of TGF-β Signaling in Human Hepatic Stellate Cells: Uncovering Novel Fibrogenic Genes
Dr. Steven L. Xius (Indonesia)

PF11-4 **#10196**
Characterization of Hepatocyte Plasma Membrane Proteins that Regulate Hepatic Stellate Cell Activation
Dr. Kirara Inoue (Japan)

PF11-5 **#10235**
Fibroblast Growth Factor (FGF) 18 Promotes Proliferation and Migration of Murine Hepatic Stellate Cells
Dr. Xingchen Liu (Japan)

18:10 - 18:40 Poster Session 12: MASLD-Clinical/Other Liver Disease-Clinical
Moderator: Dr. Akira Uchiyama (Japan)

PF12-1 **#10028**

Optimal Hemoglobin A1c (HbA1c) Target for Preventing Liver-related Complications in Individuals with Type 2 Diabetes Mellitus (T2DM) with and without Cirrhosis: A Territory-wide Retrospective Cohort Study from 2000 to 2023

Dr. Mary Yue Wang (Hong Kong)

PF12-2 **#10099**

Liver Stiffness Measurement, Doppler Ultrasound, and Serum Non-Invasive Markers as Predictors of Varices and Variceal Bleeding in Cirrhotic Patients

Dr. Waleed Attia Hassan (Egypt)

PF12-3 **#10209**

Hemobilia Due to Spontaneous Arterioportal Fistula in a Liver Abscess: A Rare Case Report

Dr. Ayush Jasrotia (India)

PF12-4 **#10034**

Analysis of Lesions of Liver in Postmortem Cases in Indian Population

Dr. Amar Ranjan (India)

PF12-5 **#10211**

Traditional Use of Gabus Fish by the Mandar People: Relevance to Liver Health and Post Surgical Healing

Dr. Jumriani Jumriani (Indonesia)

17:40 - 18:10 Poster Session 13: Liver Transplantation-Clinical/Public Health/ Viral Hepatitis-Clinical

Moderator: Dr. Hironao Okubo (Japan)

PF13-1 **#10166**

Predicting Spontaneous Clinical Recompensation in Liver Transplant Candidates: A Competing Risks Analysis of the UNOS Registry

Dr. Wen Hui Lim (Singapore)

PF13-2 **#10202**

Impact of Deep Breathing, Laughter Yoga, and Clapping Exercises on Hypoglycemia and Quality of Life in Post-Liver Transplantation Patients in Central Delhi

Dr. Ranbir Singh (India)

PF13-3 **#10068**
Regional Differences in HCC Etiology: Interim Report from the A-HOC Consortium
Dr. Shuntaro Obi (Japan)

PF13-4 **#10077**
Temporal Relationship between Hepatocarcinogenesis after Sustained Virologic Response and Insulin Resistance in Patients with Chronic Hepatitis C
Dr. Tomoko Tanaka (Japan)

18:10 - 18:40 Poster Session 14: Liver Tumor-Clinical

Moderator: Dr. Kaoru Tuchiya (Japan)

PF14-1 **#10180**
Lenvatinib Plus TACE for HCC: A Comparison of the Protocols and the Clinical Utility of Lenvatinib Continuation
Dr. Nami Mori (Japan)

PF14-2 **#10185**
Therapeutic Sequences of Systemic Therapy after Atezolizumab pulus Bevasizumab Based on BR-HCC Expert Consensus 2023
Dr. Takashi Nishimura (Japan)

PF14-3 **#10188**
Mass-forming Eosinophilic Hepatitis Mimicking Recurrent Hepatocellular Carcinoma after Surgical Resection: A Case Report
Dr. Naruyas Kakita (Japan)

PF14-4 **#10118**
Impact of PNPLA3 Genetic Variant on NBNC-HCC Recurrence
Dr. T.Motomura (Japan)

PF14-5 **#10158**
Evaluation of the Diagnostic Performance of the GAAD Score with a 2.57 Cutoff for Hepatocellular Carcinoma in Vietnamese Patients
Dr. Toan Bao Nguyen (Viet Nam)

17:40 - 18:10 Poster Session 15: Liver Tumor-Clinical

Moderator: Dr. Hisamitsu Miyaaki (Japan)

PF15-1 #10055
Metastatic Liver Tumors: A Retrospective Spectrum of Differential Diagnoses from a North Indian Tertiary Health Center
Dr. Monirujjaman Biswas (India)

PF15-2 #10096
Imaging-Pathology Discordance in a Rare Case of Mucinous Intrahepatic Cholangiocarcinoma Presenting as a Cystic Liver Lesion
Dr. Jobel Feliz C. Castillo (Philippines)

PF15-3 #10054
Clinicopathological Insights into Pediatric Liver Tumors: A North Indian Tertiary Hospital Setting
Dr. Monirujjaman Biswas (India)

PF15-4 #10131
XRCC1 Gene Polymorphism and the Risk of Hepatocellular Carcinoma in Egypt
Dr. Mohamed Abdel-Samiee (Egypt)

PF15-5 #10089
Hepatocyte Nuclear Factor 1 Alpha Variants as a Risk Factor for Hepatocellular Carcinoma Development with/without Diabetes Mellitus
Dr. Amany Rashad (Egypt)

18:10 - 18:40 Poster Session 16: Other Liver Disease-Clinical/ Other Liver Disease-Experimental
Moderator: Dr. Sangwook Cheon (Korea)

PF16-1 #10004
Histological Stage as Predictor of the Complications of Primary Biliary Cholangitis
Dr. Tadashi Namisaki (Japan)

PF16-2 #10215
The Role of Non-Invasive Methods and Serological Biomarkers in the Diagnosis and Morphological Characterization of Autoimmune Hepatitis with Correlation to Liver Biopsy Findings

Dr. Nazugum A. Ashimova (Kazakhstan)

PF16-3 #10030
Drug- induced Autoimmune Hepatitis
Dr. Ngan Thanh Quynh Le (Viet Nam)

PF16-4 #10184
The Liver That Looked Malignant: Autoimmune Hepatitis Masquerading as Malignancy-A case for Clinical Judgment in Hepatology
Dr. Lim Kai (Singapore)

PF16-5 #10120
Inhibitory Effects of Haskap Fruit Extract on Animal Models of Primary Biliary Cholangitis and Primary Sclerosing Cholangitis
Dr. Erdenetsogt Dungubat (Japan)

17:40 - 18:10 Poster Session 17: Viral Hepatitis-Clinical
Moderator: Dr. Tatsuo Kanda (Japan)

PF17-1 #10056
Prevalence and Genotypes Distribution of Virus Hepatitis B and Hepatitis Delta Virus in Chronic Liver Diseases in Kazakhstan
Dr. Balzhan Abzhaparova (Kazakhstan)

PF17-2 #10069
Fat Accumulation as a Risk Factor for HCC and Extrahepatic Cancers After SVR: A Prospective Study Based on Fibro Scan Derived Stratification
Dr. Shuntaro Obi (Japan)

PF17-3 #10070
Post-SVR Dynamics of Hepatic Steatosis: Divergent Patterns by Fibrosis Stage and Implications for HCC Risk
Dr. Shuntaro Obi (Japan)

PF17-4 #10138
Evaluation of Shortened DAA Regimens (Sofosbuvir + Velpatasvir, Sofosbuvir + Daclatasvir) in Chronic Hepatitis C Patients Based on Early Virological Response
Dr. Hien T. T. L.(Viet Nam)

PF17-5 #10204
Evaluation of HCVDuo as a Primary Tool for Hepatitis C Screening in Japan
Dr. Tomiko Koyama (Japan)

Day 2: October 3 (Friday) 2025
"Matsu", "Subaru" and Foyer, 5th Floor

13:00-13:30 Poster Session 18: Liver Tumor-Experimental/Public Health
Moderator: Dr. Hiroo Fukada (Japan)

PF18-1 #10189
PARPBP as a Prognostic Biomarker Linked to Tumor Differentiation and Immune Microenvironment in Hepatocellular Carcinoma
Dr. Misako Sato-Matsubara (Japan)

PF18-2 #10083
ANGPTL6 Regulates Epithelial Mesenchymal Transition in Liver Cancer
Dr. Ming-Syuan Shih (Taiwan)

PF18-3 #10107
The Effectiveness of Hepatitis Medical Care Coordinator Certification among Dentists: Seven Years of Progress by the Aichi Dental Association
Dr. Takako Inoue (Japan)

PF18-4 #10168
Photocatalytic Degradation of Methylene Blue to Mitigate Liver Disease: A Step Toward Sustainable Wastewater Treatment
Dr. Fatimah Bt Abd Kadir (Malaysia)

PF18-5 #10123
Comparison of Machine Learning Algorithm in Predicting Living Status of Hepatitis Patients
Dr. Nahya Nur (Indonesia)

13:30-14:00 Poster Session 19: Liver Tumor-Experimental/Other Liver Disease-Experimental/Public Health
Moderator: Dr. Kei Ishizuka (Japan)

PF19-1 #10198

Photothermally Modulated Liposome Enabling Efficient Release of Glucose Analogue Safely Displays Vigorous Antitumor Effect against Liver Cancer
Dr. Sohji Nishina (Japan)

PF19-2 #10088
Inhibition of HAV Replication by Azathioprine in Vitro
Dr. Tatsuo Kanda (Japan)

PF19-3 #10101
Novel Multi-Epitope Subunit Vaccine for Hepatitis Viruses: An Immunoinformatic Approach
Dr. Shah Shahik (Bangladesh)

PF19-4 #10037
Influence of Gut Microbiota on the Gut-Brain Axis and Neurological Disorders
Dr. Xinyue Wang (China)

PF19-5 #10086
Rice Contamination and Liver Disease Risk: A Study on Pesticide Effects on Rice Nutritional Quality
Dr. Nisrin bt Abd Kadir (Malaysia)

13:00-13:30 Poster Session 20: Liver Transplantation-Clinical/Liver Transplantation-Experimental/Viral Hepatitis-Clinical
Moderator: Dr. Takahiro Nishio (Japan)

PF20-1 #10002
Comparison of Effectiveness of Mycophenolate Mofetil Associated with Standard Dose or Low Dose Tacrolimus for Liver Transplantation Immunosuppression
Dr. Ulil Albab Habibah (Indonesia)

PF20-2 #10234
Assessment of Segment 5 and Segment 8 Congestion In Right Lobe Liver Graft
Dr. Muhammad Zakria Wahla (Pakistan)

PF20-3 #10061
Liver-Targeted Nanoparticle Delivery of Tacrolimus Enhances Immunosuppression and Minimizes Systemic Toxicity in a Rat Liver Transplant Model

Dr. Parag K Rane (India)

PF20-4 #10090
Role of Fibroscan in the Early Detection of Hepatocellular Carcinoma in 1000 Cirrhotic Egyptian Patients
Dr. Abdelghani Badran (Egypt)

PF20-5 #10127
DNA Methyltransferases as Biomarkers for HCV Related Hepatocellular Carcinoma
Dr. Mohamed Abdel-Samiee (Egypt)

13:30-14:00 Poster Session 21: Liver Transplantation-Experimental/ Viral Hepatitis-Clinical
Moderator: Dr. Kyoko Fukuhara (Japan)

PF21-1 #10079
Establishment of a Reproducible Rat Model for Orthotopic Liver Transplantation to Study Post Transplant Immunomodulation and Regeneration
Dr. Shatrughna Nagrik (India)

PF21-2 #10062
Hepatic Neuro Axis Crosstalk after Liver Transplantation: Neuroinflammatory Consequences and Pharmacological Neuroprotection in a Rodent Model
Dr. Ashish Dhote (India)

PF21-3 #10134
Paradoxical Association between Steatotic Liver Disease and Favorable Hepatic Outcomes in HCV Patients with SVRs
Dr. Zing-Ling Chang (Taiwan)

PF21-4 #10029
A Pilot Study on Hepatitis B Core Related Antigen (HBcrAg) as a Novel Marker for Monitoring Antiviral Therapy in Chronic Hepatitis B Patients
Dr. Pravinkumar Pyarelal Rejliwal (India)

PF21-5 #10049
Acute Viral Hepatitis in Hospitalized Children: Clinico-Biochemical, Ultrasonographic and Etiological Findings from North India

Dr. Monirujjaman Biswas (India)

13:00-13:30 Poster Session 22: Viral Hepatitis-Clinical

Moderator: Dr. Sachiyo Yoshio (Japan)

PF22-1 #10053

Dual Burden of Infections: Seroprevalence of Acute Viral Hepatitis among Dengue Patients in Northern India

Dr. Monirujjaman Biswas (India)

PF22-2 #10050

Clinicoepidemiology and HCV Core Antigen Assay Diagnosis of Hepatitis C: Findings from a Tertiary Care Hospital of North India

Dr. Monirujjaman Biswas (India)

PF22-3 #10052

Clinical Profile and Outcomes of Hepatitis A Virus Associated with Severe Acute Liver Injury in Adults: A Case Study of Delhi, India

Dr. Monirujjaman Biswas (India)

PF22-4 #10222

Hepatocellular Risk Outcomes of Long-term Treatment of Chronic HBV Infection: Network Meta-analysis

Dr. Evannelson E. P. Wardhana (Indonesia)

PF22-5 #10144

Co-occurrence Hepatic Steatosis and Hepatitis B Virus, Hepatic Steatosis and Hepatitis C Virus at a Tertiary Referral Hospital in Indonesia

Dr. Laode Kardin (Indonesia)

13:30-14:00 Poster Session 23: Liver Fibrosis-Clinical/MASLD-Clinical

Moderator: Dr. Maki Morinaga (Japan)

PF23-1 #10041

Creatinine-to-cystatin-C Ratios Predict Liver Fibrosis in Patients with Metabolism-associated Steatotic Liver Disease for Reducing Risk of Liver-related Death

Dr. Masafumi Oyama (Japan)

PF23-2 #10043

Allyl Nonanoate: A Bile Metabolite and Potential Biomarker for Hepatic Fibrosis in MASLD
Dr. Dae Won Jun (Korea)

PF23-3 #10073
Pathophysiological Mechanisms Linking MASLD and NCDs and Their Association with Mortality
Dr. Minjeong Kang (Korea)

PF23-4 #10087
Pediatric Nonalcoholic Steatohepatitis in a Patient with Heterozygous Familial Hypobetalipoproteinemia
Dr. Sonoko Kondo (Japan)

PF23-4 #10231
Unveiling the True Burden of Steatotic Liver Disease: Mortality Risks by Subtype and Fibrosis Stage in a UK Nationwide Cohort
Dr. Qi Feng (United Kingdom)

13:00-13:30 Poster Session 24: Liver Fibrosis-Experimental/Other Liver Disease-Clinical
Moderator: Dr. Kosuke Kaji (Japan)

PF24-1 #10125
Deep Learning-Based Inference of Monocyte-Stromal Crosstalk Predicts Fibrosis-Linked Lower Urinary Tract Dysfunction in Males
Dr. Rifaldy Fajar (Indonesia)

PF24-2 #10022
Beneficial Effects of Milk-Derived Extracellular Vesicles on Liver Fibrosis Progression by Restoring Intestinal Barrier Integrity
Dr. T. Nakatani (Japan)

PF24-3 #10076
miR-4449 Modulates the Progression of MASH-induced Fibrosis by Regulating the Merlin-TAZ Pathways
Dr. Ji Hoon Kim (Korea)

PF24-4 #10157

Usefulness of the Stroop Test to Predict Decompensation Events in Patients with Cirrhosis: A Prospective Cohort Study
Dr. Masashi Aiba (Japan)

PF24-5 **#10227**
Role of Interleukin-6 as Risk Factor of Hepatic Encephalopathy Incidence Compared to Amonia in Liver Cirrhosis Patient
Dr. Muhammad Bilal Saifulhaq (Indonesia)

13:30-14:00 Poster Session 25: Liver Tumor-Clinical/Liver Tumor-Experimental/MASLD-Clinical
Moderator: Dr. Tomomi Kogiso (Japan)

PF25-1 **#10108**
PNPLA3 I148M is not Associated with HCC Risk but Correlates with Tumor Differentiation in MASLD Patients
Dr. Dong Yeup Lee (Korea)

PF25-2 **#10129**
Latent Transforming Growth Factor-Beta Binding Protein 1 as A Molecular Diagnostic marker for Hepatocellular Carcinoma
Dr. Mohamed Abdel-Samiee (Egypt)

PF25-3 **#10051**
Steatotic Liver Disease: An Important Upstream Risk Factor for the Development of Metabolic Syndrome-related Diseases
Dr. Yoshihiro Kamada (Japan)

PF25-4 **#10075**
Short Term and Long Term Regression of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) in Older Adults
Dr. Taeho Kwak (Korea)

13:00-13:30 Poster Session 26: Liver Tumor-Experimental/MASLD-Clinical
Moderator: Dr. Yoshinari Asaoka (Japan)

PF26-1 **#10176**
Establishment of a Mouse Model of Liver Tumorigenesis with Concurrent Steatotic Liver Disease
Dr. Saki Muronaga (Japan)

PF26-2 **#10098**

The Utility of Non-invasive Imaging Modalities for Diagnosing Cirrhosis in Metabolic-dysfunction Associated Steatotic Liver Disease: A Systematic Review

Dr. Talia Yi Hui Chan (Singapore)

PF26-3 **#10017**

Prognostic Significance of Bioelectrical Impedance Analysis in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Dr. Karen Cheuk-Ying Ho (Hong Kong)

PF26-4 **#10032**

Impact of Hypothyroidism on Liver-related Events among People with Metabolic Dysfunction-associated Steatotic Liver Disease

Dr. Xinrui Jin (Hong Kong)

PF26-5 **#10003**

Association Between Sitting Time and Frailty in Patients with MASLD: A Survey Using the Global Physical Activity Questionnaire (GPAQ)

Dr. Takumi Kawaguchi (Japan)

13:30-14:00 Poster Session 27: MASLD-Clinical

Moderator: Dr. Seung Up Kim (Korea)

PF27-1 **#10044**

Molecular Clustering of Metabolic Dysfunction-Associated Steatotic Liver Disease Based on Transcriptome Analysis

Dr. Dae Won Jun (Korea)

PF27-2 **#10045**

Cost-effectiveness Analysis of MASLD Screening Using FIB-4 Based Two-step Algorithm in the Medical Check-up

Dr. Dae Won Jun (Korea)

PF27-3 **#10084**

Changes in ALT Levels Following Tirzepatide Initiation in Patients with MASLD

Dr. Yusuke Johira (Japan)

PF27-4 **#10104**

Uncovering Patient Awareness of Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) in Singapore: Risk Factors, Complications and Management Strategies
Dr. Jasmin Lim (Singapore)

PF27-5 #10137
Differences in the Prevalence of NAFLD, MAFLD, and MASLD According to Changes in the Nomenclature in a Health Checkup Using MRI erived Proton Density Fat Fraction
Dr. Sunyoung Lee (Korea)

13:00-13:30 Poster Session 28: Liver Transplantation-Experimental/MASLD-Clinical
Moderator: Dr. Mohamed Abdel-Samiee (Egypt)

PF28-1 #10186
Gene Expression Analysis of Immune Rejection in a Mouse Liver Transplantation Model
Dr. Nanoha Maeda (Japan)

PF28-2 #10142
The Association between Metabolic Abnormalities and the Development of Fatty Liver: A Cohort Study Using a Large Scale Health Check-up Database in Japan
Dr. Yayoi Yoshinaga (Japan)

PF28-3 #10155
Prevalence of Risk Factors for Non Alcoholic Fatty Liver Disease in Cryptogenic Cirrhosis: A Case Control Study
Dr. Premasish Kar (India)

PF28-4 #10165
Changing Trends and Survival Outcomes in MASLD-related Hepatocellular Carcinoma: A Multicenter Retrospective Cohort Analysis
Dr. Darren J. H. Tan (Singapore)

PF28-5 #10170
Incretin-Based Therapies for MASLD with Type 2 Diabetes: Results from Two Prospective Studies
Dr. Taeang Arai (Japan)

13:30-14:00 Poster Session 29: MASLD-Experimental

Moderator: Dr. Akiko Eguchi (Japan)

PF29-1 #10175
The Mechanism of BGB324 and the Effect of AXL Family Inhibitors in MAFLD
Dr. Mengmeng Wang (Singapore)

PF29-2 #10178
Strain-Dependent Susceptibility to Diet-Induced Fatty Liver Disease in Mice
Dr. Nanoka Nishida (Japan)

PF29-3 #10187
Effect of the Emulsifier Polysorbate 80 on a Diet-Induced MASLD Mouse Model
Dr. Mana Hanasaki (Japan)

PF29-4 #10192
PNPLA3 I148M GG Variant Promotes Immune Cell Infiltration and is Linked to Metabolic Dysfunction-associated Steatotic Liver Disease Progression
Dr. Jung Hoon Cha (Korea)

PF29-5 #10219
Hepatocyte-specific (pro)renin Receptor Knockout Attenuated Diet-induced Steatosis in Mice with Improved Insulin Resistance and Metabolic Rates
Dr. Y. C. Hsieh (Taiwan)

13:00-13:30 Poster Session 30: MASLD-Experimental

Moderator: Dr. Kenji Takemoto (Japan)

PF30-1 #10016
RNA Binding Protein TIA1 Protects Hepatic Lipid Homeostasis and Prevents Fibrotic Nonalcoholic Steatohepatitis through Stress Granule Assembly
Dr. Rong Liu (China)

PF30-2 #10042
Nintedanib Alleviates Metabolic Dysfuction-Associtated Steatohepatitis by Suppressing THBS1 Expression in Activated Fibroblasts
Dr. Sung Woo Cho (Korea)

PF30-3 #10100

Mitochondrial ROS Accumulation as a Key Pathogenic Driver in MASLD: Impact of Disrupted Mitochondrial Protein Processing of Antioxidant Enzymes
Dr. Hyun Ae Woo (Korea)

PF30-4 #10106
Intestinal Epithelial Peroxisome Proliferator-activated Receptor Gamma; Deficiency Deteriorates Insulin Resistance in Mice with Metabolic Dysfunction-associated Steatohepatitis
Dr. Hsin-Hua Lai (Taiwan)

PF30-5 #10115
Maintenance of Mitochondria-driven Oxysterol Metabolism is a Key to Early MASLD Prevention
Dr. Kei Minowa (Japan)

13:30-14:00 Poster Session 31: Liver Fibrosis-Clinical/Other Liver Disease-Clinical
Moderator: Dr. Reiko Yaginuma (Japan)

PF31-1 #10113
Evaluation of Non-Invasive Fibrosis Markers in HBV-Infected Pregnant Women from the Kyrgyz Republic
Dr. Ainura Z. Kutmanova (Kyrgyz)

PF31-2 #10039
Wilson's Disease in Adults in Vietnam from 2012-2022
Dr. Vu Van Khien (Viet Nam)

PF31-3 #10031
Sanger Sequencing in the Diagnosis of Rare Liver Diseases in Southern Vietnam
Dr. Ngan Thanh Quynh Le (Viet Nam)

PF31-4 #10074
A Case of PFIC Type7, Demonstrating the Utility of whole Exome Sequencing
Dr. Naoki Shikano (Japan)

PF31-5 #10152
Frailty is an Independent Predictor of Mortality in Patients with Chronic Liver Disease: A Multicenter Retrospective Cohort Study
Dr. Shinji Unome (Japan)

13:00-13:30 Poster Session 32: Other Liver Disease-Clinical

Moderator: Dr. Yoichiro Uchida (Japan)

PF32-1 **#10048**

Evaluation of the Efficacy of Lusutrombopag in Chronic Liver Disease: Impact of Liver Disease Etiology and Pretreatment Platelet Count

Dr. Satoru Kakizaki (Japan)

PF32-2 **#10136**

Intergrated Surgical Approach for Hepatic Cystic Echinococcosis: Experience from the Syzganov National Scientific Center of Surgery

Dr. Madiyar Nagasbekov (Kazakhstan)

PF32-3 **#10220**

Integrated Liver Care in Indonesia: A Model Study of Collaboration in the Management of Chronic Liver Disease in Communities

Dr. Andi Makkasau (Indonesia)

PF32-4 **#10201**

Impact of Partial Splenic Embolization on Pancreatic Congestion with Portal Hypertension

Dr. Hironao Okubo (Japan)

PF32-5 **#10033**

Evaluation of Chemotherapy-associated Fatty Liver Disease in Epithelial Ovarian Cancer: The Clinical Significance

Dr. Harshita Dubey (India)

Poster Session 33: Liver Fibrosis-Clinical/Other Liver Disease-Clinical

Moderator: Dr. Hitoshi Maruyama (Japan)

PF33-1 **#10035**

Comparison of Noninvasive Test for Histological Cirrhosis in Primary Biliary Cholangitis

Dr. Manabu Hayashi (Japan)

PF33-2 **#10226**

Body Mass Index as a Predictor of Liver Fibrosis and Steatosis Grades in Patients with Chronic Liver Disease

Dr. Resha Dermawansyah Rusman (Indonesia)

PF33-3 #10193
Dengue-Induced Coagulopathy Presenting with Hemorrhagic and Ischemic Stroke: A Rare but Life-Threatening Complication
Dr. Yohannes Christian Silalahi (Indonesia)

PF33-4 #10135
Endoscopic Ultrasound (EUS)-guided Portal Pressure Gradient Measurement Assessment of Acute Hemodynamic Response to Intravenous Propranolol
Dr. Rafael Romero-Castro (Spain)

PF33-5 #10132
The Role of Serum Kallistatin Level in Comparison to Other Non-Invasive Panels for Evaluating Portal Hypertension in Egyptian Cirrhotic Patients
Dr. Abdelaziz Farag (Egypt)

13:00-13:30 Poster Session 34: Liver Tumor-Clinical

Moderator: Dr. Maki Tobari (Japan)

PF34-1 #10094
Prognostic Value of Circulating cfDNA in Patients with Unresectable HCC Receiving Atezolizumab and Bevacizumab
Dr. Akimitsu Meno (Japan)

PF34-2 #10195
A Rare Case of Hepatogastric Fistula Induced by Radiofrequency Ablation Combined with Atezolizumab plus Bevacizumab in the Treatment of Hepatocellular Carcinoma
Dr. Naoto Kose (Japan)

PF34-3 #10110
High Proximity of Treg-CD4T Cell Interactions in Spatial Omics Analysis Regulating Cancer Progression in Patients with Hepatocellular Carcinoma
Dr. Junki Yamashita (Japan)

PF34-4 #10117
Dr. Michihiko Kawahara (Japan)

A Case of Immune-related Adverse Event Arthritis During Atezolizumab plus Bevacizumab Therapy for Hepatocellular Carcinoma

Dr. Michihiko Kawahara (Japan)

PF34-5 **#10172**

Pre-treatment GLIM-defined Malnutrition Predicts Poor Prognosis in Patients with Unresectable Hepatocellular Carcinoma Undergoing Systemic Therapy

Dr. Mikita Oi (Japan)

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

State of the Art Lectures

State of the Art Lecture 1

Dr. Rohit Loomba
Professor of Medicine,
Chief, Division of Gastroenterology and Hepatology,
University of California at San Diego,
USA

Emerging Therapies for MASH Related Fibrosis

Metabolic dysfunction associated steatohepatitis (MASH) is one of the most common causes of chronic liver disease worldwide. MASH is characterized by presence of steatosis, lobular inflammation, ballooning with or without fibrosis on liver histology and is associated with progressive fibrosis and can lead to cirrhosis and hepatocellular carcinoma and may lead to liver related morbidity and mortality. It is commonly associated with obesity, diabetes, and metabolic risk factors. Lifestyle interventions such as reducing free sugar intake, weight loss, and exercise are helpful in reducing the risk of progression and reversing MASH. However, majority of patients suffering from MASH related fibrosis may require pharmacologic therapies in addition to lifestyle interventions to reverse fibrosis and resolution of MASH. Over the last 2 years, resmetirom, a thyroid Beta receptor agonist, and semaglutide, a glucagon-like peptide 1 (GLP-1), have been conditionally approved for the treatment of MASH related moderate to advanced fibrosis without cirrhosis. Multiple therapies have shown promising phase 2b data and are in Phase 3 trials. In addition to currently approved therapies, here, we will discuss emerging therapies such as tirzepatide, survodutide, retadutide, lanifibranor, pegozafermin, effruxifermin, efimosfermin, DGAT-2 inhibitor, FASN-inhibitor in MASH related fibrosis.

State of the Art Lecture 2

Dr. David A. Brenner
Professor of Eminence,
Sanford Burnham Prebys Medical Discovery Institute, La Jolla,
USA

A Rationale Approach to Drug Discovery in MetALD

Background & Aims: The extent of liver fibrosis correlates closely with morbidity and mortality in patients. Excessive alcohol consumption and/or the metabolic syndrome result in a synergistic development of liver fibrosis (MetALD), which is characterized by increased Collagen Type I deposition, produced by activated Hepatic Stellate Cells (HSCs). However, there are no therapies that target liver fibrosis. Targeting collagen production in activated HSCs is an important strategy to halt liver fibrosis.

Methods: Gene expression profiles of human HSCs were analyzed using single nucleus (sn)RNA-seq of NORMAL, MASL, MASH, and MetALD livers. The mRNA of La-related protein 6 (LARP6), an RNA-binding protein which binds to the 5' stem-loop region of collagen mRNAs, was highly induced in activated HSCs from MetALD patients. To determine the role of LARP6 in HSC activation, isolated primary human HSCs were transfected with LARP6-specific (or control) dsiRNA and used to generate human liver spheroids. Human liver spheroids were composed of human liver cells in physiological ratios: 57% hepatocytes, 28% NPCs, and 15% dsiRNA-transfected HSCs. Upon formation of spheroids at day 7, human liver spheroids were cultured in MASH- or MetALD-cocktails for an additional 7 days. The MASH-cocktail contained palmitate, oleate, fructose, glucose, LPS, and human TGF-β1, while MetALD cocktail was prepared by adding 100 mM ethanol to the MASH-cocktail. To identify a LARP6 inhibitor, we delveloped a high through put assay using FRET that fluorometrically distinguished between LARP6 binding to the 5'UTR SL and unbound RNA.

Results: snRNA-sequencing identified LARP6 as one of the most highly induced genes in activated human HSCs from MASH and MetALD livers (vs NORMAL or MASL HSCs). The binding of LARP6 to collagen mRNA was validated using an enhanced CLIP (eCLIP) assay, with eCLIP peaks enriched at the 5'UTR regions of COL1A1, COL1A2, and COL3A1, demonstrating the specific binding of LARP6 to Collagen Type I/III mRNAs. Ribosome profiling revealed a significant reduction in the translation of COL1A1, COL1A2, and COL3A1 in LARP6-knockdown human HSCs. Knockdown of LARP6 suppressed TGFβ1-induced expression of fibrogenic genes in human HSCs. The development of liver fibrosis was examined in human liver spheroids which contained LARP6-knocked down human HSCs. Knockdown of LARP6 markedly reduced Collagen Type I/III deposition in MASH- or MetALD-induced human liver spheroids. The HTP screening identified hundreds of potential LARP6 inhibitors. A counter-screen eliminated artifactual fluorescence and a secondary screen identified four compounds with high binding affinity.

Conclusions: LARP6 regulates the activation of human HSCs from MASH or MetALD livers through specific binding to Collagen Type I/III mRNAs. Our results suggest that targeting LARP6 in human HSCs may provide new strategies for anti-fibrotic therapy.

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Special Lectures

Special Lecture 1

Dr. Shiv K. Sarin
Professor of Eminence,
Chancellor and Director
Institute of Liver and Biliary Sciences, New Delhi,
India

Precision Medicine for Metabolic Dysfunction Associated Fatty Liver Disease (MAFLD)

Metabolic dysfunction–associated fatty liver disease (MAFLD) is a heterogeneous, systemic disorder whose variable trajectories—from benign steatosis to inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma—demand individualized care. Precision medicine for MAFLD requires combining inherited risk, objective disease staging, and advanced computational models to predict risk, select therapies, and monitor response. The use of polygenic risk scores (PRS) help to define inherited susceptibility (e.g., PNPLA3, TM6SF2, GCKR, HSD17B13 and many additional loci) and stratify individuals by probability for hepatic fat accumulation, inflammatory activity, and fibrosis progression. When used together with clinical variables, PRS improves early identification of high-risk asymptomatic individuals and guides surveillance intensity. Additionally, the gut microbiome is a modifiable, disease-relevant axis. Microbiome signatures and metabolomic readouts both act as biomarkers and therapeutic targets (probiotics/synbiotics, donor-specific FMT, postbiotics, bile-acid modulators) that can be chosen for therapeutic end-points based on individual microbial profiles.

Accurate fibrosis staging (noninvasive elastography, MRI-PDFF + MR elastography, serum fibrosis panels) is an important clinical determinant for prognosis and treatment allocation. Combining fibrosis stage with metabolic phenotype (eg, lean or obese, T2DM), PRS, and microbiome profile enables proper therapy selection; lifestyle ± precision nutrition for low-risk; incretin-based metabolic therapies for obesity/T2DM predominant disease; antifibrotic and FXR/FGF-based agents for ≥F2 fibrosis or for rapid progressors; microbiome-targeted interventions when specific dysbiotic signatures predict benefit. Precision medicine may be more important in lean MAFLD subjects who would otherwise remain undetected. Measurement of waist/hip ratio and visceral fat needs to be included in surveillance.

We sequenced 68 genes in nearly 900 Indian patients with MAFLD. In this cohort, PNPLA3 and GCKR mutations were common irrespective of CAP parameters. PNPLA3.Ile148Met was found to increase the LSM-based fibrosis. TM6SF2 was uncommon in the Indian population. On the other hand, SOD2.Ala16Val was significantly associated with high ALT levels in patients with normal CAP values. Similarly, the mutation in MBOAT7, commonly seen in the Caucasian populations was not found to be informative in Indian population

The future of precision medicine will depend on multi-ethnic genomic datasets, prospective multi-omic cohorts and randomized evaluation of PRS/microbiome-guided interventions. By uniting genetics, microbiome science, objective staging, and AI, precision medicine can shift MAFLD care from reactive disease management to proactive, individualized prevention and therapy.

Special Lecture 2

Dr. Takeshi Okanoue
Honorary Director,
Saiseikai Suita Hospital,
Specially Appointed Professor,
Kyoto Prefectural University of Medicine
Japan

AI Diagnostic Systems can Accurately Diagnose Stage of Liver Fibrosis and Predict HCC Development in MASH

Background: Hepatic fibrosis is the most important variable to stratify the risk for LRE in MASH. We constructed the new AI neural network algorithm ”Fibro-Scope” identifying liver fibrosis stage by using 10 parameters (age, sex, height, weight, AST, ALT, GGT, cholest, TG, PLT and T4C7S). Abdominal ultrasound and with or without serum AFP has served as HCC surveillance testing but its sensitivity is suboptimal. The frequency of elevation of serum AFP was very low and DCP is suboptimal in early stage MASH-HCC but the elevation of serum IgM-free apoptosis inhibitor of macrophage (fAIM) was high frequency. We established a simple and effective surveillance method for early stage HCC in MASH using AI/neural network system (HCC-Scope).

Methods: 1) Fibro-Scope was constructed using data from NASH with F2 or F3 (STELLAR-3) and F4 (STELLAR-4) in two phase III with Japanese MASLD data. The total of 898 MASLD patients were analyzed

2) 175 MASLD and 55 MASH-HCC patients were enrolled. Of the 55 HCC patients 27 were very early stage HCC and 6 were early stage HCC. HCC-Scope was conducted using 15 items: age, sex, height, weight, body mass index, AST, ALT, GGT, cholest, TG, PLT, diabetes, AFP, DCP, and fAIM.

Results: 1) The discrimination of F0–2 from F3,4 through Fibro-Scope was characterized by a 99.8% sensitivity, a 99.6% specificity, a 99.8% PPV, and a 99.6% NPV with gray zone analysis; similar effectiveness was also revealed in the analysis without a gray zone.

2) Differential diagnosis between not HCC and HCC using the HCC-Scope revealed 100.0% sensitivity, 100.0% specificity, 100.0% PPV, and 100.0% NPV in a training study with gray-zone analysis. HCC-Scope showed significantly better sensitivity and specificity than GALAD (gender, age, AFP-L3, AFP, DCP) score (its sensitivity: 85.3%, specificity: 85.1%).

Conclusion: Fibro-Scope can accurately diagnose fibrosis stage. The newly developed AI system algorithms termed HCC-Scope is easy to use and can accurately differentially diagnose between MASH without HCC and MASH-HCC including early stage HCC.

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"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Symposiums

Dr. Lai Wei
Dean and Professor,
Hepatopancreatobiliary Center, Beijing Tsinghua Changgung Hospital,
School of Clinical Medicine, Tsinghua University, Beijing,
China

The Non-invasive Assessment of Liver Fibrosis in Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) in the Asia Population

In the recommended algorithm of APASL MAFLD guideline 2025, the methods to diagnose, evaluate, and monitor disease severity in suspected patients with MAFLD and management approach for confirmed cases are HDL-cholesterol, high-density lipoprotein cholesterol; FIB-4, Fibrosis-4 index; NFS, MAFLD fbrosis score; ELF, enhanced liver fbrosis; SSI, supersonic shear imaging; ARFI, acoustic radiation force impulse; VCTE, vibration-controlled transient elastography; MRE, magnetic resonance elastography.

In the meantime, there are a bit variation at Country level in Asia-Pacific region. In Japan, VCTE, FIB-4, and NFS were recommended for suspected NAFLD patients and with fibrosis. In China, LSM (8 kPa to rule out and 12 kPa to rule in advanced fibrosis) can be used for non-invasive assessments of hepatic steatosis and advanced fibrosis and the FIB-4 score can serve as an initial tool to evaluate the risk of advanced fibrosis in MAFLD patients and high-risk populations. Individuals with FIB-4 ≥ 1.3 should undergo LSM by transient elastography for further risk stratification of fibrosis. In Korea, serum markers can be used to exclude advanced fibrosis among patients with NAFLD, however, in patients with NAFLD, liver fibrosis can be assessed using VCTE, SWE, or MRE. In India, they recommends using APRI, FIB-4 as the initial screening tools for the assessment of hepatic fibrosis at the primary and secondary healthcare levels and also suggests that patients with high or intermediate results of APRI and FIB-4 or those with discordant results may be referred to tertiary health care levels and further using VCTE at tertiary care levels to corroborate the results of APRI and FIB-4 with suggests that an LSM cut-off of 8.2 kPa and 13.6 kPa may be used for detecting the presence of significant fibrosis and cirrhosis, respectively, in clinical practice. Last year, resmetirom was approved as first drug targetting to NASH/MASH, to prescribe resmetirom, AASLD recommended using VCTE, ELF, MRE to identify patients with MASH and significant/advanced fibrosis, and using FAST, MAST, MEFIB as alternative composite tests to identify at-sisk MASH. AASLD also recommended using VCTE to assess of treatment response on-treatment.

Therefore, VCTE is well recommenced for fibrosis assessment in Asia, it could be develop for treatment patient identification and treatment response assessment. ELF should be studied more and incorporated into NASH/MASH new drug clinical trials.

Dr. Suthat Liangpunsakul
Professor of Medicine, Biochemistry, and Molecular Biology,
Dean's Scholar in Medical Research
Division of Gastroenterology and Hepatology
Department of Medicine, Indiana University School of Medicine, Indiana, USA

Screening for Patients with MetALD in At-Risk Populations: A Practical Approach to Early Detection

Metabolic dysfunction-associated alcohol-associated liver disease (metALD) represents a growing and under-recognized phenotype at the intersection of metabolic dysfunction and alcohol-related liver injury. Individuals with coexisting metabolic risk factors and alcohol use are at particularly high risk for progressive liver disease, including advanced fibrosis and cirrhosis. However, routine screening for liver disease in this dual-risk population remains limited in clinical practice.

This talk will review current concepts in the pathogenesis and epidemiology of metALD and present a pragmatic, stepwise approach to identifying at-risk patients in real-world settings. We will define the target population, individuals with both hazardous alcohol consumption and metabolic comorbidities such as obesity, type 2 diabetes, dyslipidemia, and hypertension, and outline evidence-based screening strategies using readily available clinical tools.

Key components of this approach include initial alcohol use assessment using validated instruments (e.g., AUDIT-C) alongside evaluation of metabolic risk factors and basic laboratory testing. Non-invasive fibrosis risk stratification using serum-based scoring systems (e.g., FIB-4, NAFLD Fibrosis Score) will be highlighted as a cost-effective first step in primary care and specialty settings. For individuals with elevated risk, we will discuss the utility of second-line tools such as transient elastography (FibroScan) to assess hepatic steatosis and fibrosis.

The talk will also address implementation strategies for integrating metALD screening into diverse clinical workflows, including primary care, endocrinology, addiction medicine, and hepatology. Finally, we will review gaps in the current evidence base, including the need for validated screening thresholds and longitudinal studies to guide risk stratification in metALD. By adopting a proactive approach to screening, clinicians can play a pivotal role in identifying patients with silent but progressive liver disease and intervene before irreversible liver damage occurs.

Dr. Seung Up Kim
Professor of Internal Medicine
Yonsei University, Seoul,
South Korea

The Role of Noninvasive Tests in the Diagnosis and Prognosis Assessment in MASLD

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as nonalcoholic fatty liver disease (NAFLD), has emerged as the most prevalent chronic liver condition globally. The traditional reliance on liver biopsy for diagnosis and staging is limited by its invasiveness, cost, and potential complications, prompting the development of noninvasive tests (NITs) to enhance patient care.

NITs encompass a range of serum biomarkers and imaging modalities. Widely validated serum-based scores such as the Fibrosis-4 (FIB-4) index, NAFLD Fibrosis Score (NFS), and Enhanced Liver Fibrosis (ELF) test effectively stratify fibrosis risk, particularly in primary care settings. Advanced imaging techniques, including vibration-controlled transient elastography (VCTE), magnetic resonance elastography (MRE), and multiparametric MRI with iron-corrected T1 (cT1) mapping, offer high diagnostic accuracy for assessing liver fibrosis and steatosis. Combining these modalities, as seen in algorithms like MEFIB (MRE + FIB-4) and FAST (FibroScan-AST), further enhances diagnostic precision.

Beyond diagnosis, NITs serve prognostic purposes by identifying patients at increased risk of liver-related events, thereby informing surveillance and therapeutic strategies. The integration of NITs into clinical practice facilitates early detection, risk stratification, and monitoring of MASLD, potentially reducing the need for invasive procedures. Ongoing research aims to refine these tools and validate their efficacy across diverse populations.

Dr. Katsuhiro Sano
Associate Professor,
Department of Radiology,
Juntendo University Graduate School of Medicine
Japan

Liver MR Fingerprinting: Tissue Characterization and Comparison with Conventional Quantitative MR Imaging

Magnetic resonance fingerprinting (MRF) is a novel MRI technique first published in Nature in 2013. It enables the simultaneous acquisition of T1 and T2 values within a very short scan time. Unlike conventional T1-weighted or T2-weighted images commonly used in clinical practice, MRF provides high-speed acquisition of quantitative T1 and T2 values.

Liver MRF allows for the simultaneous, co-registered quantification of T1, T2, T2*, and fat fraction (FF) maps in a single breath-hold scan. Multiparametric liver MRF has demonstrated excellent repeatability and high agreement with conventional separate quantitative mapping techniques in patients with liver disease. These MRF-derived quantitative values correlate with key histopathological features such as steatosis, inflammation, fibrosis, and siderosis, enabling noninvasive estimation of their extent in cases of diffuse liver disease.

Dr. Kenichi Harada
Professor,
Department of Human Pathology,
Graduate School of Medical Sciences, Kanazawa University, Ishikawa
Japan

Pathology of Steatotic Liver Disease

Steatotic liver disease (SLD) is the comprehensive term for conditions characterized by abnormal lipid deposition in the liver. Although hepatic steatosis is found in other diseased livers including hepatitis C virus infection and some kinds of pediatric liver diseases as well as metabolic dysfunction-associated steatotic liver disease (MASLD). Metabolic dysfunction-associated steatohepatitis (MASH) is a heterogeneous liver disease, of which incidence was led by multiple etiologies, including obesity, metabolic syndrome, and genetic risk. As its pathogenesis, hepatic lipid accumulation generally triggers lipotoxicity and induces MASLD or progress to MASH by mediating endoplasmic reticulum stress, oxidative stress, organelle dysfunction, and ferroptosis. Pathologically, in addition to steatosis, hepatitic change consists of hepatocellular degeneration and necrosis and infiltration of inflammatory cells. Hepatic stellate cells are the primarily cells responsible for hepatic fibrogenesis, irrespective of liver diseases. The pathological diagnosis of MASH is based on the findings of steatosis, lobular inflammation and hepatocellular ballooning, to make the diagnosis of steatohepatitis. There are no changes to the pathological diagnostic criteria for steatohepatitis, irrespective of MASH or conventional termed non-alcoholic steatohepatitis (NASH). Typical cases with these findings are not difficult to diagnose, but there are many cases where the presence or absence of these findings and the diagnosis of steatohepatitis are difficult to make for general pathologists. In addition, chronic liver diseases, irrespective of their etiologies, are characterized by the heterogeneous distribution of each finding in the liver, and it is necessary to estimate the pathology of the whole liver from the limited tissue samples obtained from liver needle biopsies. Furthermore, the degree of fibrosis is also irregularly distributed within the liver biopsied tissue, making staging difficult. Fibrosis score generally displays increased HCC incidence and mortality, but a number of MASH patients develop HCC without cirrhosis, approximately 15% of HCC derived from MASLD cases. In recent years, as the population of patients with metabolic dysfunction has increased, it is important to exclude other liver diseases in pathological diagnosis, especially to differentiate from drug-induced liver injury and autoimmune liver diseases and also diagnose the overlap with these differential diseases.

Dr. Bin Gao
Deputy Scientific Director,
Chief, Laboratory of Liver Diseases
NIAAA, National Institutes of Heath Bethesda,
USA

Single Cell RNA Seq Analysis of Inflammation in Alcohol-associated Liver Disease: Identification of Novel Therapeutic Targets

Alcohol-associated hepatitis (AH) is an acute inflammatory response that can occur in patients with chronic alcohol-associated liver disease (ALD), and severe AH is associated with high short-term mortality. Over the last several years, our lab extensively characterized liver inflammation in severe AH by using multiplex immunofluorescent staining and single-cell RNA (scRNA) sequencing. Our scRNA-seq analysis revealed a distinct IL-8+ neutrophil population enriched in sAH livers but not in alcohol-associated cirrhosis livers. Multiplex immunofluorescence staining analyses of liver tissues revealed that the majority of hepatic neutrophils in sAH are IL-8 positive, whereas circulating neutrophils in the same patients have minimal IL-8 expression. Immunofluorescence staining analyses of isolated neutrophils also confirmed neutrophils from sAH livers expressed much higher levels of IL-8 than those from the blood. In addition to IL-8, several other neutrophil chemokines such as CXCL1, CXCL5 and CXCL6, also upregulated in sAH livers, as shown by RNA sequencing and ELISA.11 Notably, scRNA seq analyses of sAH livers demonstrated that hepatocytes express CXCL1, hepatic stellate cells produce CXCL5, neutrophils predominately express IL-8, while macrophages and hepatocytes express low levels of IL-8. Thus, an autocrine IL-8 loop may drive recruitment and activation of neutrophils in sAH, and IL-8 expression in neutrophils is sustained by elevated IL-1β and TNF-α levels in the liver via the activation of p38 MAPK activation. In addition, our data revealed that ALD is associated with loss of duodenal CD8+ T cells but elevation of intrahepatic CD8+ T cells, which aggravates and ameliorates ALD, respectively. ScRNA seq analysis of ALD patient livers revealed several populations of CD8+ T cells expressing activation and survival genes, playing diverse roles in the pathogenesis of ALD. Restoration of survival and functions of intestinal and intrahepatic CD8+ T cells may represent a novel therapeutic strategy for ALD patients.

Dr. Ina Bergheim
Full Professor,
Department of Nutritional Sciences,
Molecular Nutritional Science,
University of Vienna,
Austria

Alterations of Alcohol Dehydrogenase (ADH) Activity in MASLD Development: Mechanisms and Implications

Results of several studies have shown that the development of MASLD in mice and humans is associated with elevated fasting ethanol levels in blood and breath despite an absence of alcohol consumption. This so called `endogenous´ ethanol has repeatedly been discussed as a critical factor in the development of MASLD. Studies further suggest that the increased ethanol levels found in peripheral blood of rodents and humans with MASLD are related with changes in intestinal microbiota composition and an elevation of intestinal microbial ethanol synthesis. Results of other studies also suggest that alcohol metabolism through alcohol dehydrogenase (ADH) may be altered. To test the hypothesis that besides an enhanced intestinal synthesis of ethanol, impairments of ethanol elimination may be critical in the development of MASLD and to assess implications of these alterations, fasting ethanol levels and ADH activity were assessed in humans and wild-type mice with MASLD. These studies were complemented with diet-induced mouse models to assess the effect of MASLD on ethanol elimination and vitamin A metabolism. Blood ethanol levels were significantly higher in patients and wild-type mice with MASLD, while relative ADH activity in blood and liver tissue was significantly lower compared to controls. Both alterations were significantly attenuated in MASLD diet-fed TNFα-/- mice and wild-type mice treated with an anti-TNFα antibody (infliximab). Moreover, alcohol elimination was significantly impaired in mice with MASLD. Retinoic acid levels in liver tissue were significantly lower in wild-type mice with MASLD. Synthesis of retinoic acids was also lower in mice with MASLD than in controls. Furthermore, a supplementation of retinoic acid but not of retinol in mice showing signs of beginning steatohepatitis was related with an improvement of liver histology and inflammation. Taken together, our data suggest that the development of MASLD is related to higher fasting ethanol levels even in the absence of alcohol intake and marked impairments of ADH activity subsequently leading to a lower elimination of ethanol and alterations in vitamin A metabolism.

Dr. Hua Wang
Professor in the Inflammation and Immune Mediated Diseases Laboratory of Anhui Province at Anhui Medical University,
China

Liver Inflammation and Injury

Background: Neutrophil infiltration and hepatocyte damage are indispensable hallmarks in alcohol-associated hepatitis (AH), yet the underlying crosstalk between neutrophils and hepatocytes and its role in AH pathogenesis remain unclear.
Objective: We investigate the regulatory role of leucocyte cell-derived chemotaxin 2 (LECT2) in hepatocyte-neutrophil interaction and its impact on AH progression.
DESIGN: We used bulk and single-cell RNA sequencing to identify hepatocyte-secreted factors targeting neutrophils. We analysed serum and liver samples from AH patients and employed genetically modified mice alongside in vitro studies.
Results: RNA-sequencing analysis identified several neutrophil chemokines that are elevated in hepatocytes from AH patients, including LECT2 whose role in AH remains largely unknown. AH patients exhibited increased levels of LECT2 in hepatocytes, positively correlating with the severity of AH. Ethanol-fed mice also exhibited elevated liver LECT2, which was abolished by inhibiting endoplasmic reticulum stress. Functional studies revealed that ethanol-induced liver injury was ameliorated in Lect2-deficient mice but was exacerbated in mice with hepatic overexpression of Lect2. Furthermore, LECT2 exacerbated ethanol-induced liver injury by promoting reactive oxygen species (ROS) through its interaction with prohibitin 2 (PHB2), a neutrophil membrane protein. By directly binding to PHB2, LECT2 disrupts the stable structure of PHB1/PHB2 heterodimerisation, consequently leading to PHB2 degradation, ROS accumulation, neutrophil activation and neutrophil extracellular trap formation. Moreover, therapeutic intervention of LECT2 via Lect2 shRNA ameliorated ethanol-induced liver injury.
Conclusion: Our studies identified a novel vicious cycle between neutrophils and hepatocytes through the LECT2-PHB2 interaction, presenting a promising therapeutic intervention by targeting LECT2 to mitigate AH in patients.

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Glutamatergic Metabolic Synapse in ASH

Alcohol-related liver disease (ALD) is induced by multiple factors that occur during various metabolic processes of hepatocyte, diverse absorption of pathogen- or damage-associated molecular patterns from intestine, and delivery of free fatty acids and pro-inflammatory cytokines from adipose tissue. These factors cause fat accumulation in hepatocyte at early stage but continuous drinking promotes more serious diseases such as inflammation, fibrosis and even tumor. However, interestingly, our team recently discovered the existence of glutamatergic signaling pathways in the liver and reported that ALD can be occurred by them. Briefly, we have revealed that chronic alcohol consumption increases glutamate production especially by aldehyde dehydrogenase 4 family member A1 (ALDH4A1) enzyme in hepatocyte, and generated hepatic glutamate is stored within the hepatocytes, and then secreted through xCT or granules. Simultaneously, metabotropic glutamate receptor 5 (mGluR5) is expressed in various non-parenchymal cells (NPCs) and exerts pathophysiological effects through interaction with secreted glutamate. In addition, released glutamate is mainly absorbed by hepatocytes and NPCs. Today, I would like to briefly introduce the roles of hepatic glutamate, as a hepatotransmitter, in inducing alcohol-associated steatohepatitis (ASH).

Glutamate, a crucial player in hepatic amino acid metabolism, has been relatively unexplored in the development of alcohol-associated steatohepatitis (ASH). Our research reveals that chronic alcohol consumption induces the formation of hepatic glutamate vesicles, driven by the aryl hydrocarbon receptor-mediated expression of vesicular glutamate transporter 3 (VGLUT3). Simultaneously, alcohol-induced changes, including perivenous hepatocyte ballooning, microvilli loss, and mitochondrial Ca2+ accumulation, bring Kupffer cells (KCs) into close contact with ballooned hepatocytes. Additional binge drinking triggers the exocytosis of glutamate vesicles by altering intracellular Ca2+ level, consequently activating NADPH oxidase 2 (NOX2) through metabotropic glutamate receptor 5 (mGluR5) in KCs which induces ROS production and promotes ASH. Accordingly, genetic or pharmacological interference of mGluR5 and NOX2 in KCs attenuates ASH. In patients, plasma glutamate and VGLUT3 vesicles correlate with ASH development. Conclusively, our findings posit that hepatocytes and KCs form a pseudosynapse through which glutamatergic signaling may induce ASH. This study highlights the intriguing roles of hepatic glutamate as a hepatotransmitter in ALD development. It is believed that these findings will contribute to the discovery of therapeutic targets and development of treatments for liver diseases.

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Genetic Variants of Alcohol-metabolizing Enzymes and Their Clinical Relevance to Psychiatry and Hepatology in Asian Populations

Epidemiological studies have demonstrated significant racial/ethnic variations in drinking patterns and the prevalence of alcohol-related adverse consequences, including alcohol use disorder (AUD). Compared to other racial/ethnic groups, Asians generally exhibit lower rates of alcohol misuse. The National Epidemiologic Survey of Alcohol Related Conditions (NESARC) showed that Asian Americans reported the lowest rates of 12-month abuse (1–2%) and dependence (2.3–2.4%). The rate of abuse was 2.5 times lower than that for European-descent and Native Americans and Hispanics, and 1.6 times lower than that for African-descent Americans. The rate of dependence was 1.6–2.6 times lower than that in other ethnic groups. These differences are attributed to various biological, genetic, and environmental factors, including the unique metabolism of alcohol in many Asians.

Research from the Kurihama Medical and Addiction Center explored the effects of genetic polymorphisms on alcohol- metabolizing enzymes in healthy individuals and patients with AUD. This presentation covers research on the genetic polymorphisms of alcohol dehydrogenase (ADH1B) and aldehyde dehydrogenase-2 (ALDH2) on subjective response to alcohol in healthy volunteers, their impact on the development of AUD, severity of alcohol withdrawal, their effect on alcoholic liver disease, and their relationship with alcohol-related cancers in patients with AUD. For example, the slow-metabolizing ADH1B genotype (ADH1B*1/*1) is associated with fatty liver disease in patients with AUD, whereas the fast-metabolizing ADH1B genotypes (ADH1B*2/*2 and ADH1B*1/*2) are associated with liver cirrhosis.

Genetic polymorphisms in alcohol-metabolizing enzymes significantly influence clinical manifestations, from subjective alcohol sensitivity to the risk of alcohol dependence, withdrawal, liver disease progression, and alcohol-related cancers. These findings highlight the interplay between genetic predispositions and environmental factors in AUD. Understanding these interactions provides a biological basis for individual differences in alcohol-related outcomes and enables personalized approaches in treatment, prevention, and risk stratification. This underscores the need for close collaboration between psychiatry and hepatology to address alcohol-related health issues.

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Aldehydes Drive the Shared Pathogenesis of Alcohol-Associated and Metabolic Dysfunction-Associated Steatohepatitis (ASH and MASH) by Inducing Mitochondrial Depolarization (mtDepo), Mitophagy, and Release of Profibrotic and Proinflammatory Mitochondrial Damage-Associated Molecular Patterns (mtDAMPs)

Intravital multiphoton microscopy and in vivo labeling with MitoTracker Red shows that ethanol (EtOH) induces reversible hepatocellular mtDepo in the central halves of liver lobules expressing cytochrome P4502E1. Similarly, mtDepo develops after feeding mice a Western diet high in fat, fructose, and cholesterol. Onset of mtDepo is driven by aldehydes, including acetaldehyde (AcAld) from EtOH metabolism and aldehydes from β-scission of hydroperoxides formed after lipid peroxidation. mtDepo, as well as an increase in mitochondrial respiratory capaticty after EtOH treatment, acts to accelerate adaptive mitochondrial respiration needed for the detoxifying oxidation of these aldehydes by mitochondrial aldehyde dehydrogenases. Simultaneously, voltage-dependent anion channels (VDAC) in the mitochondrial outer membrane close to block exchange of bilayer-impermeant metabolites but not membrane-permeant aldehydes. VDAC closure acts to prevent futile mitochondrial ATP hydrolysis after mtDepo, inhibit β-oxidation of fatty acids, and promote steatosis. mtDepo also induces mitophagy. Chronically, overburdened mitophagy and impaired processing of mitophagosomes by lysosomes leads to release of mtDAMPs like mitochondrial DNA that activate hepatic stellate cells and Kupffer cells to cause fibrosis and steatohepatitis. This shared aldehyde-driven pathogenesis of ASH and MASH accounts for the nearly identical histopathology of the two diseases and the synergism between them. This pathogenesis suggests novel preventative and therapeutic strategies against (M)ASH.

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From Degradome to Defense: CAPN4 Modulation as a Novel Therapeutic Strategy for MASH

Background: Extracellular matrix (ECM) remodeling and tissue architecture disruption are hallmarks of metabolic associated steatotic hepatitis (MASH), yet early detection and targeted interventions remain limited. Recent proteomic analyses of plasma samples from both experimental models and human MASH patients revealed distinct protein degradation patterns compared to healthy controls, with bioinformatic analysis identifying enhanced calpain-mediated protein cleavage as a key mechanism. Building on our translational findings that early degradome signatures predict post-liver transplant MASH progression, we investigated calpain 4 (CAPN4) as a novel therapeutic target.
Methods: We developed a targeted gene therapy approach using recombinant adeno-associated virus type 8 vectors (rAAV8) encoding shRNA against Capn4 under albumin promoter control to achieve liver-specific knockdown. C57Bl6/J mice received either Capn4-targeting or scrambled control vectors (1×10^{11} PFU/mouse, i.v.). Following a 4-week establishment period, mice were challenged with either a control diet (CD: 13% saturated fat) or a 'Western'-style diet (WD: 42% saturated fat) for 12 weeks. Comprehensive assessment included histological analysis, ECM composition, inflammatory markers, fibrosis progression, and matrix-bound nanovesicle (MBV) characterization.
Results: Liver-specific Capn4 knockdown provided remarkable protection against diet-induced metabolic liver disease. While WD feeding typically induces substantial hepatic steatosis, inflammation, and early fibrosis, Capn4 knockdown mice showed preserved tissue architecture with significantly reduced inflammatory markers (TNF-α, IL-1β, IL-6) and fibrosis markers (COL1A1, ACTA2, TGF-β, PDGF). The intervention also altered ECM dynamics, with changes in matrix-bound nanovesicle protein content suggesting modified tissue remodeling pathways. Notably, CAPN4 suppression delayed adipose tissue expansion and fundamentally altered the trajectory of metabolic stress responses.
Conclusions: Our findings establish CAPN4 as a critical mediator of pathological tissue remodeling during metabolic stress, with its therapeutic suppression preserving hepatic architecture and function through multiple mechanisms. This work identifies a novel druggable target for preventing MASH progression and suggests potential applications for biological scaffold development in liver tissue engineering. The dynamic nature of ECM remodeling and the ability to track degradation products may enable development of "liquid biopsy" approaches for early MASH detection and risk stratification. Understanding calpain-mediated tissue remodeling mechanisms opens new avenues for precision medicine approaches in metabolic liver disease.
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The Hepatic Lymphatic System in Cholestatic Liver Disease: Mechanisms and Therapeutic Potential

The hepatic lymphatic system is critical for maintaining interstitial fluid balance, immune cell trafficking, and macromolecule clearance, yet its role in cholestatic liver disease remains poorly defined. Primary biliary cholangitis (PBC), a chronic autoimmune disorder characterized by bile duct destruction, portal inflammation, and fibrosis, provides a model to investigate this link. Importantly, bile ducts and lymphatic vessels (LVs) lie in close proximity, suggesting that lymphatic dysfunction may directly exacerbate bile duct injury during autoimmune-mediated damage.

Using a murine model of PBC, we observed a biphasic change in LV density: expansion during early disease, followed by decline in advanced stages. Loss of lymphatic density correlated with increased inflammation and fibrosis, implicating impaired lymphatic clearance and lymphatic endothelial cell dysfunction in disease progression.To test therapeutic potential, we employed VEGF-C, a lymphangiogenic factor. VEGF-C overexpression restored LV density, improved lymphatic phenotype, and reduced hepatic inflammation and fibrosis.

These findings identify hepatic lymphatic remodeling as a key contributor to PBC progression and suggest that enhancing lymphangiogenesis may offer a novel therapeutic approach for cholestatic liver disease.

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Novel Insights into LSECs Dedifferentiation in CLD: Role of miRNAs

Chronic liver disease (CLD) remains a global health burden, characterized by progressive hepatic fibrosis, vascular remodeling, and eventual organ failure. Liver sinusoidal endothelial cells (LSECs) play a pivotal role in maintaining hepatic homeostasis through their unique fenestrated structure and anti-fibrogenic phenotype. However, during CLD progression, LSECs undergo a process of dedifferentiation, losing their characteristic fenestrae and acquiring a capillarized, pro-fibrotic phenotype that exacerbates disease progression. Despite recent advances, the molecular mechanisms orchestrating LSEC dedifferentiation remain incompletely understood. Emerging evidence highlights microRNAs (miRNAs) as key post-transcriptional regulators of cellular phenotype and intercellular communication within the liver microenvironment.

This lecture will present novel insights into the roles of both endogenous and exogenous miRNAs in the dedifferentiation of LSECs in CLD. We will explore the regulatory networks governed by endogenous miRNAs within LSECs that control the expression of genes involved in fenestrae maintenance, angiogenesis, and extracellular matrix remodeling. Particular attention will be given to miRNAs that are downregulated during CLD, leading to the alteration of pro-fibrotic and capillarization pathways.

Additionally, this lecture will delve into the increasingly recognized impact of miRNAs transferred from neighboring cells, such as hepatocytes, through extracellular vesicles (EVs). These transferred miRNAs can significantly influence LSEC phenotype by modulating gene expression profiles that drive dedifferentiation, capillarization, and pro-inflammatory signaling. We will discuss recent findings demonstrating how pathogenic cell-to-cell miRNA transfer contributes to the fibrogenic microenvironment and the loss of LSEC specialization and viability.

Understanding the dual role of miRNAs—both those intrinsically regulated within LSECs and those exogenously supplied by neighboring cells—provides a more comprehensive view of the molecular landscape underpinning LSEC dedifferentiation in CLD. This integrative perspective not only advances our fundamental knowledge of liver vascular biology but also identifies potential therapeutic targets. The modulation of specific miRNAs or the interruption of pathogenic miRNA-modulated pathways may offer promising strategies to preserve LSEC phenotype, attenuate fibrosis, and potentially reverse vascular dysfunction in chronic liver disease.

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Reduced Expression of Fatty Acid Desaturase 2 Exacerbates Diet-induced Steatohepatitis in Mice

We previously reported that age-related decreases in the expression of fatty acid desaturase (FADS) 1 and 2 alter hepatic lipid profiles and contribute to the progression of diet-induced steatohepatitis in mice (Ishizuka K et al., J Gastroenterol Hepatol, 2020). However, it remains unclear whether a reduction in the expression of FADS directly contributes to the progression of steatohepatitis. Therefore, this study aimed to investigate the impact of a reduction in the expression of FADS2 on high-fat, high-cholesterol (HFHC) diet–induced steatohepatitis using heterozygous FADS2 knockout mice.

Methods: Male 8-week-old heterozygous FADS2 knockout (FADS2+/−) mice and wild-type controls were fed an HFHC diet or a control diet for 8 weeks. The expression of mRNA in liver tissue was quantified by RT-PCR, intrahepatic macrophages were detected by F4/80 immunohistochemistry, and liver fibrosis was assessed by Sirius Red staining. Lipid composition was analyzed using LC-MS.

Results: In the control diet groups, serum ALT levels and liver histology were comparable between FADS2+/− and wild-type mice. In contrast, HFHC-fed FADS2+/− mice developed more severe steatohepatitis with prominent infiltration of F4/80-positive cells and significantly elevated serum ALT levels compared to wild-type mice. The expression of mRNA for TNF-α in the liver was more than two-fold higher in HFHC-fed FADS2+/− mice, accompanied by significant increases in the expression of mRNA for CCL2, CXCL2, and HO-1 in the liver. These mice also exhibited marked pericellular fibrosis, with significantly increased expression of mRNA for TGFβ1, TIMP1, and type I collagen in the liver compared to wild-type controls. Lipidomics revealed reduced levels of PUFA-containing phosphatidylethanolamines and lysophosphatidylcholines, whereas diacylglycerols (DAGs) and triacylglycerols (TAGs) enriched in saturated and monounsaturated fatty acids were significantly increased. In addition, ceramide d18:1/24:1 and lactosylceramide d18:1/24:1 were upregulated, while sphingomyelins d18:1/20:0 and d18:1/22:0–24:0 were decreased, indicating a shift in ceramide metabolism from the sphingomyelin pathway toward the glycosphingolipid pathway.

Conclusions: These findings demonstrate that HFHC-fed FADS2+/− mice develop exacerbated steatohepatitis characterized by macrophage accumulation, enhanced chemokine and oxidative stress responses, and accelerated progression of fibrosis. This phenotype is associated with a reduction in PUFA-containing phospholipids, an increase in SFA/MUFA-rich DAGs and TAGs, and a shift in ceramide metabolism toward glycosphingolipid synthesis. A reduction in the expression of FADS2 alters hepatic lipid composition, thereby promoting lipotoxicity and aggravating steatotic liver disease.

Symposium 4: Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)

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New Pathways in Lipid Metabolism

Lipids are key signals controlling gene expression in the enterohepatic axis. Our long-term objective is to reveal fundamental mechanisms by which lipid signals orchestrate cellular and systemic lipid homeostasis. The flux of cholesterol and fatty acids through liver and intestine is an important determinant of tissue and systemic metabolism. Excess lipid accumulation in the enterohepatic axis is linked to diabetes and gastrointestinal diseases, including Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), intestinal inflammation, and cancer. We have characterized a family of mammalian proteins (Aster-A, -B and -C) that play an important role in nonvesicular cholesterol transport from plasma membrane to ER. Asters are integral ER proteins that are recruited to the plasma membrane in response to excess cholesterol. We have defined important roles for Aster proteins in liver and intestinal metabolism. Hepatic Aster-C and Aster-A play key roles in reverse cholesterol transport (RCT) and fasting in liver, and that Aster-B and Aster-C are important for dietary cholesterol absorption and chylomicron production by the intestine. We also validated small molecule Aster inhibitors as tool compounds for the study of Aster function. Collectively, our findings to date establish the Aster pathway as a physiologically important and pharmacologically tractable node in dietary lipid absorption and hepatic lipid metabolism.

Symposium 4: Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)

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Stress Response by Co-creation of Phase-separated p62 Body and Liver Autophagy

When degenerated and subsequently ubiquitinated proteins accumulate in the cytoplasm due to extensive stress, liquid-liquid phase separation occurs via multivalent interactions between these ubiquitinated proteins and p62, resulting in the formation of a large membraneless organelle called the “p62 body.” The p62 body undergoes maturation and activates the cellular stress response pathway, particularly the KEAP1–NRF2 axis. Ultimately, the p62 body, which contains large amounts of denatured proteins, is degraded together with its client proteins in a selective autophagy-dependent manner. In other words, this dynamically transforming p62 body plays a central role in both cellular robustness (via stress response activation) and proteostasis (via clearance of denatured proteins) under stress conditions.

Importantly, it has become increasingly clear that dysregulation of p62 body formation and clearance is associated with disease states. For instance, persistent accumulation of p62 bodies has been observed in liver diseases, where they are referred to as Mallory–Denk bodies, a pathological hallmark of various hepatic disorders including alcoholic and non-alcoholic steatohepatitis. These findings suggest that impaired phase separation dynamics and defective autophagic turnover of p62 bodies contribute to disease pathogenesis.

In this talk, I would like to introduce the stress response and autophagic degradation mechanisms regulated by various post-translational modifications of the p62 body, and discuss their pathological implications in liver diseases.

Symposium 4: Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)

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The Liver-Heart Axis in MASLD: Drivers of Cardiometabolic Remodeling

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a major global health burden strongly linked to cardiovascular disease (CVD), particularly heart failure with preserved ejection fraction (HFpEF). Overall, CVD is the leading cause of mortality in patients with MASLD, followed by cancer and liver-related death. In MASLD patients, HFpEF is the most common cardiovascular complication. While emerging clinical data has correlated MASLD with CVD and left ventricular (LV) dysfunction, the molecular mechanisms underlying the bidirectional crosstalk driving this liver-heart axis remain enigmatic. The challenge is exacerbated by the absence of translatable models that mimic human cardiovascular-liver-metabolic pathophysiology, hampering our ability to fully unravel this complex condition. We established a mouse model that recapitulates the full spectrum of MASLD and associated cardiac dysfunction. Integrated molecular and physiological profiling revealed that MASLD initiates subclinical cardiac impairment through shared stress signaling and metabolic remodeling. Cardiac dysfunction progressed from mild impairment to severe HFpEF in parallel with worsening hepatic fibrosis, ultimately driving increased mortality. Although lifestyle modifications, such as a healthy diet, exercise and weight management, are the cornerstone of CVD and MASLD management, very little is known regarding how lifestyle modifications affect the liver-heart axis concurrently during disease resolution. Strikingly, switching from a Western diet to standard chow not only reversed the liver pathology but also prevented HFpEF and cardiac mortality. These studies provide insights into the liver-heart axis, allowing us to map changes in LV gene signatures both during disease progression and resolution and uncover molecular pathways across the MASLD spectrum.

Symposium 4: Frontier of Lipid Metabolism and Autophagy (Southern California Research Center for ALPD and Cirrhosis Joint Session)

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Impaired Autophagy in Hepatic Macrophages: A Key Contributor to MASH Progression

Background: We previously demonstrated that autophagy is suppressed in hepatocytes of patients with MASLD, contributing to the progression of MASH. However, the role of macrophage autophagy in MASH pathogenesis remains poorly understood.

Methods and Results: Using a Western diet (WD)-induced MASH mouse model, hepatic macrophages exhibited p62 accumulation, indicating impaired autophagic activity. In vitro, palmitic acid treatment of macrophages suppressed autophagic flux, accompanied by p62 accumulation, and significantly increased IL-1β secretion. Single-cell RNA sequencing of livers from MASH model mice revealed that IL-1β was expressed in macrophages, while Il1r1, the gene encoding the IL-1β receptor, was most highly expressed in liver sinusoidal endothelial cells (LSECs), along with increased expression of the chemokines Ccl2 and Cxcl10. Moreover, deletion of Atg7 in macrophages led to increased IL-1β levels in the culture supernatant. When LSECs were cultured with this conditioned medium, CCL2 and CXCL10 expression was upregulated via activation of the JNK signaling pathway.

To further investigate the functional relevance of IL-1β signaling through IL1R1 in LSECs, we generated tamoxifen-inducible, endothelial cell-specific Il1r1 knockout mice. When fed a MASH-inducing diet, these mice exhibited significantly reduced hepatic expression of Ccl2 and Cxcl10, along with attenuated liver fibrosis. In addition, Cxcl10-deficient mice showed lower serum ALT levels and reduced fibrosis under the same dietary conditions, underscoring the contribution of chemokine signaling to disease progression.

In liver biopsy samples from MASLD patients, expression levels of CCL2 and CXCL10 were significantly higher in MASH cases than in non-MASH cases and were positively correlated with NAFLD activity scores. Spatial transcriptomic profiling of human MASH liver tissues revealed periportal LSECs with high IL1R1, CCL2, and CXCL10 expression located adjacent to macrophages. Neighborhood analysis further identified monocyte-derived macrophage (MoMF)–rich regions with increased expression of inflammation- and fibrosis-related genes.

Conclusion: This study identifies suppressed autophagy in hepatic macrophages as a key pathological feature of MASLD. Impaired autophagy enhances IL-1β secretion, which activates IL1R1 signaling in periportal LSECs, leading to chemokine production and immune cell recruitment. This macrophage–LSEC interaction promotes hepatic inflammation and fibrosis, thereby driving MASH progression. Spatial mapping highlights immune cell–rich niches near the portal vein, where MoMFs are abundant and inflammation- and fibrosis-related gene expression is elevated.

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Tumor-promoting Lipid Reprogramming by Hepatic Stellate Cells

Hepatic stellate cells (HSC) store lipids including but not limited to vitamin A. These intracellular lipids are lost in activation of HSC due in part to anti-lipogenic reprogramming caused by morphogens such as WNT, DLK1, and SHH. Paradoxically, the lipogenic gene *Scd2* is upregulated in activated HSC (aHSC) by β-catenin (CTNNB1) via its ability to associate with SREBP1c and accentuate its trans-activity within a proximal *Scd2* promoter. This leads to selective PUFA biosynthesis despite lost lipid storage. The biologic causality of this regulation is supported by abrogation of HSC activation and liver fibrosis in mice by *Scd2* conditional ablation (cKO). Mechanistically, SCD2 increases intracellular MUFA (oleic acid) which inhibits Ran1 binding to TNPO1 required for nuclear import of the mRNA binding protein ELAV1. This increases cytosolic ELAV1 and ELAV1-mediated mRNA stability of the Wnt co-receptor LRP5/6, establishing a novel positive forward loop for Wnt-CTNNB1 pathway in aHSC. *Scd2* cKO also suppresses liver tumor development promoted by MetALD because SCD2 deficiency suppresses HSC generation of the oxylipin 12-HHTrE and its ability to activate the cognate receptor LTB4R2 for downstream CTNNB1-mediated YAP1 intronic enhancer activation in liver tumor cells. CYP1B1 whose expression is dependent on SCD2, is identified as the source of 12-HHTrE by aHSC, and scRNA-seq identifies a unique subpopulation of aHSC co-expressing the portal fibroblast marker *Fbln2*, as the primary cellular site of *Cyp1b1* upregulation. Indeed, selective *Cyp1b1* ablation in *Fbln2*+ aHSC, suppresses liver tumor development in mice, and this tumor suppression is associated with global yet unique inhibition of tumor-promoting lipid reprogramming in TME, unlimited to 12-HHTrE generation. Further, translational relevance of this notion is supported by spatial transcriptomic analysis of MetALD patient HCC revealing localization of CYP1B1-expressing aHSC in HCC nodules in proximity of YAP1-expressing HCC cells.

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Multi-Modal Analysis of Human Hepatic Stellate Cells Identifies Novel Therapeutic Targets for MASH and MetALD

Background and Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) ranges from Metabolic dysfunction-associated steatotic liver (MASL) to Metabolic dysfunction-associated steatohepatitis (MASH) with fibrosis and MetALD in patients with excessive alcohol consumption. Activation of Hepatic Stellate Cells (HSCs) into fibrogenic myofibroblasts plays a critical role in the pathogenesis of liver fibrosis. We compared transcriptome and chromatin accessibility of human HSCs from NORMAL, MASL, MASH and MetALD livers at single cell resolution using single-nucleus (sn)RNA-seq and snATAC-seq. High priority targets were identified, then tested in 2D human HSC cultures, 3D human liver spheroids, and HSC-specific gene knockout mice. We identified that MASH/MetALD-enriched highly activated aHSC subclusters are the major source of extracellular matrix proteins. Expression of fibrogenic genes, including SERPINE1 (encoding for PAI-1 protein) was regulated via crosstalk between lineage-specific (JUNB/AP1), cluster-specific (RUNX1/2) and signal-specific (FOXA1/2) transcription factors. The pathological function of SERPINE1 was evaluated using dsiRNA-based HSC-specific gene knockdown or pharmacological inhibition of PAI-1 in 3D human MASH liver spheroids, and HSC-specific Serpine1 knockout mice. Targeting SERPINE1 (PAI-I) may become a novel strategy to treat liver fibrosis in patients with MASH and MetALD.

Symposium 5: Fibrogenesis in SLD

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Involvement of Cannabinoid 1 Receptors in Liver Fibrosis

Background: Cannabinoid 1 receptor (CB1R) belongs to the endocannabinoid system that plays an important role in the pathogenesis of liver diseases such as Metabolic dysfunction-associated steatohepatitis (MASH) and liver fibrosis. In this study, we aimed to clarify the role of CB1 in liver fibrosis using mice deleting CB1 in peripheral tissues outside the central nervous system (CB1□MX1) and mice deleting hepatic stellate cell CB1 (CB1□HSC).

Methods: CB1F/F mice was crossed with Lrat-cre mice to generate HSC specific CB1 deleted mice (CB1□HSC). To generate mice that lacks peripheral CB1 while sparing the gene in the brain, CB1F/F mice was crossed with MX1-cre mice (CB1□MX1). CB1□MX1 mice when injected with poly (I:C) recombines and deletes CB1 in peripheral tissues with little to no recombination in the brain. CB1F/F mice injected with poly (I:C) were used as controls. 10 to 12 weeks old male mice were used in three distinct preclinical models: (1) MASH model: Fructose + Western diet for 6 months, (2) cholestatic liver injury model: mice underwent bile duct ligation (BDL) for 2 weeks and (3) CCl4 induced liver fibrosis model: CCl4 administered intraperitoneally for 6 weeks. Hepatic gene expression was determined by qRT-PCR. Hepatic fibrosis was evaluated histologically using Sirius red staining. Immunohistochemical (IHC) staining was performed to evaluate α smooth muscle actin (αSMA) and F4/80 expression.

Results: Poly (I:C)-treated CB1□MX1 mice reduced CB1 expression in peripheral tissues but did not affect the CB1 expression in the brain. When subjected to MASH diet for 6 months, the peripheral absence of CB1 had overall protection towards development of liver steatosis and fibrosis. The expression of F4/80 and αSMA was decreased. The expression of inflammatory cytokines (TNFα, IL1b) and fibrosis-related genes (Col1a1, TIMP1, MMP12, MMP13, αSMA, TGFβ) were also significantly decreased. In models of cholestatic liver injury and CCl4-induced liver fibrosis, poly(I:C)-treated CB1□MX1 mice showed reduced hepatic fibrosis and decreased expression of F4/80 and αSMA. The expression of inflammatory cytokines and fibrosis-related genes was also significantly decreased. In contrast, inhibition of liver fibrosis was not observed in either model in CB1□HSC mice.

Conclusion: This study provides genetic foundational and proof-of-concept studies indicating that peripheral CB1 antagonists (sparing the CNS and the brain) have potential therapeutic applications in multiple liver diseases. However, deletion of CB1 specifically in HSC did not have a protective effect in our models of liver disease.

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Intercellular Communication between Hepatic Stellate Cells and Myofibroblasts Mediated by Osteopontin and FGF18 Promotes Liver Fibrosis

Hepatic stellate cells (HSCs) play a central role in the development of liver fibrosis. We previously showed that fibroblast growth factor 18 (FGF18) promotes liver fibrosis by increasing HSC proliferation. However, the underlying mechanisms remain incompletely understood. Here, we showed that FGF18 efficiently induced osteopontin (Spp1/OPN) expression in culture-activated αSMA$^+$ HSCs, but not in freshly prepared quiescent HSCs. Notably, OPN upregulated profibrotic genes only in quiescent HSCs, suggesting that the activation status of HSCs influences their responsiveness to FGF18 and OPN. Furthermore, FGF18 and TGFβ synergistically increased Spp1/OPN expression in culture-activated αSMA$^+$ HSCs. Immunohistochemical analyses of murine liver fibrosis models revealed that OPN was expressed predominantly in αSMA$^+$ myofibroblasts, but not in desmin$^+$ quiescent HSCs. The cell–cell communication analyses further revealed that myofibroblast-derived Spp1 signaled to HSCs in fibrotic livers. Together, FGF18 initiates a feed-forward loop between quiescent and activated αSMA$^+$ HSCs/myofibroblasts via OPN signaling, thereby driving fibrosis progression.

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A Single-cell Fixed RNA Profiling Uncovers Key Transcriptional and Signalling Programs in Liver Fibrosis Progression and Regression

Liver fibrosis progression and regression involve complex interactions among hepatic and immune cell populations. Using single-cell fixed RNA profiling (FLEX) in a TAA-induced mouse liver fibrosis model with and without a recovery phase, we mapped the cellular and molecular mechanisms underlying fibrosis resolution. Regression was marked by pericentral hepatocytes expressing detoxification genes (Cyp2e1, Txn1) and secreting Rarres2. This was accompanied by increased expression of scar-resolving genes (Mmp14, Ctsl), fenestrae restoration in liver sinusoidal endothelial cells, anti-inflammatory Kupffer cells, reduced fibrogenic cholangiocytes, and recovery-associated immune signatures. Conversely, during fibrosis progression, monocyte-derived macrophages secreted SEMA4D, activating PLXNB2^{+} HSCs; SEMA4D blockade attenuated fibrosis in vivo. LMCD1 emerged as a novel marker for HSC activation and fibrosis modulation. This single-cell atlas highlights key transcriptional programs and cell–cell communication pathways, offering insights into condition-specific drivers of fibrosis and potential therapeutic targets.

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Australia

The Dawn of the Age of Pharmacotherapies for MASH

MAFLD is the most common liver disease globally affecting nearly 40% of the world's population either as the sole entity, or as a contributor to other liver diseases. While there are standard treatment regimens for most other liver diseases, MAFLD, in this regard, has been an orphan disease bereft of pharmacotherapies. Until recently, the cornerstone of treatment has been lifestyle intervention focusing on reduced calorie consumption and the intake of whole foods, predominantly of plant based origin, as well physical activity, both aerobic and resistance. Equally important, since most patients die of cardiovascular disease or extrahepatic cancer, has been the focus on cardiovascular risk factor control, optimal diabetes management and surveillance as per guidelines for cancer, particularly colorectal cancer. This paradigm of management, at a population level, still represents the optimal care pathway for the patient with MAFLD, given their causes of death.

For the hepatologist, liver-directed pharmacotherapies have evaded our armamentarium, to reduce the risk of decompensated liver disease and liver cancer. The therapeutic graveyard has been littered with suboptimal treatments including vitamin E, PPAR gamma agonists, biguanides and omega three supplements. However, the last few years have seen a raft of positive trials, some of which have progressed from phase 2 to landmark phase 3 registration trials. The classes of drugs tested include those in two broad categories, liver-directed drugs and those that target the dysfunctional systemic metabolic milieu. First among the former has been the thyroid hormone receptor beta agonist resmetirom which gained approval in the US in 2024 and in the EU a year later, after meeting both primary endpoints of improvements in steatohepatitis with no worsening of fibrosis and improvement in fibrosis with no worsening of steatohepatitis in those with fibrosis stage 2 and 3. In 2024, the GLPIRA semaglutide was shown to also meet both primary endpoints and has received approval, with recent data suggesting that it has both indirect and direct beneficial effects on liver health. Importantly, both drugs have beneficial cardiovascular profiles. A raft of new agents are now in phase 3 studies such as the FGF21 analogues and pan-PPAR agonists, including for those with cirrhosis. The arrival of these exciting new drugs will place Hepatologists at the centre of the new genre of metabolic physicians. However, it remains critical to determine whether the promise of these pharmacotherapies extends to preventing adverse liver related outcomes.

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Epidemiology and Treatment of MASLD in Japanese Real-world Setting

AASLD indicated that the most common cause of death in patients with MASLD was related to cardiovascular diseases (CVDs). Liver-related mortality was reported to be the second or third cause of death, and cancer-related mortality was among top three causes of death. Incidence of three complications was investigated in 552 Japanese patients with biopsy-proven MASLD. The yearly incidence rates of CVDs, malignancies, and liver-related events (LREs) were found to be 1.0%, 0.8%, and 0.3%, respectively. The impacts of diet and exercise, and diabetes therapeutics were evaluated in MASLD patients. Regarding diet and exercise treatment, subjects of retrospective cohort study were cumulative total of 1 403 Japanese SLD patients. All of them were introduced hospitalization program of personalized diet and exercise for 6 days. Liver function tests, physical findings, and CVD risk score at 6 months improved significantly. Especially, regular and repeated hospitalizations every 6 months were effective for improvement of liver function at 2 years. Regarding diabetes therapeutics, histological impacts at 5 years after start of SGLT2 inhibitors were investigated retrospectively in 6 Japanese patients with MASLD and T2DM. Histological improvement, defined as decrease in MASLD activity score of one point or more without worsening in fibrosis stage, was 50%, and none developed CVDs. In conclusion, the most common event in Japanese MASLD patients was CVDs. Personalized medicine with diet and exercise, and diabetes therapeutics are expected to improve the pathology of MASLD, including the suppression of CVDs and LREs. As the future perspective of new drugs development for MASLD, firstly, treatment for suppression of CVDs due to metabolic syndrome, regardless of liver fibrosis stage, should be performed. Especially, GLP-1RA and SGLT2i are expected to improve prognosis of T2DM complicated by MASLD, according to reduction of CVDs. Secondly, treatment for suppression of LREs, due to advanced fibrosis stage, should be performed. Especially, resmetirom was approved by FDA, and semaglutide as one of GLP-1RAs showed the favorable treatment efficacy with phase 3 trial. The addition of these drugs is expected to suppress LREs with histological improvement.

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Beyond Glycemic Control: Hepatic and Oncologic Potentials of SGLT2 Inhibitors

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are widely used anti-diabetic agents that have demonstrated beneficial actions on hepatic function. We recently conducted a pooled meta-analysis of five phase III clinical trials using luseogliflozin, an SGLT2i. A 24-week treatment with luseogliflozin significantly improved hepatic steatosis and fibrosis indices in diabetic patients with liver injury. Additionally, luseogliflozin exerted favorable effects on cardiometabolic risk factors and hepatic inflammatory markers. Given that metabolic dysfunction and inflammation contribute to the progression of metabolic dysfunction-associated steatotic liver disease (MASLD), luseogliflozin may offer therapeutic potential for MASLD in patients with diabetes.

Expression of SGLT2 was detected in several human hepatocellular carcinoma (HCC) cell lines, including Hep3B and Huh7. Notably, SGLT2 was localized to the mitochondria in these cells. SGLT2i significantly inhibited cell proliferation in both Hep3B and Huh7 lines. Multi-omics analyses of metabolomics and absolute quantification proteomics (iMPAQT) revealed that SGLT2i markedly downregulated ATP synthase F1 subunit alpha, a key component of the mitochondrial electron transport chain. Concurrently, SGLT2i upregulated 3-hydroxybutyrate, a metabolite associated with β-oxidation. These findings suggest that SGLT2i may suppress HCC cell proliferation by modulating mitochondrial oxidative phosphorylation and fatty acid metabolism.

Furthermore, we conducted a retrospective cohort study using a Japanese medical claims database. Among patients with type 2 diabetes mellitus (T2DM) prescribed either SGLT2i or dipeptidyl peptidase-4 inhibitors (DPP4i) (n = 1,628,656), individuals with suspected MASLD were matched into SGLT2i (n = 4,204) and DPP4i (n = 4,204) groups. Over a 12-month period, SGLT2i significantly reduced the FIB-4 index and significantly lowered the incidence of esophageal varices (HR 0.12, P = 0.044) compared to DPP4i. SGLT2i also significantly suppressed the incidence of extrahepatic malignancies (HR 0.50, P = 0.009) compared to DPP4i. These anti-tumor effects were particularly pronounced in patients aged ≥65 years, with a FIB-4 index >1.3, HbA1c ≥7.0%, and triglyceride levels ≥150 mg/dL.

In this seminar, I will present the diverse hepatic actions of SGLT2i. Particular attention will be given to their potential role in the management of MASLD and related malignancies. The discussion will integrate findings from clinical trials, basic studies, and real-world data to highlight the therapeutic relevance of SGLT2i in liver disease and oncology.

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Ferroptosis in MASLD -from Mechanism to Development of New Drugs

Background: Ferroptosis is a new form of cell death, characterized by the iron-dependent accumulation of lipid hydroperoxides to lethal levels. MASLD is also characterized by excess oxidative stress and iron storage in the liver. However, the role of ferroptosis in MASLD remains largely unknown, and few drugs are available to inhibit ferroptosis.

Methods: In vitro experiments were conducted using Huh7 cells and primary cultured mouse hepatocytes. Male hepatocyte-specific PTEN KO (PTEN KO) mice, 8-10 weeks old, were served as the MASLD model. We tested ferrostatin-1, a known ferroptosis inhibitor, and apomorphine, a Parkinson's disease medication, for their ability to inhibit ferroptosis. Additionally, we developed apomorphine derivatives that lack dopamine agonist activity but retain ferroptosis- inhibiting property.

Results: The ferroptosis inducer RSL-3 triggered cell death in both Huh7 cells and primary cultured hepatocytes. This cell death was suppressed by ferrostatin-1, apomorphine, and apomorphine derivatives, but not by inhibitors of necrosis or apoptosis. Among ferroptosis inhibitors, apomorphine derivatives showed particularly strong inhibitory effects. These ferroptosis inhibitors also reduced lipid peroxidation of cell membrane. In vivo, PTEN KO mice at 10 weeks exhibited moderate steatosis, increased oxidative stress, upregulation of proinflammatory and profibrogenic genes in the liver, and elevated serum transaminases. While some hepatocytes death occurred, there were few necrotic or apoptotic hepatocytes. Necrosis inhibitor had little effects on hepatocyte death or MASLD features in mice. In contrast, two weeks of treatment with ferrostatin-1, apomorphine, or apomorphine derivatives reduced hepatocyte death and improved MASLD characteristics. Apomorphine and its derivatives demonstrated strong radical-trapping activity. In addition, apomorphine and its derivatives for mice activated nrf2 and its downstream molecules in the liver. Hepatic iron content remained unchanged after treatment with ferroptosis inhibitors.

Conclusions: Ferroptosis contributes to MASLD development. Ferroptosis inhibitors, especially apomorphine derivatives, show promise as potential therapeutic agents for MASLD.

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The Role of Bile Acid in Metabolic Dysfunction Steatotic Liver Disease & Its Treatment Implication

Non-alcoholic fatty liver disease (NAFLD) is one of the challenging etiologies in chronic liver disease (CLD) as it would need comprehensive evaluation and management. Currently, the term of NAFLD has changed to MASLD (Metabolic Dysfunction Steatotic Liver Disease), where it comprises to metabolic dysfunction in the fatty condition or steatosis condition only, or metabolic dysfunction with steatohepatitis, where inflammation is a very important pathology condition as it might lead to significant fibrosis and its complications in the setting of liver cirrhosis. Portal hypertension complications, and liver cancer are two main key players in the liver disease progression and will determine the prevention strategy approach.

Bile acid (BA) is one of the important wing players in CLD. BA metabolism would be happened in the liver, as well as in the gut. This phenomenon is well-known as entero-hepatic circulation. In fatty liver disease, the role of BA is strongly associated with farnesoid X receptor (FXR), where the process of activation will be related to the lipogenesis, beta oxidation, PPAR alfa, free fatty acid (FFA) oxidation, and ketogenesis process. The BA will also be involved in the inflammatory process as it would interferes with some inflammatory cytokines. It can inhibit the interleukins (ILs) secretion and can inhibit the tumor necrosis factor secretion by the Kupffer cells. On the other side, in the setting of CLD, there will be BA synthesis, metabolism, and excretion disturbance, and these conditions will lead to BA dysregulation. In return, this will give more damage condition inside the liver.

There have been clinical trials looking at potential of BA as a treatment in MASLD population, such as FXR agonist, TGR agonist, UDCA, and BA sequestrant. However, there are still many conflicting data results, and concern about its safety despite its efficacy. The newcomer, such as ileal bile acid transporter is still under investigation. In the future, BA therapy will hold an important position to prevent liver disease progression in MASLD.

Symposium 7: Cancer Development in SLD

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MASLD Drives CRC Liver Metastasis by Remodeling the Fibrotic Tumor Microenvironment

Steatotic liver has been shown to facilitate liver metastasis of colorectal cancer. Previously, we demonstrated that hepatocyte-derived extracellular vesicles carrying oncogenic microRNAs and M2-like tumor-associated macrophages promote liver metastasis in the context of metabolic dysfunction-associated steatotic liver disease. However, the contribution of the fibrotic tumor microenvironment shaped by cancer-associated fibroblast (CAF)-derived extracellular matrix remained poorly understood. High-fat diet (HFD)-induced steatosis leads to increased infiltration of CAFs and elevated levels of collagen and hyaluronic acid (HA). In this study, we explored the role of hyaluronan synthase 2 (HAS2) in forming the fibrotic tumor microenvironment within steatotic liver. Has2ΔHSC mice, which lack Has2 expression in hepatic stellate cells, exhibited decreased metastatic growth of MC38 colorectal cancer cells in steatotic livers. Mechanistically, low-molecular-weight HA activated YAP in cancer cells, leading to the release of CTGF, which further stimulated HAS2 expression in CAFs. Single-cell analysis indicated that CAF-derived HAS2 interacts with M2 macrophages and colorectal cancer cells via CD44, establishing connections with exhausted CD8 T cells through the PD-L1/PD-1 axis. Inhibition of HA synthesis effectively reduced steatotic liver-associated metastasis of colorectal cancer. Notably, co-administration of a HA synthesis inhibitor with anti-PD-1 effectively reversed the resistance to anti-PD-1 therapy in the steatotic liver. In summary, these findings suggest that steatotic liver promotes a fibrotic tumor microenvironment that increases metastatic potential through a bidirectional interaction between CAFs and metastatic cancer cells, thereby promoting colorectal cancer progression in the liver.

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Study on the Applications of Nanocarrier as Therapeutic Candidates for Liver Fibrosis

Liver fibrosis, a key pathological feature of chronic liver disease, is characterized by the excessive accumulation of extracellular matrix (ECM) components, leading to progressive architectural distortion of the liver parenchyma and ultimately resulting in hepatic dysfunction, cirrhosis, and organ failure. Despite the increasing global burden of liver fibrosis and its association with high morbidity and mortality, effective and targeted antifibrotic treatments remain elusive. Recent advances in nanocarrier-based drug delivery systems have opened new strategies for the development of precision therapeutics that can modulate disease-driving molecular pathways with enhanced specificity and reduced off-target effects. In this study, we investigated two innovative nanocarrier-based therapeutic strategies for treating liver fibrosis in experimental animal models. The first approach employed exosome-based delivery of a super-repressor form of IκB (Exo-SrIκB), designed using EXPLOR (Exosome engineering for Protein Loading via Optically Reversible interactions) technology to inhibit nuclear factor-κB (NF-κB) signaling, a central mediator of inflammation and fibrogenesis. In both mouse and minipig models of cholestatic liver fibrosis, Exo-SrIκB administration effectively suppressed NF-κB nuclear translocation and significantly attenuated liver fibrosis, as evidenced by reduced collagen deposition, decreased α-smooth muscle actin (α-SMA) expression, and downregulation of fibrogenic gene signatures. The second strategy involved the development of a hepatocyte-targeted lipid nanoparticle (LNP) delivery platform encapsulating small interfering RNA (siRNA) against G2 and S-phase expressed 1 (GTSE1), a gene implicated in cell cycle regulation and fibrotic remodeling. Treatment with siGTSE1-LNPs in a carbon tetrachloride (CCl_4)-induced model of toxic liver injury led to marked reductions in fibrosis and restoration of hepatic function. Moreover, GTSE1 silencing promoted the re-expression of hepatocyte nuclear factor 4 alpha (HNF4α), a master regulator of hepatocyte differentiation, indicating recovery of hepatocellular identity and phenotype. Collectively, our findings provide compelling evidence that nanocarrier-based modulation of pro-fibrotic pathways through target protein delivery and RNA interference represents a promising therapeutic strategy for combating liver fibrosis.

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Clinical Aspects of Hepatocarcinogenesis in Steatotic Liver Disease

MASLD (Metabolic dysfunction-associated steatotic liver disease), MetALD (Metabolic and alcohol-related liver disease), and ALD (Alcohol-related liver disease) are recent categories of steatotic liver disease (SLD). MASLD involves liver steatosis and metabolic risk factors without excessive alcohol intake, while MetALD combines both metabolic factors and moderate alcohol consumption, and ALD is primarily driven by high alcohol consumption without metabolic risk factors. The global increase in SLD is directly linked to a rapid rise in HCC rising from SLD. SLD share underlying pathophophysiological mechanisms. SLD begins with fat accumulation in the liver, driven by factors like obesity, diabetes, and alcohol intake. This leads to dysregulated lipid metabolism within hepatocytes. The metabolic imbalance triggers hepatocyte damage, inflammation, and oxidative stress, which can further progress the disease. The chronic damage can cause liver scarring (fibrosis), and in more severe cases, develop into cirrhosis, though HCC rising from SLD can occur even without advanced fibrosis. The microenvironment in SLD can be remodeled, promoting tumor expansion by involving immune cells and suppressing antitumor immunity. Extracellular vesicles released from the steatotic liver play a role in both local tumor promotion and distant cancer development. Furthermore, alcohol accelerates hepatocarcinogenesis, including the mutagenic effects of acetaldehyde toxicity through the formation of protein and DNA adducts and the production of reactive oxygen species, inflammation and an impaired immune response and modifications to DNA methylation through several signaling pathways including Gut - Liver axis. In SLD patients, the HCC diagnosis is often delayed and less frequently detected through screening programmes. From a clinical perspective, it is well known that alcohol interacts with other factors, such as age, gender, obesity, and diabetes leading to an increased risk of HCC. There is a critical need for more effective screening programs to detect SLD-associated HCC in its early stages, especially in the large population of patients without cirrhosis. Addressing the root causes of SLD, such as obesity and metabolic dysfunction, and excessive alcohol intake through public health policies is essential to curb the rising tide of HCC.

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The Immune Landscape of Steatotic Hepatocellular Carcinoma

MASH has emerged as the fastest-growing cause of hepatocellular carcinoma (HCC). Steatotic HCC displays distinct biological and immunological features, leading to unique responses to immune checkpoint inhibitors. In this presentation, we will demonstrate how advanced mouse models, combined with cutting-edge immunophenotyping technologies, can be used to map the immune landscape of steatotic HCC. Our goal is to identify effective therapeutic strategies tailored to this subtype, with a focus on activating myeloid cells to enhance anti-tumor immunity.

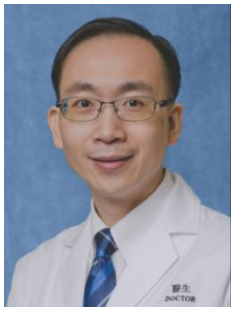
Furthermore, our research shows that HCC cells evade ferroptosis—a form of cell death driven by lipid-derived oxidative stress in steatotic HCC—through activation of the mevalonate pathway. We demonstrate that targeting the mevalonate pathway with statins and 6-FMEV sensitizes HCC cells to ferroptosis and significantly suppresses steatotic HCC. Notably, these agents act synergistically with tyrosine kinase inhibitors and anti-PD-1 monoclonal antibodies, offering promising avenues for combination therapies in this disease.

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Panel Discussions



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Classification and Epidemiology of SLD/FLD in Lean Individuals

Metabolic dysfunction-associated fatty liver disease (MAFLD, also known as metabolic dysfunction-associated steatotic liver disease and nonalcoholic fatty liver disease) is primarily linked to obesity, yet around 20% of individuals with hepatic steatosis maintain a normal body mass index (BMI), referred to as lean MAFLD. The new classification distinguishes between lean MAFLD, which includes cardiometabolic risk factors, and cryptogenic steatotic liver disease, where no such factors are present. This differentiation is essential for understanding varied liver disease presentations and risks in lean individuals.

Traditionally, obesity has been viewed as a problem in Western countries. However, urbanization in many Asian nations over the past two decades has led to sedentary lifestyles and overnutrition, contributing to an obesity epidemic. Currently, the prevalence of MAFLD in Asia is approximately 30%, comparable to Western nations. Notably, 8-19% of Asians with a BMI under 25 kg/m² also exhibit MAFLD. While this condition tends to be less severe than in obese patients, steatohepatitis and fibrotic disease are recognized. Central adiposity, insulin resistance, and weight gain are major risk factors, with genetic predispositions like the PNPLA3 polymorphism playing a critical role in the development of MAFLD in the non-obese population. Cardiometabolic risk factors often remain critical for developing hepatic steatosis and liver injury. In the general population, the PNPLA3 gene polymorphism correlates with a higher risk of MAFLD, more severe liver histology, and increased chances of hepatocellular carcinoma and cirrhosis.

The classification of lean individuals with liver disease is crucial for effective diagnosis and management. Understanding the epidemiological trends in Asia and the genetic factors contributing to lean MAFLD can help identify at-risk populations and guide interventions. Despite lifestyle modifications being the cornerstone of management, achieving and maintaining weight reduction remains challenging for many patients. Pharmacological agents for steatohepatitis are in development, yet Asian patients are often under-represented in clinical trials. Future studies must focus on optimizing MAFLD management strategies in Asia.

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MAFLD in Lean Individuals: What do We Know?

Excessive calorie consumption relative to expenditure, intake of unhealthy diets, and lack of physical activity are globally fuelling an increase in the prevalence of poor metabolic health, even in individuals of normal weight. Consequently, this trend entails increased risk of various metabolic disorders, including metabolic dysfunction associated fatty liver disease (MAFLD), which affects up to a third of the global population.

MAFLD burden has grown in parallel with rising rates of type 2 diabetes and obesity and increases the risk of end-stage liver disease, hepatocellular carcinoma, death, and liver transplantation, and has extrahepatic consequences including cardiometabolic disease and cancers. Although classically is associated with obesity, there is accumulating evidence that not all overweight or obese develop fatty liver disease. On the other hand, a considerable proportion of patients with MAFLD are lean, indicating the importance of metabolic health in disease pathogenesis regardless of body mass index. A complex and dynamic interaction between a multitude of factors, including genetic, epigenetic, dietary, and lifestyle factors, enterohepatic circulation, and gut microbiota is likely to shape individual metabolic health status.

The clinical profile, natural history and pathophysiology of lean patients with MAFLD is not well characterised. In this talk, I am going to provide the recent epidemiological data on this group of patients. The talk will illustrate the novel concept considering the overall metabolic health and metabolic adaptation as a framework to best explain the pathogenesis of MAFLD and its heterogeneity, both in lean and non-lean individuals. This framework provides a conceptual schema for interrogating the MAFLD phenotype in lean individuals that can translate to novel approaches for diagnosis and patient care. I will also touch briefly on the prospective aspects including the initiatives bringing together diverse stakeholders across the metabolic disease spectrum that are pivotal in our efforts to firstly understand and then to provide personalized, timely, equitable and affordable health interventions for lean patients with MAFLD.

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Clinical Manifestations of MASLD Based on the New Diagnostic Criteria in Japan

Background: The recent redefinition of fatty liver disease under the term Metabolic dysfunction-associated steatotic liver disease (MASLD) has provided a new diagnostic framework aimed at improving clarity and clinical relevance. However, real-world data on the clinical characteristics of MASLD patients based on these new criteria remain limited, particularly in the Japanese population.
Methods: We retrospectively analyzed 1,150 Asian patients diagnosed with MASLD at our hospital between 1980 and 2021, based on the new diagnostic algorithm that incorporates metabolic dysfunction components. Patients were categorized into the MASLD (n = 803), MASLD and increased alcohol intake, (MetALD, n = 81), and alcohol-associated liver disease (ALD, n = 266) group. Data on demographics, laboratory values, imaging findings, and liver fibrosis scores were collected and metabolic profiles, liver-related parameters, and disease severity compared across subgroups.
Results: Among 1,150 patients (MASLD, MetALD, ALD; medianage 53, 65, and 62 years; male: 49.3, 82.7, and 86.8%), metabolic comorbidities were complicated with type 2 diabetes (50.4, 49.4, and 47.0%), dyslipidemia (65.6, 34.6, and 21.8%), and hypertension (51.7, 58.0, and 40.2%), respectively. During a median follow-up of 10.6 years, the proportions of patients who developed extrahepatic malignancies were 7.2%, 9.9%, and 5.6%, and those who experienced CVD events were 5.7%, 3.7%, and 4.1%, respectively. However, Cox proportional hazards analysis revealed no significant difference in the risk of extrahepatic complications among the groups after adjusting for confounding factors. The mortality risk was significantly higher in ALD patients.
Conclusion: The application of the new MASLD criteria in a Japanese cohort revealed that the incidence of CVD and extrahepatic malignancies was similar between MetALD and ALD, despite low mortality rates. These complications require close monitoring.

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Diabetes Connection: A Bidirectional Relationship in Steatotic Liver Disease

Steatotic liver disease (SLD) illustrates the strong link between liver and metabolic disorders. Among these, type 2 diabetes mellitus (T2DM) stands out as both a cause and a consequence of SLD, emphasizing a bidirectional relationship that is becoming increasingly important clinically. Several pathophysiological processes contribute to hepatic steatosis in people with diabetes: chronic insulin resistance increases hepatic de novo lipogenesis, impairs the suppression of adipose lipolysis, and elevates free fatty acid flux to the liver; glucotoxicity and lipotoxicity induce oxidative stress and damage to the endoplasmic reticulum; meanwhile, adipokine imbalance and low-grade inflammation promote hepatocellular injury and fibrosis. These mechanisms explain why patients with diabetes face a much higher risk of developing progressive SLD, advanced fibrosis, and hepatocellular carcinoma compared to those without diabetes.

Conversely, SLD itself predisposes individuals to develop diabetes. The steatotic liver is not just a passive target but an active endocrine organ that contributes to systemic insulin resistance. The buildup of toxic lipid intermediates disrupts insulin signaling pathways, while hepatocellular stress triggers the release of pro-inflammatory cytokines and hepatokines like fetuin-A, which impair pancreatic β-cell function and worsen peripheral insulin resistance. The progression of fibrosis further increases hepatic insulin resistance, creating a vicious cycle that accelerates the transition from normal blood sugar levels to prediabetes and full-blown diabetes. Epidemiologic studies consistently show that the presence and severity of SLD nearly double the risk of incident T2DM, even after adjusting for traditional metabolic risk factors.

This interconnected pathophysiology highlights the importance of a dual approach in screening and treatment. Patients with diabetes should be regularly evaluated for SLD and fibrosis, while those with SLD must be closely observed for developing glucose intolerance. Recognizing the liver as both a victim and a contributor to metabolic dysfunction shifts the care paradigm, stressing the need for integrated treatment plans that address common mechanisms like insulin resistance, lipotoxicity, and inflammation.

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Multidisciplinary Management of Hepatocellular Carcinoma in Steatotic Liver Disease: A Hepatologist's Perspective

The incidence of hepatocellular carcinoma (HCC) arising from metabolic dysfunction–associated steatotic liver disease (MASLD) is increasing worldwide, reflecting the decline of viral hepatitis–related cases and the growing burden of obesity, type 2 diabetes, and other metabolic risk factors. MASLD-related HCC frequently develops in patients with preserved hepatic function but with significant extrahepatic comorbidities. These factors influence treatment eligibility, peri-procedural safety, and long-term outcomes, requiring a comprehensive and individualized approach. From the hepatologist's perspective, the cornerstone of effective care lies in early detection through structured surveillance programs, accurate staging using high-quality imaging, and integration of liver function assessment with metabolic risk profiling. In the therapeutic phase, decision-making must weigh tumor stage, hepatic reserve, and patient comorbidities while coordinating with a multidisciplinary team including hepatobiliary surgeons, interventional radiologists, and medical oncologists. Locoregional therapies, surgical resection, liver transplantation, and systemic therapies such as immune checkpoint inhibitors each have unique considerations in MASLD, particularly regarding peri-treatment cardiovascular risk and metabolic optimization. Importantly, management extends beyond tumor-directed interventions. Dietitians are essential in addressing the dual challenges of sarcopenia and obesity, tailoring dietary strategies to support adequate protein intake, weight control, and metabolic stability. This nutritional optimization is particularly relevant before surgery or during systemic therapy, where malnutrition and frailty can compromise outcomes. Physical therapists contribute by designing individualized exercise programs that improve muscle mass, functional capacity, and physical resilience, thereby reducing postoperative complications and enhancing tolerance to systemic treatments. These supportive interventions are not ancillary but integral to the therapeutic plan, directly influencing survival and quality of life. This presentation will share case-based experiences and real-world treatment algorithms for MASLD-related HCC, focusing on the hepatologist's role as the coordinator of multidisciplinary input. Strategies for integrating dietetic and physiotherapy support from the point of diagnosis will be discussed, alongside approaches to minimize treatment-related liver decompensation and prevent metabolic deterioration. The discussion will highlight how collaboration across specialties—including nutrition, physical rehabilitation, hepatology, surgery, oncology, and radiology—can be operationalized in daily practice, ensuring that patient management is both tumor-focused and holistic. By adopting a multidisciplinary model that prioritizes metabolic health, physical function, and hepatic reserve, we can improve not only oncologic outcomes but also the long-term wellbeing of patients with MASLD-related HCC.

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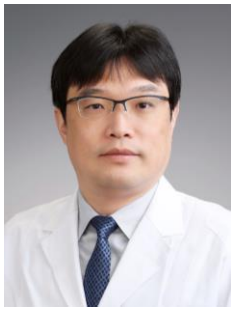
Innate Immune Receptor Profiles in Steatotic Liver Disease: Sex and Etiology

Background: Steatotic liver disease (SLD), encompassing metabolic dysfunction–associated steatotic liver disease (MASLD) and alcohol-related liver disease (ALD), is strongly influenced by gut-derived pathogen-associated molecular patterns (PAMPs). Alcohol consumption and metabolic stress disrupt the intestinal barrier, promoting microbial translocation into the portal circulation. These PAMPs activate hepatic pattern recognition receptors (PRRs), such as RIG-I-like receptors (RLRs) and Toll-like receptors (TLRs), leading to hepatic inflammation. However, sex- and etiology-specific expression profiles of these receptors remain incompletely characterized.

Methods: We analyzed liver biopsy specimens from 62 patients with biopsy-proven SLD (MASLD: n=44; ALD/MetALD: n=18) treated at Juntendo University Hospital. Clinical features, laboratory data, and hepatic mRNA expression of RLRs (RIG-I, MDA5) and TLRs (TLR3, TLR4) were assessed by quantitative PCR. To further investigate microbial nucleic acid translocation, stool and portal blood samples were collected from six cirrhotic patients undergoing endoscopic variceal treatment. Microbial DNA was extracted and subjected to 16S rRNA sequencing.

Results: Among patients with SLD, females were significantly older and exhibited higher serum albumin and γ-GTP levels compared with males. Hepatic expression of RIG-I and TLR3 was significantly higher in females, with a similar trend for MDA5. No sex differences were observed for TLR4 or inflammatory cytokines (TNF-α, IL-1β, IFN-α, IFN-β). Stratification by etiology showed that ALD patients had significantly higher hepatic RIG-I and TLR4 expression than MASLD patients, whereas TLR3 expression did not differ. Cytokine expression tended to be higher in ALD but did not reach statistical significance. In the cirrhotic cohort, microbial diversity was markedly reduced in portal blood compared with stool; however, specific taxa such as Proteobacteria (Enterobacteriaceae) and Firmicutes (Veillonellaceae) were consistently detected in both, suggesting selective translocation of bacterial DNA into the portal circulation.

Conclusions: Hepatic innate immune receptor expression in SLD is modulated by sex and disease etiology. Female patients display enhanced expression of nucleic acid–sensing receptors (RIG-I and TLR3), potentially reflecting estrogen-mediated regulation, whereas ALD patients show upregulated RIG-I and TLR4, consistent with alcohol-induced microbial translocation. Detection of bacterial DNA in portal blood of cirrhotic patients provides direct evidence that gut-derived microbial nucleic acids can access the liver, where they may drive hepatic inflammation and disease progression.



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Developing New Therapy for SLD-related Cirrhotic Patients Using Extracellular Vesicles from Human iPS-derived Mesenchymal Stem Cell

Hepatitis C has been the most common cause of cirrhosis in the past, but now alcohol consumption is the most common cause and fatty liver disease is steadily increasing. In 2023, the concept of steatotic liver disease (SLD) was proposed, which includes the replacement of the word "fatty" with "steatotic. Thus, cirrhosis caused by SLD is expected to increase from hepatitis viruses in the future, and the development of hepatocellular carcinoma surveillance methods and antifibrotic therapy are needed. So far, we have developed a liver regeneration therapy for decompensated liver cirrhosis using cultured autologous bone marrow-derived mesenchymal stem cells (BMSCs). From September 2020, " self-contained liver cirrhosis regeneration therapy (robot culture with new culture medium, autologous bone marrow-derived MSCs, hepatic artery administration)" is being conducted as a clinical trial (jRCT2063200014). On the other hand, we developed human iPSC-derived MSCs (iMSCs) and assessed the therapeutic effects of iMSC-extracellular vehicles (EVs) on murine MASH-related liver fibrosis by feeding Gubra-Amylin-NASH (GAN) diet and a single intraperitoneal injection of carbon tetrachloride. In this model, we confirmed that human iMSC-EVs improved serum albumin levels and reduced dyslipidemia compared to the control group, consistent with significant reduced liver fibrosis and increased number of CD163-positive M2 macrophage histologically. Therefore, we concluded that human iMSC-EVs might be able to be a new therapy for SLD-related cirrhotic patients.

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Digital Pathology Using Fibrosis Pattern Analysis to Predict Hepatocellular Carcinoma Development in Patients with MASLD

Purpose: Fibrosis progression is a major risk factor for the development of hepatocellular carcinoma (HCC) in metabolic dysfunction-associated steatotic liver disease (MASLD). However, the annual incidence of HCC in MASLD-related cirrhosis is approximately 1–2%, which is lower than that in viral cirrhosis. In recent years, the application of artificial intelligence (AI) has enabled comprehensive analysis of pathological parameters using digitized tissue specimens. In this study, we aimed to identify specific fibrotic patterns associated with HCC development.

Methods: Study 1: Seventeen patients who underwent liver transplantation for MASLD-related cirrhosis were included. Among them, eight had HCC and nine did not. Sirius Red-stained noncancerous areas were scanned as whole slide images (WSIs) for analysis. Fibrotic parameters were assessed in the noncancerous regions. Fiber characteristics were examined with and without HCC.

Study 2: Thirteen patients with biopsy-proven MASLD and advanced fibrosis, who were followed for more than five years after liver biopsy, were included. Similarly, the characteristics of fibers involved in the development of HCC or not were examined.

Results: Study 1: No significant differences in collagen content or structural patterns were observed between the HCC and non-HCC groups. However, when fibrotic phenotypes were weighted and scored, the HCC group could be distinguished from the non-HCC group with a sensitivity of 75% and a specificity of 100%.

Study 2: Among MASLD biopsy cases, there was no significant difference in collagen volume between those who developed HCC and those who did not. However, cases with HCC were characterized by significantly lower fiber torsion kurtosis and skewness, greater fiber width and density kurtosis, and lower length kurtosis. When these fiber parameters were combined and scored, future HCC development could be predicted with a sensitivity of 85% and a specificity of 100%.

Conclusion: Quantitative analysis and integration of fibrotic parameters enabled high-accuracy discrimination of MASLD cases at risk for HCC development.

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"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Workshops

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Multi-Omic Deep Learning Model Predicts IVA337 Response in MASLD Patients Using Liver Transcriptomics, Serum Proteomics, and Immune Single-Cell RNA-seq

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) presents a therapeutic challenge due to heterogeneous responses to emerging agents such as IVA337 (lanifibranor), a pan-PPAR agonist. We aimed to develop a non-invasive, deep learning-based predictive model of IVA337 histologic response by integrating transcriptomic, proteomic, and immune single-cell data from MASLD patients.

Methods: We utilized human omic datasets from the Gene Expression Omnibus (GEO): liver transcriptomics from IVA337-exposed spheroid models (GSE292999), serum proteomics from MASLD patients using SomaScan v1.3k (GSE251855), and peripheral immune single-cell RNA-seq from MASLD and control cohorts (GSE267033). A transformer-based multi-branch deep learning model was built to classify responders (NAS ≥2 reduction and ≥1-stage fibrosis improvement) versus non-responders. Cross-omic attention fusion layers integrated key features, with model performance assessed using five-fold stratified cross-validation and bootstrapped confidence intervals. SHAP interpretation was applied for biomarker identification.

Results: The model achieved an AUROC of 0.812 (95% CI: 0.765-0.853), AUPRC of 0.791, sensitivity of 75.6%, and NPV of 88.9%. Top predictors included hepatic PPARγ and FABP4, serum CK-18 and C7, and immune CD8+ PD-1+ T cell exhaustion signatures, supporting IVA337's known anti-inflammatory and anti-fibrotic effects. Additional stratified analyses showed improved performance in patients with baseline NAS ≥5 and fibrosis stage F2-F3, where predictive accuracy reached 0.842, indicating enhanced model performance in clinically advanced MASLD subgroups.

Conclusion: This computational and clinically interpretable multi-omic model provides a non-invasive approach to predict therapeutic response to IVA337 in MASLD, supporting its potential use in guiding personalized treatment strategies.

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Improvement Effect of Metabolic and Bariatric Surgery on Steatotic Liver Disease and its Mechanism

The bariatric surgery has been recognized as a most effective treatment modality for morbid obesity. Furthermore, it has been shown to improve obesity-related comorbidities, including type 2 diabetes and steatotic liver disease, independent of weight reduction and it is referred to as metabolic and bariatric surgery (MBS). In Japan, the prevalence of NASH in morbidly obese patients who have undergone MBS is reported 77%. According to data based on periodic health checkup, the prevalence of NAFLD was 63.4% in patients 25≤BMI≤30 kg/m2, and 89.1% in those BMI≥30 kg/m2. In the meta-analysis reported in 2008, in 766 patients who underwent MBS, fatty liver improved in 91.6%, NASH improved in 81.3%, and fibrosis improved in 65.5% postoperatively, and the complete remission rate of NASH was 69.5%. In the RCT reported in 2023, 288 patients with NASH were randomly assigned to lifestyle modification (LM) group, RYGB group, and sleeve gastrectomy (SG) group. The remission rate was significantly higher in RYGB (56%) and SG (57%), compared to 16% in LM.

Although above mentioned results after MBS, there are few studies on the mechanisms underlying this metabolic improvement. We investigated the NASH improving mechanism of the duodenal-jejunal bypass (DJB), a component of MBS, using diet-induced rodent NASH model, which were fed with high fat and high fructose diet. In this study, DJB model showed significant reduction of liver volume and serum transaminase, and significant improvement of liver fibrosis. Besides, DJB model presented the significant elevation of portal bile acids concentration and a marked suppression of various inflammatory mediators such as TNF-alpha, Ip-10 and MCP-1. A transcription factor of lipid metabolism, SREBP1c also seemed decrease, not statistically significant though. Moreover, it has been suggested that lipopolysaccharide (LPS) derived from intestinal bacteria induces inflammation in the liver, and DJB improves NASH by suppressing the transfer of LPS from the intestine to the liver. In this model, the stomach was not resected to eliminate the effects of changes in food intake, and it is understood that these effects are purely the result of DJB.

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Paradoxical Effects of Fat Accumulation on Immune Checkpoint Inhibitor Efficacy in HCC Treatment

Immunotherapy, particularly the combination of anti–PD-L1 and anti–VEGF antibodies (atezolizumab plus bevacizumab, Atez/Bev), has emerged as a first-line treatment for advanced hepatocellular carcinoma (HCC). However, treatment response of immune checkpoint inhibitors (ICIs) varies significantly, with underlying tumor biology and the tumor immune microenvironment (TIME) playing critical roles.

In our previous multi-omics analysis of non-viral HCC, we demonstrated that approximately one-quarter of tumors exhibited intratumoral steatosis, a feature associated with an immune-enriched yet exhausted TIME. These steatotic tumors were infiltrated by cytotoxic T lymphocytes, M2 macrophages, and cancer-associated fibroblasts, and expressed high levels of PD-L1 and TGF-β signaling. Patients with steatotic HCC experienced significantly improved progression-free survival (PFS) following Atez/Bev treatment, suggesting enhanced sensitivity to ICI-based therapy.

In contrast, immune resistance in metabolic dysfunction-associated steatohepatitis (MASH)-related HCC appears to arise from a distinct mechanism. In MASH-HCC, lipid accumulation primarily occurs in the peritumoral liver. A Nature study previously reported that MASH-HCC is associated with cytoplasmic accumulation of p62, a selective autophagy adaptor protein. Notably, p62 is known to stabilize and activate NRF2, a key transcription factor involved in oxidative stress responses and immune regulation. In our recent work, we demonstrated that NRF2 activation, via the NRF2–COX2–PGE2 axis, induces an immune COLD TIME, characterized by exclusion of tumor-infiltrating lymphocytes and upregulation of immunosuppressive mediators, thereby conferring resistance to Atez/Bev in both mouse models and human HCC samples.

Together, these studies suggest that the spatial context of fat accumulation—within the tumor versus in the surrounding liver—critically determines ICI responsiveness. Intratumoral steatosis fosters a targetable immune exhaustion phenotype responsive to Atez/Bev, whereas peritumoral steatosis in MASH-HCC contributes to a systemic immunosuppressive milieu resistant to immunotherapy. These findings underscore the necessity of refined stratification strategies based on lipid distribution and immune profiling, which may inform personalized immunotherapeutic approaches and improve clinical outcomes in HCC.

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Inhibitory Effect of Pemafibrate on Fatty Acid-Induced Mitochondrial and Cellular Damage by Induction of Autophagy

Background and Aim: Dysfunction of autophagy is closely associated with the progression of metabolic dysfunction-associated steatotic liver disease (MASLD). Recently, the selective PPARα modulator pemafibrate has been reported to exert protective effects against liver injury and fibrosis in patients with MASLD. Here, we investigated the autophagy-inducing effects of pemafibrate and its protective role against fatty acid-induced cellular injury.

Methods: HepG2 cells were treated with a fatty acid mixture (oleic acid + palmitic acid, 2:1, 300 μM) with or without 2 μM pemafibrate. Cell viability was assessed using the WST-1 assay. Intracellular lipid droplet formation was visualized with LipidTOX™, and autophagosomes were evaluated after GFP-LC3 plasmid transfection. Mitochondrial damage was assessed using the JC-1 probe and confocal laser microscopy.

Results: After 24 h of fatty acid treatment, cell viability decreased to 77.6% compared with controls, whereas co-treatment with pemafibrate restored viability to 106.4 ± 10.6%. The number of GFP-positive autophagosomes increased approximately four-fold with pemafibrate compared with controls. In fatty acid-treated cells, lipid droplets accumulated in the cytoplasm, with 13% co-localizing with GFP-positive autophagosomes. In contrast, co-treatment with pemafibrate markedly increased co-localization to 74.7 ± 8.0%. Fatty acid treatment induced mitochondrial membrane potential abnormalities in 85.0 ± 3.2% of cells, whereas co-treatment with pemafibrate reduced this to 22.6 ± 4.4%.

Conclusions: Pemafibrate induced autophagy and lipophagy, thereby reducing the accumulation of damaged mitochondria and preventing cellular injury. These findings suggest that pemafibrate-mediated autophagy induction plays a protective role and may underlie its beneficial effects on MASLD pathology.

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The Role of SASP in the Liver Tumor Microenvironment: The Gut-liver Axis-mediated Mechanism

Recently, metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH) have been recognized as major contributors to hepatocellular carcinoma (HCC). However, the precise mechanisms of how MASLD/MASH-associated conditions promote HCC development remain to be understood. In our previous studies, we demonstrated that high-fat diet (HFD)-induced obesity profoundly alters the gut microbiota composition. We identified that hepatic stellate cells (HSCs) exposed to elevated levels of deoxycholic acid (DCA), a microbial metabolite increased by obesity, promoted a senescence-associated secretory phenotype (SASP), characterized by the secretion of pro-inflammatory cytokines, chemokines, and proteases (1,2). In addition, hepatic translocation and accumulation of the gut microbial component, lipoteichoic acid (LTA), were observed (2,3). This microbial stimulation further enhanced the SASP phenotype in HSCs via activation of Toll-like receptor 2. Besides IL-1β (1), we found that IL-33 was highly induced in liver tumor regions, particularly in senescent HSCs, in an IL-1β-dependent manner in an HFD-induced MASH-associated liver cancer mouse model. Notably, IL-33 knockout mice developed significantly fewer tumors compared to wild-type controls, suggesting a critical role for IL-33 in HCC development (3). Furthermore, we discovered a novel release mechanism of SASP factors involving membrane pore formation by the N-terminal domain of gasdermin D, triggered by LTA. The secreted short form of IL-33 suppressed antitumor immunity by activating ST2-positive regulatory T (Treg) cells, thereby contributing to the progression of MASH-associated HCC. Importantly, IL-33 overexpression and accumulation of the gasdermin D N-terminal domain were also observed in HSCs within tumor areas of human MASH-associated HCC, implying that a similar mechanism may underlie liver cancer progression in humans (3). More recent findings on this topic will be presented in the conference.

References:

(1) Yoshimoto et al. 499:97-101, Nature, 2013,
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Surgical Treatment for SLD-related HCC: Trends in Liver Resection and Transplantation

The advent of anti-viral therapy has led to a decline in hepatitis B (HBV) and C (HCV) cases. Concurrently, a marked increase has been observed in hepatocellular carcinoma (HCC) with hepatitis virus-unrelated etiologies (non-B non-C; NBNC), which predominantly result in steatotic liver diseases (SLD), including metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-associated liver disease (ALD). The association between SLD-related HCC and cardiometabolic risks, including central obesity, type 2 diabetes, hypertension, and dyslipidemia, as well as alcohol consumption, is well-documented. In the context of surgical interventions for HCC, encompassing liver resection (LR) and liver transplantation (LT), the influence of SLD on post-treatment outcomes was examined.

In cases of LR, NBNC etiologies accounted for approximately one-third of the total, with a significantly increasing trend observed across age groups. Among NBNC cases, ALD was the most prevalent at 30%, followed by MASLD at approximately 25%, MetALD at 10%, and cryptogenic cases at 33%. Approximately 25% of the total cases exhibited coexisting MASLD, irrespective of the baseline disease, with an increasing trend observed by age group. NBNC cases exhibited markedly superior postoperative overall survival and recurrence-free survival when compared to HCV cases. Patients diagnosed with MASLD-related HCC exhibited superior hepatic function, a comparatively reduced tumor stage, and a more optimistic long-term prognosis following LR compared to those with non-SLD. Non-SLD cases, including cryptogenic cases, exhibited a propensity for advanced tumors, and those with metabolic risk factors demonstrated unfavorable long-term outcomes following liver resection.

In the context of LT cases involving hepatocellular diseases, the prevalence of hepatitis B (HBV) was 20%, while hepatitis C virus (HCV) accounted for 50%. The remaining 30% was attributed to NBNC, including ALD and pure-MASLD. The survival outcomes for NBNC-HCC recipients were comparatively superior to those with HCV. The coexistence of MASLD in the overall cohort was associated with a relatively favorable prognosis. Regarding the comorbidity of post-LT SLD, baseline MASLD was associated with high risk of SLD recurrence, with a 5-year incidence rate of approximately 50%. The prevalence of visceral adiposity and diabetes was associated with the occurrence of post-LT-SLD. The incidence of post-LT SLD exhibited a strong correlation with the occurrence of cardiovascular events following LT.

Conclusion. The treatment outcomes of LR and LT for SLD-related HCC are feasible. Nevertheless, the perioperative management of concomitant cardiovascular and metabolic risks remains challenging.

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Spatial Profiling Identifies GPNMB-positive Macrophages as Regulators of Fibrosis and Tumor Growth and as Predictive Biomarkers in Hepatocarcinogenesis

Background: GPNMB (Glycoprotein non-metastatic melanoma protein B) is a lysosomal stress-induced, senescence-associated molecule. Its role in liver macrophages and relevance in chronic liver disease remain unclear.

Methods: CosMx spatial transcriptomics was applied to liver tissues from patients with metabolic dysfunction-associated steatohepatitis (MASH) and hepatitis C virus (HCV)-related disease. Single-cell RNA sequencing profiled immune cells in chronic liver diseases. In vitro, THP-1-derived macrophages were exposed to fatty acids, bafilomycin, or apoptotic HepG2 cells. GPNMB-knockout (KO) THP-1 macrophages were analyzed. Serum GPNMB levels were assessed in 936 MASLD or HCV patients to evaluate HCC risk and in 290 HCV-cirrhosis patients for prognosis.

Results: scRNA-seq showed consistent GPNMB expression in CD68-positive hepatic macrophages across etiologies. Spatial analysis revealed GPNMB-positive macrophages expressed genes associated with lipid metabolism, phagocytosis, and SASP. Ligand-receptor analysis incorporating proximity scores identified GPNMB-CD44 signaling enriched between neighboring macrophages. Hepatic stellate cells near GPNMB-positive macrophages upregulated fibrotic genes, while those near GPNMB-negative macrophages were less activated than distant cells. In tumors, GPNMB-positive macrophages upregulated tumor-promoting genes. In vitro, lysosomal stress triggered GPNMB and SASP cytokines, whereas apoptotic body uptake suppressed inflammation despite GPNMB induction. GPNMB-KO experiments indicated that GPNMB plays a role in promoting M2 polarization of macrophages in response to chronic stress. Serum GPNMB was an independent predictor of HCC risk in both MASLD and HCV cohorts. In HCV cirrhosis, levels ≥18.8 ng/mL were associated with significantly shorter transplant-free survival.

Conclusion: GPNMB-positive macrophages shape fibrogenic and tumor-promoting niches via spatial and autocrine signaling. Serum GPNMB may serve as a biomarker.

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Toxic Relationships:
When Environmental Exposures Meet Metabolic Liver Disease

Environmental chemical exposures represent an underrecognized but critical component of liver health, serving as risk modifiers that influence disease development, severity, and complications. While traditional hepatology focuses on genetic, viral, and lifestyle factors, mounting evidence demonstrates that environmental toxicants significantly modify liver disease risk, particularly in metabolic dysfunction-associated steatotic liver disease (MASLD).

The liver serves as a primary target organ for environmental chemicals, with major pollutants consistently associated with MASLD development and progression. These exposures exhibit substantial health disparities across populations, creating differential vulnerability patterns. Environmental chemicals function through diverse pathways including mitochondrial dysfunction, inflammatory activation, oxidative stress, and disruption of cellular metabolism.

Our research demonstrates that low-level vinyl chloride exposure, at concentrations previously considered safe, significantly enhances Western diet-induced liver injury. This interaction transforms manageable dietary stress into severe hepatotoxicity characterized by inflammation, necrosis, and accelerated tumorigenesis. Transcriptomic analyses reveal that Western diet backgrounds amplify toxicant responses 4.6-fold and uniquely enable carcinogenic pathway activation.

Beyond single chemicals, environmental mixtures present complex challenges. Military burn pit exposures cause rapid-onset hepatic pathology within days, characterized by disrupted liver architecture and ultrastructural alterations. Chemical mixtures containing metals and emerging contaminants like PFAS synergistically enhance liver injury, promoting severe inflammation while activating cancer-related pathways.

Human epidemiological studies consistently demonstrate associations between environmental exposures and liver dysfunction across diverse populations. Particulate matter (PM2.5) significantly associates with liver dysfunction and chronic liver diseases, with developing countries showing slightly higher MASLD risk levels than developed nations. Chemical disasters and industrial accidents provide natural experiments demonstrating how acute exposures can trigger long-term hepatic consequences.

The mechanisms underlying these interactions involve complex cellular processes. Environmental chemicals disrupt mitochondrial function, alter gene expression patterns, activate inflammatory cascades, and impair cellular detoxification systems. These effects are particularly pronounced when combined with underlying metabolic stress, suggesting that environmental factors may explain inter-individual variability in MASLD progression.

Clinical translation requires incorporating environmental exposures into precision medicine approaches for liver health. This includes developing exposure reduction strategies, enhancing toxicant clearance, and understanding exposure sources. Future directions involve longitudinal studies to understand how environmental factors influence disease progression, therapy response, and patient outcomes, ultimately advancing environmental hepatology as a critical component of comprehensive liver care worldwide.

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Impact of Fatty Acid Desaturase (FADS) 2 Gene Variants on Progression of Hepatic Fibrosis in MASLD

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Background and Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) arises from genetic predisposition and acquired factors, and progresses to cirrhosis in a subset of patients. While the contribution of single-nucleotide polymorphisms (SNPs) for lipid-metabolizing enzymes (i.e., PNPLA3, TM4SF2) to MASLD is well-established, the interaction among multiple genetic determinants remains uncertain. Since our previous experimental work indicated that fatty acid desaturase (FADS) gene expression decreases in advanced steatohepatitis in mice, here we evaluated the clinical impact of SNPs for FADS genes, in relation with other lipid-metabolizing gene variants, in the progression of MASLD.
Methods: We analyzed 48 biopsy-proven MASLD patients diagnosed between January 2021 and September 2024. Patients were stratified into non-progressive fibrosis (stage 0–2, n = 32) and progressive fibrosis (stage 3–4, n = 16) groups. Genomic DNA was extracted from peripheral blood, and SNPs of PNPLA3 (rs738409), MBOAT7 (rs641738), TM6SF2 (rs58542926), FADS1 (rs174556), and FADS2 (rs174583) were genotyped using TaqMan PCR. Group differences were assessed by chi-square and Student's t-tests, with logistic regression applied for multivariate analysis.
Results: Age and sex distributions did not differ significantly between non-progressive and progressive fibrosis groups. The PNPLA3 G/G allele occurred in 62.5% of progressive cases versus 43.8% of non-progressive cases., whereas the FADS2 T/T allele was present in 56.3% and 40.6%, respectively. Other alleles (MBOAT7 C/C, TM6SF2 C/T, FADS1 T/T) showed no significant group differences. Importantly, carriers of both PNPLA3-GG and FADS2-TT were significantly more frequent in the progressive group (43.8%), as compared to the non-progressive group (12.0%, p = 0.027). Logistic regression adjusting for age and sex identified the combination of PNPLA3-GG/FADS2-TT genotype as an independent predictor of fibrosis progression (odds ratio 7.171, 95% CI 1.284–40.047).
Conclusions: The PNPLA3 and FADS2 risk alleles not only independently, but also synergistically increase the likelihood of fibrosis progression in MASLD. These findings suggest the importance of combined genetic risk profiles rather than the evaluation of a single gene variant. Genetic validation for PNPLA3 and FADS2 most likely provides a optimal approach regarding precise fibrosis risk-stratification and early intervention for MASLD patients.

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ALDH2 Variants and Liver Disease

Aldehyde dehydrogenase 2 (ALDH2) is a pivotal mitochondrial enzyme central to the detoxification of acetaldehyde, the primary toxic metabolite of alcohol. This enzymatic function is crucial for safeguarding cells from the detrimental effects of acetaldehyde accumulation. In addition to its canonical role in alcohol metabolism, ALDH2 is implicated in a range of biological processes, including the regulation of cellular redox homeostasis, mitochondrial integrity, and modulation of inflammatory pathways. A well-established genetic polymorphism in the ALDH2 gene leads to a loss-of-function variant that affects a significant portion of the global population (~8%), with markedly higher prevalence in East Asia, where approximately 30% to 45% of individuals harbor the mutant allele. This genetic variant results in a substantial reduction or complete loss of ALDH2 enzymatic activity, culminating in the accumulation of acetaldehyde and an increased susceptibility to cellular damage, particularly in the liver.

Emerging evidence increasingly underscores the critical role of ALDH2 deficiency in the pathogenesis of a variety of liver disorders, including viral hepatitis, alcoholic liver disease (ALD), and metabolic-associated steatotic liver disease (MASLD). Moreover, ALDH2 deficiency has been strongly correlated with the progression of liver fibrosis and the subsequent development of liver carcinoma. Mechanistic studies have begun to elucidate the diverse mechanisms through which ALDH2 dysfunction contributes to liver disease progression. These include disturbances in lipid and bile acid metabolism, alterations in exosome-mediated intercellular signaling, and the impairment of T-cell responses, all of which collectively facilitate the progression of liver pathology.

This report will comprehensively elaborate on the relationship between ALDH2 variant and liver diseases by integrating our own work and the latest research progress.

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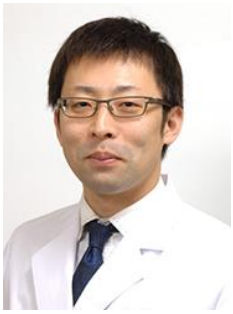
Decoding Cell-State Specific Expression Quantitative Trait Locus Regulation of Fibrosis Progression in Human Metabolic Liver Disease Using Single-Cell Transcriptomic Analysis

Background: Fibrosis progression in metabolic-associated liver disease may be influenced by cell-type specific genetic regulation, but these mechanisms remain poorly characterized in human liver. This study aimed to identify expression quantitative trait loci that regulate fibrosis at the level of specific cell states using integrated single-cell transcriptomic and genotype data.
Methods: We analyzed single-nucleus RNA sequencing and matched genotype data from the Gene Expression Omnibus (GEO) dataset GSE289173, comprising 48 human liver biopsies (25 disease, 23 control). Cell types were identified using canonical markers, and pseudotime analysis inferred dynamic cell states across hepatocytes, Kupffer cells, hepatic stellate cells, and endothelial cells. We applied tensor-based regression models to map expression quantitative trait loci and genotype-by-cell state interaction loci. Fibrosis-linked loci were tested for enrichment using stratified linkage disequilibrium score regression based on published genome-wide association summary statistics. Druggable gene targets were predicted using OpenTargets and DGIdb databases.
Results: We identified 3,642 significant regulatory loci and 297 interaction loci, including a Kupffer cell-specific variant near TREM2 (rs1990622; $p = 2.3x10-5$; OR = 1.84 [95% CI: 1.43-2.33]) and an endothelial-specific variant near VCAM1 (rs4762; $p = 7.2x10-4$) associated with fibrosis stage. Heritability was enriched 10.27-fold within interaction regions ($p < 1x10-6$), and colocalization confirmed 22 high-confidence overlaps. Prioritized druggable targets included SPP1 and LGALS3, including enhancer-linked signals, splicing regulation effects, and transcription factor binding disruptions.
Conclusion: These findings establish a precision genomics framework for identifying cell-state specific drivers of fibrosis in metabolic liver disease and inform future therapeutic targeting strategies.



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Metabolic and Bariatric Surgery as a Strong Alternative for MASH in Patients with Severe Obesity

Steatotic liver disease (SLD) is one of the important liver disease in current life circumstances, and metabolic dysfunction associated steatotic liver disease (MASLD)/metabolic dysfunction associated steatohepatitis (MASH) can be the leading disease in patients with metabolic syndrome and/or severe obesity. As surgical option for MASLD/MASH, metabolic and bariatric surgery (MBS) is the strong option for MASLD MASH in patients with severe obesity except for liver transplantation for end-stage MASH and liver resection for hepatocellular carcinomas due to SLD. We can choose either laparoscopic sleeve gastrectomy (LSG) or bypass procedure with LSG within national health insurance. We have focused on MASLD/MASH as the most important obesity-related disease from introducing MBS in 2008, and we clarified that intraoperative liver biopsy revealed that MASH prevalence rate was more than 60% (Nikai H, Sasaki A, et al. Obes Surg. 2020). However, we also demonstrated that histopathological MASH improved after MBS by metabolic effects (Sasaki A, et al. Biomedicines. 2022). Moreover, hepatocyte ballooning and liver fibrosis were closely related to insulin resistance in patients undergoing MBS (Kakisaka K, Sasaki A, et al. Sci Rep. 2021、Nikai H, Sasaki A, et al. Surg Today. 2021), moreover, we also demonstrated that the changes of adipokines, hepatokines, ketone bodies, lipid profiles, microbiota, and cytokines after MBS improved MASH (Umemura A, Sasaki A, et al. Endocr J. 2014, Umemura A, Sasaki A, Takamura T, et al. Surg Today. 2024, Ummeura A, Sasaki A, et al. Obes Surg. 2024, Takahashi N, Sasaki A, et al. Biomedicines. 2022, Kumagai H, Sasaki A, et al. Endocr J. 2023); therefore, MBS can be a candidate of surgical treatments for SLD and further investigations in MBS are warranted in near future.

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Preoperative HbA1c Predicts Postoperative Liver Inflammation after Metabolic Bariatric Surgery in Patients with Severe Obesity and Steatotic Liver Disease

Aim: Metabolic dysfunction-associated steatotic liver disease (MASLD) is commonly diagnosed in individuals with obesity and liver steatosis. Patients with MASLD and elevated alanine aminotransferase (ALT >30 U/L) are at increased risk of liver fibrosis progression. In 2024, MASLD was included as an indication for metabolic bariatric surgery (MBS). This study aimed to identify MASLD related metabolic factors and evaluate the impact of MBS.

Methods: A prospective study was conducted on 69 patients with severe obesity who underwent laparoscopic sleeve gastrectomy. A control group of 19 age- and sex- matched non-obese healthy volunteers was included. Intraoperative liver biopsies were performed, serum cytokines and adipokines were measured using multiplex and ELISA, amino acids were analyzed using HPLC-ninhydrin method. Blood sampling and clinical data were collected preoperatively and at 6 months and 1 year postoperatively.

Results: Of 69 patients, 66 (95.7%) had fatty liver, consistent with a diagnosis of MASLD. Median age was 45 years, BMI 43.6 kg/m^2, ALT 47 U/L, and HbA1c 6.2%. Brunt stage $\geqq$ 2 was observed in 44 patients (66.7%). Patients exhibited elevated levels of 16 inflammatory cytokines compared to non-obese healthy volunteers, indicating systemic inflammation. Patients with ALT > 30 U/L group (n=45, 68%) were predominantly younger males with more hypertension, insulin resistance, and advanced fibrosis. One year after surgery, liver inflammation, systemic inflammation, and metabolic parameters improved significantly. Of the 45 patients with the preoperative ALT >30 U/L group, 5 (11 %) exhibited postoperative ALT >30 U/L. To clarify the risk factors associated with poor improvement in liver inflammation after MBS, we compared preoperative clinical findings and laboratory data between the preoperative and postoperative ALT > 30 U/L groups. Univariate analysis revealed that significant differences in preoperative levels of GGT, HbA1c, HOMA-IR, BCAA were higher in the postoperative ALT > 30 U/L groups. Multivariate analysis identified high preoperative HbA1c as a predictor of persistent ALT elevation. Although preoperative ALT levels did not differ significantly between high and low HbA1c groups, ALT declined more slowly in the high HbA1c group, resulting in significantly elevated levels at 48 weeks.

Conclusions: MBS improves liver inflammation in severely obese patients with MASLD. However, this benefit may be less pronounced in individuals with HbA1c > 7.2%, suggesting a possible role for glycemic control in influencing hepatic outcomes.

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Liver Transplantation for Steatotic Liver Disease: Current Problems and Future Challenges

Liver transplantation (LT) remains the only curative treatment for hepatocellular carcinoma (HCC). In January 2024, the recipient criteria for deceased donor LT in Japan were revised, expanding eligibility from Child-Pugh classification C to B or higher in patients with decompensated liver failure. This revision is expected to increase the number of deceased donor LT cases for HCC. In parallel, the remarkable progress in antiviral therapy has led to a decline in HBV- and HCV-related cases, whereas LT for non-B, non-C cirrhosis, particularly those due to alcohol-associated liver disease (ALD) and metabolic dysfunction-associated steatotic liver disease (MASLD), has been increasing. With the increase in steatotic liver disease (SLD), approximately 40% of deceased donor livers exhibit steatosis, and many of them are not suitable for LT. In particular, steatotic grafts with moderate-to-severe macrovesicular steatosis are prone to severe ischemia-reperfusion injury after transplantation, leading to early graft dysfunction, thus, strategies to optimize the use of steatotic grafts are required. At our institution, analysis of LT for hepatocellular diseases between 2017 and 2022 revealed that MASLD accounted for 20% of cases (vs. 4% a decade ago), ALD 45% (7%), HBV 11% (24%), and HCV 18% (64%), demonstrating a marked increase in SLD-related recipients. The cumulative 5-year incidence of de novo MASH after LT in non-MASH recipients was 3.8%, whereas the recurrence rate in pre-existing MASH recipients was as high as 56%. Although overall outcomes of LT in MASLD recipients were favorable, post-transplant SLD recurrence was strongly associated with diabetes mellitus and myosteatosis.

A newly emerged clinical challenge is the prolonged hospitalization after LT, despite the stabilization of surgical techniques and improvement in short-term outcomes. The primary cause is insufficient oral intake during hospitalization. Despite active nutritional management through multidisciplinary teams (e.g., Nutrition Support Team), patients frequently develop obesity due to overeating after discharge, resulting in early post-transplant steatosis. At the time of discharge, the prevalence of obesity (defined as Body Mass Index ≥25) was 7.3%, whereas obesity progression or new-onset obesity was observed in 25.5% of patients during outpatient follow-up. Therefore, in LT for SLD, perioperative management of systemic metabolic risks is essential.

Furthermore, our department has established a novel mouse steatotic liver graft transplantation model to investigate the mechanisms of ischemia-reperfusion injury in fatty liver grafts, and we will present our latest findings in this session.

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Conversion Surgery following Chemotherapy for Advanced Hepatocellular Carcinoma with Underlying SLD

Background: Recently, systemic therapy followed by conversion surgery has been proposed as a novel treatment strategy for patients with highly advanced hepatocellular carcinoma (HA-HCC). The aim of this study was to assess the feasibility and short-term outcome of conversion surgery after administrating systemic therapy for HA-HCC underlying SLD.

Methods: We defined initially unresectable when R0 resection was technically impossible or residual liver reserve was inadequate, and borderline resectable when oncologically unresectable: more than 4 tumors or macroscopic vascular invasion. Our strategy is to perform systemic chemotherapy first for initially unresectable and borderline resectable HCC. Patients with extrahepatic metastases was excluded from this study.

Results: From September 2019 to June 2023, 167 HCCs without extrahepatic metastases were referred to our outpatient department. Of these, 114 had SLD. Of 167 HCCs, 19 cases were borderline resectable, and 10 cases were initially unresectable. Of the 19 borderline resectable cases, we treated 7 with ATBV and 7 with LEN, and the remaining 5 had already received hepatic arterial infusion chemotherapy at other centers. Six of the 7 cases treated with ATBV could have undergone surgery, and 5 of the 7 cases treated with LEN could have undergone surgery. Of the 10 initially unresectable cases, we treated 3 with ATBV and 4 with LEN, and the remaining 3 had already started hepatic arterial infusion chemotherapy at other centers. None of the 3 cases treated with ATBV could have undergone surgery, and 2 of the 4 cases treated with LEN could have undergone surgery. Pathologic complete response was achieved in 2 of 6 patients who could undergo surgery after receiving ATBV in borderline resectable and in 2 of 6 receiving LEN in borderline resectable.

Conclusion: Conversion surgery after ATBE or LEN might be the option for treating borderline resectable HCC.

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Management of MASLD-Related Comorbidities

The FDA has approved resmetirom (a thyroid β receptor agonist) and semaglutide (a GLP-1 receptor agonist) as targeted therapies for MASH, based on international phase 3 trials. In addition, optimal management of type 2 diabetes (T2D) and dyslipidemia, as comorbidities associated with MASLD, is crucial to prevent fibrosis progression and to improve both overall and liver-related mortality. We conducted the LEAD study and the PORTRAIT study to address MASLD with T2D and hypertriglyceridemia, respectively. The LEAD study evaluated the efficacy of the SGLT2 inhibitor luseogliflozin in MASLD patients with T2D. A total of 39 patients with NAFLD were enrolled and treated with luseogliflozin for 24 weeks, with serial monitoring of clinical and biochemical parameters. Hepatic fat fraction was quantitatively measured using MRI, while metabolic indices were assessed by fasting blood glucose, HbA1c, and BMI, in addition to liver function tests (AST, ALT, and γ-GTP). After 24 weeks, MRI-derived hepatic fat fraction decreased significantly from 21.46% (±7.17) to 15.66% (±6.82) ($p<0.001$). AST, ALT, and γ-GTP levels were all significantly reduced ($p<0.01$–0.001). HbA1c, fasting glucose, and BMI also improved. These findings demonstrate that luseogliflozin effectively reduces hepatic steatosis and improves biochemical markers in MASLD patients, supporting its potential as a therapeutic strategy. The PORTRAIT trial investigated treatments for MASLD with hypertriglyceridemia, comparing pemafibrate (a selective PPARα modulator) with omega-3-acid ethyl ester in a randomized, controlled, multicenter trial. Eighty patients with MASLD and hypertriglyceridemia were enrolled and randomized. At week 24, the adjusted mean change in ALT was significantly greater in the pemafibrate group (-19.7±5.9 U/L) compared with the omega-3-acid ethyl ester group (+6.8±5.5 U/L), yielding an intergroup difference of -26.5 U/L (95% CI: -42.3 to -10.7; $p=0.001$). Pemafibrate also significantly improved other hepatic enzymes (AST, γ-GTP), lipid parameters (triglycerides, total cholesterol, HDL-C, and non-HDL-C), as well as the fibrosis marker Mac-2 binding protein glycan isomer. These results demonstrate that pemafibrate was superior to omega-3-acid ethyl ester in improving liver enzymes, lipid profiles, and fibrosis markers, offering new evidence for MASLD treatment. In conclusion, both SGLT2 inhibitors and pemafibrate represent promising therapeutic options for MASLD, with potential to improve hepatic, metabolic, and fibrotic outcomes.

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Metabolic Dysfunction-Associated Steatotic Liver Disease as a Cardiovascular Risk Equivalent

The causal relationship between metabolic dysfunction-associated steatotic liver disease (MASLD) and cardiovascular disease (CVD) remains an area of active scientific debate. Epidemiological studies have consistently demonstrated an increased prevalence of CVD in patients with MASLD; however, determining causality requires careful analysis beyond mere associations. This presentation explores the causal relationship between MASLD and cardiovascular disease (CVD), synthesizing recent evidence from large-scale genetic and epidemiological studies. Key mechanisms linking MASLD to CVD—including insulin resistance, inflammation, oxidative stress, lipotoxicity, endothelial dysfunction, and gut microbiota alterations—are explored in depth. Additionally, genetic insights from Mendelian randomization studies provide perspective on potential causal pathways. Clinical evidence from cohort studies and meta-analyses suggests a gradient relationship between MASLD severity and CVD risk, but confounding factors and reverse causation remain important considerations. Two distinct MASLD subtypes were identified through data-driven clustering: i) liver-specific type and ii) cardiometabolic type. Genetic studies reveal variants like PNPLA3 rs738409 that increase liver disease risk but may protect against CVD, suggesting a complex causal relationship. Partitioned polygenic risk scores (pPRS) also demonstrate differential associations: i) liver-specific pPRS and ii) systemic pPRS. Transcriptomic and metabolomic analyses support distinct biological profiles for these MASLD subtypes. Long-term follow-up data from the UK Biobank confirm divergent clinical trajectories for the identified MASLD types. These findings challenge the notion of a simple causal relationship between MASLD and CVD, highlighting the disease's heterogeneity and the need for personalized risk assessment and management strategies. The identification of distinct MASLD subtypes with different underlying biology and clinical outcomes suggests potential for tailored therapeutic approaches and more precise prognostication. Ultimately, while compelling data support a significant association between MASLD and increased cardiovascular risk, definitive evidence establishing direct causality remains elusive. Further prospective studies and randomized controlled trials are imperative to clarify this complex relationship and inform targeted clinical interventions.

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Predicting HCC Risk in MASLD Using NILDA and Clinical Background Factors

Metabolic dysfunction-associated steatotic liver disease (MASLD) is now the most common chronic liver disease worldwide, and it represents a systemic disorder in which not only liver-related complications but also cardiovascular disease and extrahepatic malignancies constitute the leading causes of death. Patients with MASLD frequently present with comorbidities such as type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, and chronic kidney disease, which significantly influence both hepatic and extrahepatic outcomes. In our long-term cohort of biopsy-proven MASLD, the cumulative incidence of hepatocellular carcinoma (HCC) was 4.5 per 1,000 person-years, and patients with T2DM had a significantly higher incidence of HCC compared with those without diabetes. Multivariate Cox proportional hazards analysis revealed that T2DM and elevated fibrosis-4 (FIB-4) index (≥2.6) were independent predictors of HCC development. Moreover, low platelet counts, low serum albumin, and elevated levels of type IV collagen 7S and M2BPGi were also strongly associated with increased carcinogenic risk.

These findings highlight the importance of incorporating non-invasive liver disease assessment (NILDA) tools into routine clinical practice for MASLD. FIB-4 is a simple and cost-effective first-line screening tool, while type IV collagen 7S, M2BPGi, and magnetic resonance elastography (MRE) provide more precise second-line assessments. A two-step NILDA strategy allows efficient identification of high-risk patients and minimizes the need for liver biopsy. Patients with T2DM, thrombocytopenia, hypoalbuminemia, or elevated fibrosis markers represent a subgroup with markedly higher HCC risk and therefore require intensive surveillance and timely intervention.

In conclusion, MASLD should be regarded as both a hepatic and systemic disease in which HCC risk is shaped by the interaction of metabolic comorbidities and fibrosis progression. NILDA-based stratification, combined with careful assessment of diabetes status, platelet count, serum albumin, and type IV collagen 7S, offers an evidence-based approach to identify patients at greatest risk. Integration of these non-invasive biomarkers into daily practice can optimize surveillance strategies and improve long-term outcomes in MASLD.

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Screening Strategies for High-Risk MASLD Populations in Health Check-Up Programs

Most liver society guidelines recommend evaluating hepatic fibrosis in individuals at risk — those with one or more metabolic risk factors such as obesity with additional metabolic abnormalities, elevated liver enzymes, or type 2 diabetes. However, current guidelines generally do not recommend screening for MASLD (Metabolic dysfunction-associated steatotic liver disease) in the general population.

In some Asian countries, however, health check-up systems are widely implemented, providing a unique opportunity for early detection. Given the high prevalence of MASLD in the general population, an effective screening algorithm within these health check-up programs is crucial for timely intervention and disease control.

The FIB-4 index is currently the most widely used tool for identifying high-risk individuals, but it was developed in populations with a higher hepatic fibrosis burden. Therefore, its sensitivity and positive predictive value (PPV) in general population settings or within health check-up programs remain uncertain.

This presentation will discuss the need for and development of an effective screening algorithm tailored to high-risk groups within a health check-up setting, where the overall hepatic fibrosis burden is relatively low.

Currently, most liver societies recommend screening algorithms for identifying high-risk groups for MASLD using more than one non-invasive test (NIT). Among these, the initial screening step is typically based on blood test–derived NITs. Several first-line blood-based NITs have been proposed, including the FIB-4 index, NAFLD Fibrosis Score (NFS), SAFE score, Liver Risk Score, and MAF-5. These tools vary in complexity, required variables, and performance metrics such as sensitivity, specificity, and predictive value.

In this presentation, we will explore in detail the advantages and limitations of these blood test–based NITs within the context of health check-up systems. We will evaluate their applicability, practicality, and performance in populations with a relatively low hepatic fibrosis burden, and discuss how they may be optimized or integrated into a more effective screening algorithm for MASLD in the general population.

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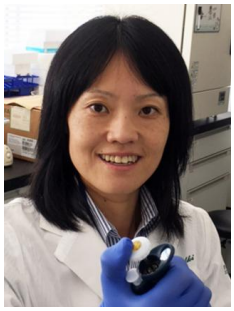
Non-Invasive Testing Strategies for Managing MASLD on Patient Referral

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a prevalent condition; its progression to steatohepatitis and fibrosis increases the risk of cirrhosis and hepatocellular carcinoma. With the increasing number of patients with MASLD, determining which individuals should be referred to hepatologists is crucial. Liver biopsy, the traditional gold standard, has limitations, including invasiveness and sampling errors. Non-invasive tests (NITs), including blood biomarkers and imaging techniques, have emerged as accurate tools for assessing liver fibrosis. This review summarizes expert opinions on the appropriate use of NITs by primary care physicians for MASLD patient referral, focusing on Japanese evidence. This presentation will provide an overview of the FIB-4 index, liver fibrosis markers (ELF test, M2BPGi, and type IV collagen 7S), a hepatocyte apoptosis marker (cytokeratin-18 fragment), and imaging diagnosis (ultrasound elastography and magnetic resonance elastography). In this presentation, we propose guidance to improve clinical practice by utilizing the NIT to identify patients with MASLD who require referral to a hepatologist.



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Exploring Biomarkers for the Diagnosis of SLD-Related Complication

Autopsy brains of patients with hepatic encephalopathy (HE) exhibit glial cell swelling and degeneration. However, these cerebral changes cannot be solely attributed to hyperammonemia or a leaky gut, suggesting the involvement of novel disease mediators. We previously reported that extracellular vesicles from damaged hepatocytes (HC-EVs) act as communicators, contributing to disease progression within the liver. Therefore, this study aimed to investigate whether HC-EVs are involved in glial cell changes and reflect the pathology of HE.

We examined glial cell abnormalities in the brains of metabolic dysfunction-associated steatotic liver disease (MASH) model mice using gene expression analysis and histological staining. In the brains of MASH mice, the glial cell activation markers Ionized calcium-binding adaptor molecule 1 (Iba1) and Glial fibrillary acidic protein (GFAP) were elevated, along with increased Monocyte chemotactic protein 1 (MCP1) and Interleukin 1 beta (IL-1b). Imaging analysis confirmed that a portion of fluorescently labeled HC-EVs from MASH mice were transmitted to glial cells. Furthermore, we investigated the introduction of HC-EVs into glial cells and subsequent intracellular changes ex vivo. We found that HC-EVs induced an increase in Iba1, MCP-1, and IL-1b, similar to observations in the brains of MASH mice. Comprehensive analysis of HC-EV-miRs revealed a significant increase in the let-7 family in MASH-HC-EVs, which contributes to glial activation. In human subjects, we comprehensively detected and compared circulating EV-miRs in patients with no HE, covert HE (diagnosed by Stroop test), and overt HE, as well as before and after rifaximin treatment. The let-7 family was also among the circulating EV-miRs that significantly increased with the exacerbation of HE. Furthermore, we identified EV-miRs that decreased following treatment and normalization of the Stroop test.

Our findings suggest that HC-EVs act as inter-organ disease communicators, participating in the development of brain damage associated with chronic liver disease. They are indicated to be novel disease mediators that could also serve as biomarkers.

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The Effectiveness of %CDT and γ GT-CDT in the Diagnosis of MetALD and ALD

Background and Aim: A new concept of fatty liver disease, including metabolic dysfunction-associated steatotic liver disease (MASLD) and MASLD and increased alcohol intake (MetALD) has been proposed, clarifying the previous definition of the intermediate alcohol drinker group. Carbohydrate-deficient transferrin (CDT)/ total transferrin ratio (%CDT) and γGT-CDT are known markers of alcohol consumption. We evaluated the utility of %CDT and γGT -CDT in assessing alcohol intake among patients with MASLD, MetALD, and ALD.

Methods: A total of 120 SLD patients who visited our department between 2018 and 2024 were classified into the MASLD group, MetALD group, ALD group, and cryptogenic SLD group. The usefulness of %CDT and γGT-CDT in distinguishing between the groups was compared with the conventional drinking markers, γGT and MCV.

Results: The MASLD, MetALD, ALD, and cryptogenic SLD groups consisted of 67, 31, 18, and 4 patients, respectively. The optimal cut-off value to identify MASLD was 1.78% for %CDT, with a sensitivity of 77.6%, specificity of 71.6%, and AUROC of 0.79, which was comparable to the AUROC of 0.80 for γGT-CDT. %CDT and γGT-CDT have been shown to have higher diagnostic abilities compared to MCV with an AUROC of 0.71 and γGT with an AUROC of 0.74. In contrast, when distinguishing between MetALD and ALD, optimal cut-off value to identify ALD was 5.00 for γGT-CDT with a sensitivity of 72.2%, specificity of 79.6%, and an AUROC of 0.76, which was superior to the AUROC of 0.68 for %CDT.

Conclusions: In distinguishing MASLD from MetALD, %CDT and γGT-CDT demonstrated comparable diagnostic utility, and both outperformed γGT and MCV. Conversely, in differentiating MetALD from ALD, γGT-CDT showed greater diagnostic value than %CDT. Although %CDT is a more reliable marker of alcohol intake than γGT or MCV, the sensitivity for detecting heavy drinking can be further enhanced by incorporating γGT-CDT.

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Translational Research in Cirrhosis

In Japan, due to the effectiveness of DAA therapy, cirrhosis caused by HCV has decreased, while cirrhosis caused by alcohol and MASH has increased, and this trend is expected to become even more obvious in the future.

Based on the course of DAA treatment, the liver has the natural ability to improve fibrosis and promote regeneration even in cases of cirrhosis. In terms of fibrosis improvement and regenerative therapy for cirrhosis, the University of Edinburgh is currently leading the field globally with its autologous macrophage therapy, but various other approaches are also being explored.

We have been developing and conducting clinical trials on treatments using mesenchymal stromal cells (MSCs), treatments using their extracellular vesicles (EVs), and treatments using peptides, and in this presentation, I would like to introduce the current status of these studies.

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Adverse Reactions in Lenvatinib Treatment for Hepatocellular Carcinoma Focusing on Carnitine Changes including the Potential of L-carnitine Supplementation

Background and Aims: During lenvatinib (LEN) treatment for hepatocellular carcinoma, the development of fatigue and progression of sarcopenia prevents long-term continuation of treatment, and carnitine deficiency has been reported to be a contributing factor. Carnitine deficiency induces fatigue by reducing ATP production. In addition, most carnitine stores are intracellular, especially in the mitochondria of skeletal muscles. Therefore, we conducted basic and clinical studies on the relationship between fatigue, muscle injury, and changes in carnitine during LEN administration.
Methods: Male Wistar rats were treated for two weeks with LEN, LEN + low-dose L-carnitine (L-CA), or LEN + high-dose L-CA, and the amount of carnitine in skeletal muscle, carnitine-related proteins within mitochondria including carnitine palmitoyltransferase I (CPT I), carnitine palmitoyltransferase II (CPT II), carnitine/acylcarnitine translocase (CACT) and oxidative phosphorylation (OXPHOS) proteins were measured. In addition, LEN was added to C2C12 myotubes and cultured for 24 h. Tube formation analysis was conducted using human umbilical vein endothelial cells (HUVEC), and aortic ring assays were performed in C57BL/6 mice. In a clinical study, serum total carnitine and free carnitine levels in the plasma and creatine kinase (CK) and aldolase (ALD) levels were measured in 85 patients with hepatocellular carcinoma receiving LEN. Fatigue was assessed using the Brief Fatigue Inventory (BFI).
Results: Although LEN significantly decreased carnitine levels in the skeletal muscle, this reduction was suppressed by both low- and high-dose L-carnitine supplementation. LEN administration significantly suppressed the protein expression of CPT I, CPT II, and CACT; however, supplementation with L-carnitine dose-dependently suppressed this decrease. LEN reduced mitochondrial protein synthesis in C2C12 myotube cells; however, this reduction was suppressed by L-CA supplementation in a dose-dependent manner. Furthermore, during LEN treatment, the blood acylcarnitine/free carnitine (AC/FC) ratio at baseline and weeks 2, 4, and 6 was significantly increased compared to baseline values ($p<0.001$, $p=0.009$, $p=0.001$, respectively). Both CK and ALD levels significantly increased at weeks 2, 4, and 6 compared to baseline values. There was a significant positive correlation between AC/FC and CK values at week 4 ($r=0.417$, $p=0.048$). In addition, BFI significantly correlated with AC/FC at week 4 ($r=0.442$, $p=0.004$).
Conclusions: LEN directly induces mitochondrial dysfunction in skeletal muscles, leading to carnitine deficiency. Furthermore, fatigue and muscle toxicity can be regarded as carnitine deficiency-related adverse reactions.

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Single-cell Proteomics and Spatial Proteomics Revealing Creative Pathogenesis of Metabolic Dysfunction-Associated Steatotic Liver Disease

Background: The MASLD prevalence has attracted attention recently, which leads to MASH, fibrosis, and cirrhosis. Currently, there are no effective treatments. Therfore, advancements in proteomics and spatial proteomics on specialized single-cell, present promising opportunities for exploring MASLD creatively mechanisms.

Method: We collected liver tissue samples from patients undergoing surgery. To characterize cellular microenvironment within MASLD , we employed Time-of-Flight Flow Cytometry (CyTOF) and Imaging Mass Cytometry (IMC) together to delineate special resolved-cells and their spatially functional-characteristics with in-vitro cellular experiments validation.

Results: Initially, CyTOF was utilited to delineate celltypes in MASLD, where it revealed notable increase of M2 macrophages in MASLD. Meanwhile, significant elevation of phosphorylation expression was detected in myeloid-cells in MASLD. Therefore, focused on MASLD myeloid-cells and phosphorylation, proteomic and phosphoproteomic were carried out, where in MASLD myeloid-cells metabolic inhibition, inflammation, immune disorder, and cell-adhesion decrease were core biological function. Based on omics, to further investigate spatial function of MASLD myeloid-cells, IMC was taken to succeed identifing M2 macrophages negative for AGXT2 and PYCR3. The infiltration proportion of inflammatory cells and Ki67 in proximity to such M2 macrophages were significantly elevated. Moreover, it indicated close spatial association between fibroblasts or myofibroblasts with such M2 macrophages. Eventually, in vitro cellular experiments with siRNA were carried out ,where it revealed that macrophages with simultaneous knockdown for AGXT2 and PYCR3 demonestrated significant elevation of inflammatory and fibrotic phenotypes.

Conclusion: We effectively identified macorphages M2 negative for AGXT2 and PYCR3, showing strong trend for inflammation and fibrosis, could be potential treatment tagret for MASLD.

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Metabolic Inflammation in MASLD Drives Memory CD8+T Cell Differentiation by Downregulating Lnk/Sh2b3, Thereby Activating the IL-15-Jak-STAT Pathway and Exacerbating Hepatic Inflammation and Fibrosis

Background: Hepatic steatosis and inflammation play a central role in driving fibrosis and disease progression in metabolic dysfunction-associated steatotic liver disease (MASLD). Lnk/Sh2b3 is a negative regulator of the IL-15-Jak-STAT pathway. MASLD patients exhibit missense mutations in the Lnk gene. We investigated the role of Lnk in regulating immune responses associated with hepatic inflammation in MASLD.
Methods: We analyzed Lnk expression in hepatic immune cells using human liver samples and MASLD mouse models fed a high-fat/high-cholesterol (HF/HCD) diet. To evaluate the role of Lnk in MASLD pathogenesis, we used Lnk-deficient (Lnk KO) mice and bone marrow chimeras with immune cell-specific deletion of Lnk. CD8+T cell phenotypes, cytotoxic activity, and IL-15-Jak-STAT pathway activation were assessed by flow cytometry.
Results: Lnk expression was reduced in hepatic CD8+T cells in both MASLD patients and mouse models. IL-15 expression was elevated in the livers of MASLD models. Lnk KO mice fed an HF/HCD diet exhibited exacerbated liver steatosis, inflammation, and fibrosis, along with expansion of hepatic CD8+T cells. Similar findings were observed in immune cell-specific Lnk KO mice, confirming the immune cell-intrinsic role of Lnk. Lnk deficiency enhanced IL-15 responsiveness, promoting effector memory CD8+T cell differentiation and increased cytotoxic activity via the NKG2D-Mult1 pathway. Suppression of IL-15 signaling mitigated MASLD exacerbation in Lnk-deficient mice. Jak inhibition reduced hepatic CD8+T cell accumulation and prevented MASLD progression.
Conclusion: Lnk suppresses IL-15-Jak-STAT signaling in CD8+T cells and acts as a negative regulator of hepatic inflammation and fibrosis in MASLD.

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Why does the Microbiome Produce Alcohol in Patients with Auto-Brewery Syndrome?

Auto-brewery syndrome (ABS) is an uncommon disorder in which gut microbes generate enough ethanol to cause recurrent intoxication. The underlying microbial and metabolic features of ABS have not been well characterized beyond isolated case descriptions. To address this gap, we carried out a prospective study enrolling 22 individuals with ABS, 21 household partners without symptoms, and 22 healthy controls. All participants underwent clinical evaluation, and stool samples were analyzed by shotgun metagenomic sequencing to profile microbial composition and function. Using an in vitro culture system, we demonstrated that microbiota from ABS patients produced ethanol and could accurately separate patient samples from those of unaffected partners. Microbial communities in ABS were enriched for genes encoding ethanol-generating pathways, including mixed acid fermentation, heterolactic fermentation, and ethanolamine utilization. In one patient, fecal microbiota transplantation normalized gut microbial function and coincided with clinical improvement. This represents the largest ABS cohort reported to date and provides evidence that therapeutic strategies aimed at reducing gut microbial ethanol production should be explored in clinical trials for ABS and possibly in other alcohol-related conditions.

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Gut Microbial Therapy in Advanced Chronic Liver Disease

Advanced chronic liver disease (ACLD), encompassing severe liver fibrosis to cirrhosis and its complications, is increasingly recognized as a systemic condition influenced by gut-liver axis disruption. The gut microbiota plays a pivotal role in modulating hepatic inflammation, fibrosis, and portal hypertension. Emerging microbial therapies offer promising avenues for intervention.

Recent studies highlight the therapeutic potential of targeting gut dysbiosis in cirrhosis. Rifaximin-α has demonstrated efficacy in reducing liver fibrosis in alcohol-related liver disease, while active vitamin D3 improves intestinal barrier integrity and attenuates bacterial translocation in cirrhotic models. Innovative approaches such as bacteriophage therapy targeting cytolytic Enterococcus faecalis and transgene delivery via native E. coli have shown promise in preclinical settings.

Fecal microbiota transplantation (FMT) has gained traction across various liver disease contexts. In cirrhosis, FMT improves hepatic encephalopathy, restores antibiotic-associated dysbiosis, and enhances short-chain fatty acid and bile acid profiles. Notably, FMT reduces alcohol craving and consumption, with favorable microbial shifts and fewer alcohol use disorder-related events. Furthermore, FMT has been associated with improved outcomes in acute-on-chronic liver failure and reduced portal pressure in animal models.

Microbial signatures also correlate with disease severity. Sarcopenia-related depletion of Ruminococcus 2 and Anaerostipes is linked to increased complications. Bacteroides species, enriched post-FMT, have shown efficacy in reducing portal pressure and enhancing gut barrier function in cirrhotic rats, suggesting their potential as targeted therapeutics.

Collectively, these findings underscore the gut-liver axis as a critical therapeutic target in ACLD. Microbiota-based interventions, particularly FMT and selective microbial modulation, represent a frontier in personalized hepatology, with implications for disease modification and improved clinical outcomes.

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Is There any Role of Gut Microbiome in Fatty Liver Pathogenesis and Treatment?

Metabolic Dysfunction Associated Fatty Liver Disease (MAFLD) has emerged as the most prevalent chronic liver disorder worldwide, ranging from simple steatosis to metabolic dysfunction associated steatohepatitis (MASH), cirrhosis, and hepatocellular carcinoma. Despite its growing burden, the exact mechanisms driving MAFLD pathogenesis remain incompletely understood, and effective targeted therapies are limited. Increasing evidence points toward the gut microbiome as a central contributor to both the initiation and progression of fatty liver disease.

Gut dysbiosis alters intestinal barrier function, bile acid metabolism, and immune responses, thereby promoting hepatic steatosis and inflammation. Specific microbial metabolites—including short-chain fatty acids (SCFAs), bile acids, lipopolysaccharides (LPS), choline derivatives, and trimethylamine-N-oxide (TMAO)—have been implicated in modulating host lipid metabolism, insulin resistance, and immune activation. For instance, butyrate enhances intestinal barrier integrity and suppresses hepatic lipogenesis, while excessive LPS translocation activates Toll-like receptor (TLR)-mediated inflammatory cascades, leading to hepatocellular injury. Moreover, disruption of bile acid signaling via farnesoid X receptor (FXR) and Takeda G-protein receptor 5 (TGR5) contributes to steatosis and metabolic dysfunction, highlighting microbiota-mediated bile acid signaling as a therapeutic target.

Parallel evidence suggests that gut-derived endogenous alcohol production may mimic the pathogenic effects of ethanol in MASH. Human studies demonstrate increased expression of alcohol dehydrogenase and aldehyde dehydrogenase pathways in NASH livers, suggesting elevated exposure to microbiota-derived ethanol. This mechanism may partly explain the histological resemblance between MASH and alcoholic steatohepatitis (ASH). High-alcohol–producing strains of Klebsiella pneumoniae and Escherichia coli have been isolated from MAFLD patients, and experimental transplantation of such strains into mice induced fatty liver changes, strengthening the causative link between microbial ethanol and liver pathology.

Beyond pathogenesis, the gut microbiota is being explored as a diagnostic and therapeutic tool. Distinct microbial signatures have been associated with MAFLD severity and fibrosis stage, suggesting potential biomarker roles. Therapeutically, modulation of gut microbiota through probiotics, prebiotics, synbiotics, antibiotics, and fecal microbiota transplantation (FMT) has shown promise in reshaping dysbiotic communities, reducing endotoxemia, and improving metabolic parameters. In clinical studies, FMT from healthy donors improved liver fat content and survival in advanced liver disease, though patient compliance remains challenging. Meanwhile, probiotics such as Lactobacillus and Bifidobacterium have demonstrated partial benefits in metabolic regulation, while phage therapy targeting high-alcohol–producing bacteria is emerging as a novel precision approach. Furthermore, synthetic agonists of FXR and TGR5 are under clinical investigation, aiming to restore bile acid homeostasis and attenuate hepatic inflammation.

In conclusion, the gut microbiome plays a pivotal role in MAFLD pathogenesis via mechanisms involving microbial metabolites, ethanol production, bile acid dysregulation, and immune modulation. Therapeutic strategies targeting gut-liver axis offer novel avenues for prevention and treatment. However, variability in microbiome profiles across populations underscores the need for personalized, microbiota-based interventions. Continued integration of multi-omics profiling, microbial biomarkers, and microbiome-targeted therapies holds promise for advancing both diagnosis and management of fatty liver disease.

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China

Gut Barrier and Immunotherapy

Immune checkpoint inhibitors (ICIs), such as anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and anti-programmed cell death protein 1 (PD-1), have revolutionized cancer treatment and significantly improved survival rates. However, ICIs can lead to immune-related adverse events, notably colitis. Our prior work highlighted the essential role of myosin light chain kinase (MLCK) mediated gut leak pathway as a driver of inflammatory bowel disease. Here, we aim to explore the tight junction related gut barrier's function in ICIs colitis and find ways to adjuvant therapy for tumors. Initially, staining in human samples with colitis induced by anti-PD1 antibodies revealed reduced expression of tight junction proteins ZO-1 and occludin and increased MLCK expression and activation. Analysis of a novel mouse model of anti-CTLA4 and anti-PD-1-induced ICIs colitis led to reduced ZO-1 and occludin expression and increased MLCK expression. ICIs colitis is alleviated in MLCK knockout mice but exacerbated in MLCK overexpressing mice. Further analysis found that ICIs increased intestinal bacterial s_Duncaniella_sp_C9 and decreased the associated metabolites Luffariellolide and 13,14-Dihydro-15-keto-PGE2 in MLCK knockout mice, but decreased s_Duncaniella_sp_C9 and increased Luffariellolide and 13,14-Dihydro-15-keto-PGE2 in MLCK overexpressing mice. In addition, Luffariellolide and 13,14-Dihydro-15-keto-PGE2 led to reduced ZO-1 and occludin expression and increased MLCK expression in intestinal organoids and caco-2 cells. Finally, tacrolimus, a calcineurin inhibitor that inhibits MLCK recruitment to tight junctions and reverses inflammation-induced barrier loss, enhanced intestinal barrier function and improved tumor immunotherapy effectiveness. These data suggest that MLCK-mediated leak pathway impact ICIs efficacy and tumorigenesis, barrier restoration may provide an approach to ICIs colitis therapy.

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Sponsored Seminars

Luncheon Seminar 1 (Gilead Sciences K.K.)

Dr. Jia-Horng Kao
Chair Professor,
Graduate Institute of Clinical Medicine,
National Taiwan University College of Medicine.
Taiwan

Real-World Evidence of Sofosbuvir/Velpatasvir and Post-SVR Strategies for HCC Risk Reduction

The introduction of direct-acting antivirals (DAAs) has revolutionized the treatment of chronic hepatitis C virus (HCV) infection, turning it into a curable condition. Among these, Sofosbuvir/Velpatasvir (SOF/VEL) has shown consistently high sustained virological response (SVR) rates across a wide range of patient populations. This presentation reviews real-world evidence supporting the effectiveness of SOF/VEL and examines strategies for post-SVR monitoring aimed at minimizing long-term complications, especially hepatocellular carcinoma (HCC).

Real-world data from global cohorts reinforce the strong efficacy and safety profile of SOF/VEL, closely aligning with clinical trial results. SVR rates exceed 95% in both treatment-naïve and treatment-experienced patients, including those with compensated cirrhosis.

Importantly, while achieving SVR significantly lowers the risk of HCC, it does not eliminate it. The stage of liver fibrosis remains a key predictor of long-term outcomes. In addition, our recent study indicated that HCV patients with metabolic dysfunction-associated steatotic liver disease (MASLD) exhibited an increased HCC risk compared to those without MASLD. Current clinical guidelines recommend continued HCC surveillance for patients with advanced fibrosis or cirrhosis; however, adherence to these surveillance protocols varies widely in real-world settings. Recent studies reveal substantial gaps in follow-up care, which may lead to delayed HCC diagnosis and worse prognoses.

Emerging tools for risk stratification—such as non-invasive fibrosis assessments and clinical scoring systems—offer promising avenues for tailoring post-SVR monitoring. This presentation aims to equip clinicians with practical insights for incorporating real-world evidence into clinical practice, ensuring that patients who achieve SVR with SOF/VEL receive ongoing, risk-adjusted care. Special focus will be given to identifying patients at highest risk, refining surveillance approaches, and addressing challenges in implementing guidelines to ultimately reduce HCC incidence and enhance long-term patient outcomes in the post-SVR setting.

Luncheon Seminar 1 (Gilead Sciences K.K.)

Dr. Hayato Nakagawa
Professor and Chairman,
Department of Gastroenterology and Hepatology,
Mie University
Japan

From HCV to SLD: Cutting-edge Research in Liver Disease

The development of direct-acting antivirals (DAAs) has greatly improved the management of hepatitis C virus (HCV). However, many individuals are still believed to remain untreated, highlighting the continued importance of public awareness and case-finding efforts to achieve complete elimination of HCV. In this talk, I will share our ongoing efforts to address these challenges, as well as strategies for appropriate follow-up after HCV eradication.

At the same time, the focus of liver disease is shifting toward steatotic liver disease (SLD). We are currently conducting research aimed at developing personalized approaches to this increasingly important condition. By combining multi-omics analysis with artificial intelligence, we are trying to identify new high-risk groups for HCC development and to better understand the disease mechanisms involved. I will present some of our recent findings in this emerging field.

Luncheon Seminar 2 (Boehringer Ingelheim)

Dr. Kanji Yamaguchi
Associate Professor,
Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine
Japan

MASLD Pathogenesis: Focus on Cellular Stress Responses

The pathogenesis of MASLD is explained by the "multiple-hit hypothesis," which supersedes the previously simplified "two-hit model." This hypothesis proposes that disease progression is driven by the integration of multiple metabolic, genetic, epigenetic, and environmental factors. According to previous studies, MASLD develops when intrahepatic fat accumulation exceeds 5% of liver weight, leading to metabolic disturbances such as alterations in fatty acid oxidation pathways, dysregulation of reactive oxygen species (ROS) signaling, mitochondrial dysfunction, impaired proteostasis, and imbalances in the gut microbiota.

Furthermore, numerous studies have investigated the specific mechanisms underlying the progression from MASLD/MASH to hepatocellular carcinoma (HCC). This process involves various contributing factors, including oxidative stress, lipotoxicity, gut dysbiosis, metabolic imbalance, chronic injury, and hypoxia. These factors are believed to promote chronic inflammation, tissue fibrosis, and ultimately the development of HCC.

To date, we have focused on cellular stress responses and have reported several studies on hepatokines such as FGF21 and GDF15, as well as on molecular chaperones. Additionally, we have investigated the impact of genetic background on the pathogenesis of MASLD through clinical studies. Given the multifaceted pathophysiology of MASLD, it is important to understand the stage-specific and individualized pathophysiology, including the consideration of extrahepatic manifestations.

Luncheon Seminar 2 (Boehringer Ingelheim)

Dr. Hirokazu Takahashi
Division of Metabolism Diabetes and Endocrinology,
Faculty of Medicine, Saga University
Japan

MASLD as a Condition Necessitating Decisions on the Management and Risk Reduction of Lifestyle-Related Diseases

Obesity, diabetes, dyslipidemia, and hypertension are major interrelated risk factors in the development and progression of metabolic dysfunction-associated steatotic liver disease (MASLD). Obesity, particularly with visceral adiposity, is highly prevalent among MASLD patients and contributes to hepatic steatosis through increased free fatty acid flux and subsequent chronic inflammation and insulin resistance. Diabetes, notably type 2 diabetes mellitus, shares a bidirectional relationship with MASLD; insulin resistance acts as a central mechanism, amplifying hepatic glucose and lipid production, which in turn leads to liver fat accumulation and inflammation. Dyslipidemia, characterized by elevated triglycerides, low HDL cholesterol, and high LDL cholesterol, is present in the majority of MASLD cases and perpetuates a cycle of altered hepatic lipid metabolism, promoting both atherogenesis and hepatocellular damage. Hypertension frequently coexists with MASLD and is linked to more severe liver injury, largely through mechanisms involving insulin resistance, systemic inflammation, and activation of the renin-angiotensin-aldosterone system. The synergistic interactions among these metabolic disorders, particularly through shared pathways such as chronic inflammation and dysregulated lipid and glucose metabolism, not only increase the risk of MASLD onset but also accelerate its progression to advanced liver disease and fibrosis. Effective prevention and management of these underlying metabolic risk factors are imperative for reducing the burden of MASLD and its associated hepatic and extrahepatic complications.

MASLD is increasingly recognized as a major risk factor for cardiovascular disease (CVD), a leading cause of morbidity and mortality globally. Emerging evidence underscores the substantial association between MASLD and the elevated risk of a range of CVD outcomes, including heart failure, atrial fibrillation, stroke, and overall cardiovascular mortality. Individuals with MASLD exhibit a markedly increased risk of CVD events, with studies highlighting a 66% higher risk of CVD and a 41% higher risk of ischemic stroke compared to those without MASLD. More severe forms of MASLD, such as advanced fibrosis or steatohepatitis, confer even greater cardiovascular risk, emphasizing the disease's severity-dependent impact on CVD outcomes. However, this positive correlation between CVD risk and hepatic severity remains unclear in Asian population. So far, guidelines and practice guidance recommend surveillance and risk reduction of CVD for all MASLD patients.

Luncheon Seminar 3 (AbbVie K.K.)

Dr. Eiichi Ogawa
Lecturer
Department of General Internal Medicine
Kyushu University Hospital, Fukuoka,
Japan

Current Landscape of HCV: Epidemiology, Treatment, and Long-Term Outcomes after HCV Cure

An estimated 50 million individuals worldwide are chronically infected with hepatitis C virus (HCV), with approximately 1 million new infections annually. Chronic hepatitis C (CHC), if untreated, leads to progressive liver disease, including cirrhosis and hepatocellular carcinoma (HCC), and is also associated with a range of extrahepatic manifestations that contribute to increased morbidity and mortality.

Since the advent of direct-acting antivirals (DAAs) in 2014, HCV therapy has undergone a transformative evolution, with sustained virologic response rates now exceeding 95% across nearly all patient populations. Current guidelines recommend prompt initiation of antiviral therapy for all patients with recently acquired or chronic HCV infection, regardless of treatment history or fibrosis stage. Despite this, by 2022, only 36% of individuals living with HCV had been diagnosed, and just 20% had received curative therapy, highlighting significant gaps in global care delivery.

Pangenotypic regimens -such as glecaprevir/pibrentasvir (GLE/PIB) for 8-12 weeks and sofosbuvir/velpatasvir (SOF/VEL) for 12 weeks- allow for simplified, genotype-independent treatment. Resistance testing is generally unnecessary prior to first-line DAA therapy. However, assessment of fibrosis severity remains critical, as protease inhibitor-based regimens are contraindicated in patients with decompensated cirrhosis. Genotype 3 patients with compensated cirrhosis may require intensified regimens including SOF/VEL plus ribavirin, SOF/VEL/voxilaprevir (VOX), or extended GLE/PIB. In patients with severe renal dysfunction, including those on dialysis, DAA therapy remains feasible and effective. For those who failed DAA therapy, resistance-associated substitutions- particularly NS5A P32 deletions- should guide retreatment strategy. In such cases, SOF/VEL/VOX or SOF/VEL plus ribavirin are recommended options.

HCC risk remains a clinical concern even after HCV cure, underscoring the importance of risk stratification tools for post-treatment surveillance. Although data on extrahepatic outcomes after HCV cure remain limited, accumulating evidence suggests that DAA therapy improves both hepatic and systemic health and may contribute to prolonged overall survival.

Luncheon Seminar 3 (AbbVie K.K.)

Dr. Takumi Kawaguchi
Professor and Chairman,
Division of Gastroenterology, Department of Medicine,
Kurume University School of Medicine
Japan

A New Era of Liver Care: MASLD and Post-SVR Outcomes

The redefinition of fatty liver disease from “NAFLD” to “MASLD” makes a significant paradigm shift in hepatology. This updated terminology more accurately reflects the underlying pathophysiology by emphasizing metabolic dysfunction and reduces stigma by replacing “fatty” with “steatotic.” MASLD is diagnosed based on the presence of hepatic steatosis and at least one metabolic risk factor. Multiple studies have demonstrated that patients with MASLD are clinically comparable to those with NAFLD. The adoption of MASLD enhances patient engagement, clarifies therapeutic targets, and aligns with current understanding of disease mechanisms. Currently, clinical trials investigating novel pharmacological agents targeting MASLD are progressing, indicating that a new era of drug-based therapy may be on the horizon.
This seminar also addresses hepatocarcinogenesis following sustained virological response (SVR) in patients with chronic hepatitis C virus (HCV) infection. MASLD confers a liver cancer risk comparable to elevated alpha-fetoprotein (AFP) levels. In a cohort of 1,280 HCV patients with ≥65 years old, SVR, and no prior history of hepatocellular carcinoma (HCC), the incidence of HCC reached 23.9% after 60-months follow-up among those with MASLD. Notably, a recent large-scale Japanese study revealed that over 80% of post-SVR deaths were due to extrahepatic causes, with digestive cancers being the most prevalent, followed by cardiovascular and cerebrovascular diseases. MASLD-related events accounted for more than 50% of these extrahepatic deaths.
Various studies have been conducted on sodium-glucose cotransporter 2 inhibitors (SGLT2i), exploring their potential associations. For example, some experimental studies have reported associations between cellular responses in liver and other cancer types and SGLT2i. Retrospective studies have shown potential association between cancer incidence and SGLT2i in diabetic patients. These findings are exploratory and further research is needed to better understand the clinical relevance of these observations.
This seminar highlights the evolving framework of MASLD, post-SVR cancer risks in patients with chronic hepatitis C, and the emerging therapeutic potential of SGLT2 inhibitors, offering new perspectives for integrated liver disease management and cancer prevention.

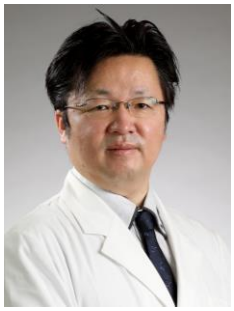
Luncheon Seminar 4 (Meiji Seika Pharma Co., Ltd.)

Dr. Masanori Atsukawa
Professor,
Division of Gastroenterology and Hepatology
Nippon Medical School Hospital
Japan

Validating the JSH Cirrhosis Guidelines from Real-world Clinical Data in Japan

Complications of liver cirrhosis are varied and strategies for diagnosis and treatment are described in the JSH guidelines. In this presentation, I would like to report the results of a validation of some of the complications such as ascites, varix, hepatic encephalopathy and portal vein thrombus described in the JSH cirrhosis guidelines using real clinical data in Japan.

Luncheon Seminar 4 (Meiji Seika Pharma Co., Ltd.)



Dr. Masahito Shimizu
Professor,
Department of Gastroenterology,
Gifu University Graduate School of Medicine
Japan

Nutritional Therapy for Cirrhosis
-Effects of BCAA on Prevention of Liver Failure-

Cirrhotic patients with reduced hepatic functional reserve are associated with several nutritional/metabolic disorders. In particular, protein-energy malnutrition (PEM) is strongly associated with poorer prognosis and quality of life (QOL) in cirrhotic patients. The progression of cirrhosis is often accompanied by abnormal glucose metabolism, including hyperinsulinemia, which contributes to the development of hepatocellular carcinoma (HCC). In addition, sarcopenia, a syndrome characterized by reduced skeletal muscle mass and strength often seen in cirrhotic patients, is predictive of patient prognosis and mortality. Therefore, it is important to assess the nutritional status and sarcopenia of patients with cirrhosis, and to provide nutritional therapy based on these findings, in order to improve their prognosis.

In cirrhosis, a decrease in branched-chain amino acids (BCAA) is commonly observed and is strongly associated with the onset of complications such as hepatic encephalopathy. BCAA supplementation in PEM increases serum albumin levels and improves QOL and survival in cirrhotic patients. BCAA supplementation is effective in improving hepatic encephalopathy. In particular, BCAA-enriched supplementation given as a late evening snack improves nutritional status and increases body protein content. Long-term administration of BCAA granules also improves event-free survival, serum albumin levels and QOL in cirrhotic patients. Evidence-based Japanese clinical practice guidelines for liver cirrhosis 2020 recommend that BCAA should be administered to cirrhotic patients with PEM.

BCAA plays an important role in maintaining and increasing skeletal muscle mass. Therefore, the decrease in BCAA in cirrhotic patients is closely related to the development of sarcopenia. In cirrhosis, the progression of PEM, the decrease in BCAA, the development of sarcopenia, and the onset of impaired glucose tolerance are observed as a series of pathological conditions. Japanese guidelines suggest that exercise and nutritional therapy as treatment for sarcopenia.

In addition to malnutrition, hypernutrition worsens the prognosis of cirrhotic patients. Obesity and diabetes increase the risk of HCC and liver cirrhosis, and metabolic dysfunction associated steatotohepatitis (MASH) associated with obesity and lifestyle diseases is also on the rise. Patients with diabetes and MASH are also prone to sarcopenia. Interestingly, BCAA supplementation has been reported to inhibit liver carcinogenesis in obese cirrhotic patients. BCAA may be a chemopreventive agent for HCC development, especially when the patients have metabolic disorders.

In conclusion, nutritional therapy using BCAA supplementation improves event-free survival, increases serum albumin levels, improves QOL and at least suppresses obesity-related HCC in patients with cirrhosis. BCAA is a key agent in the overall management of cirrhosis.

Teatime Seminar 1 (Novo Nordisk Pharma Ltd.)

Dr. Yoichi Hiasa
Professor,
Department of Gastroenterology and Metabology,
Ehime University Graduate School of Medicine,
Japan

Proposals for the Management of MASLD/MASH in Japan

In recent years, the prevalence of metabolic associated steatosis liver disease (MASLD) and metabolic dysfunction associated steatohepatitis (MASH) has increased significantly, and addressing these diseases has become an extremely important issue in preventing the progression to cirrhosis and reducing hepatocellular carcinoma. On the other hand, patients with MASLD/MASH often have comorbidities such as diabetes and obesity, necessitating an integrated approach that includes these areas to identify patients, screen for MASH, and implement dietary and exercise therapy for MASH patients not only by physicians but also through multidisciplinary collaboration. Hepatologists play a central role in this collaborative framework, working closely with general practitioners, diabetologists, obesity specialists, other endocrinologists, cardiologists and other healthcare professionals to ensure comprehensive management of the patient's overall health. To achieve this, it is essential to appropriately and effectively utilize non-invasive liver disease assessments (NILDA), and to accurate evaluation for hepatic functional reserve of MASH, as well as prognosis, and the risk of hepatocellular carcinoma.

This presentation will outline the collaborative care models led by hepatologists, as well as the interdepartmental collaboration involved in the management of MASLD/MASH in Japan. Because of the pathophysiological characteristics of MASLD/MASH, collaboration with registered dietitians is essential. We have already established a training program for "Certified Specialist of Registered Dietitian for Liver Diseases (CSRDLD)" in collaboration with the Japan Dietetic Association, the Japan Society for Metabolism and Clinical Nutrition, and the Japan Society of Hepatology. Providing appropriate "nutritional treatment as a therapy" to MASLD/MASH patients facilitate lifestyle modifications and support effective treatment strategies, which are expected to yield improvements in patient outcomes. These initiatives will be further explored in this presentation.

Teatime Seminar 1 (Novo Nordisk Pharma Ltd.)

Dr. Hideki Fujii
Lecturer, Department of Hepatology,
Graduate School of Medicine, Osaka Metropolitan University
Japan

Management of MASLD/MASH: Current Situation and Challenges

In recent years, the number of patients with Metabolic Associated Steatotic Liver Disease (MASLD) and its advanced form, Metabolic Associated Steatohepatitis (MASH), has been increasing globally, with similar trends observed in Japan. MASLD/MASH is closely linked to metabolic disorders such as obesity, diabetes, and hyperlipidemia, with lifestyle changes and Westernized diets identified as primary contributors. Research has demonstrated that the progression of MASLD/MASH significantly impacts patient prognosis and can lead to liver cirrhosis and hepatocellular carcinoma. Therefore, early diagnosis and prediction of disease progression are essential, along with rapid screening and appropriate treatment pathways to improve patient outcomes.

Regarding diagnosis, the evaluation of liver fibrosis is particularly important, as accurate assessment is crucial for determining treatment strategies and predicting long-term patient outcomes. However, liver biopsy, which has traditionally been regarded as the gold standard procedure, presents various challenges due to its costs and invasiveness. Consequently, a shift toward non-invasive diagnostic methods is urgently needed. Recent advancements in non-invasive testing methods, including blood tests and imaging techniques, have enabled better management of liver fibrosis. These approaches not only significantly reduce the burden on patients but also provide effective means for monitoring the progression of liver fibrosis.

This presentation will discuss the epidemiology and pathophysiology of MASLD/MASH in Japan, as well as the genetic factors involved in these conditions. Additionally, an overview of the diagnostic approaches for MASLD/MASH currently utilized in Japan will be provided.

Teatime Seminar 2 (AbbVie G.K.)

Dr. Nobuharu Tamaki
Deputy Director, Gastroenterology and Hepatology,
Musashino Red Cross Hospital, Tokyo,
Japan

Efficacy of HCV Treatment and Challenges in Disease Progression Following Viral Eradication

Chronic hepatitis C can now be effectively treated in nearly all patients with direct-acting antivirals (DAAs). In a cohort of 1,275 patients treated with glecaprevir/pibrentasvir, the sustained virologic response (SVR) rate was 99.1%. Genotype-specific analyses showed SVR rates ranging from 98% to 100% across all genotypes. Even among patients with FIB-4 index >3.25 who received only 8 weeks of treatment, the SVR rate was 100%. Achieving SVR with DAA therapy not only reduces liver-related complications but also lowers the risk of non-liver-related comorbidities, compared with untreated cases. Therefore, all patients with hepatitis C should be considered for treatment, and identifying untreated individuals and linking them to appropriate care is of critical importance.

While the risk of hepatocellular carcinoma (HCC) decreases after achieving SVR, it does not disappear entirely—particularly in older patients, or those with diabetes or hepatic steatosis. Careful management of comorbidities and continued follow-up of high-risk individuals remain essential to preventing post-SVR complications, especially HCC.

Teatime Seminar 2 (AbbVie G.K.)

Dr. Taro Yamashita
Professor,
Department of Gastroenterology
Kanazawa University School of Medicine
Kanazawa University Hospital
Japan

Prediction of Hepatocellular Carcinoma by Serum Biomarkers

Chronic liver diseases (CLDs) associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) infection are major causes of hepatocellular carcinoma (HCC), the most prevalent primary liver malignancy and the third leading cause of cancer-related death worldwide. Therefore, regular surveillance for HCC is recommended in patients with CLDs even after viral eradication, especially those with cirrhosis, to detect the tumors at an early stage when curative resections/ablations are available. In addition to the diagnostic imaging such as ultrasonography, computed tomography, and magnetic resonance images, the use of biomarkers is also recommended for HCC surveillance in those patients. Several serum biomarkers, including alpha-fetoprotein (AFP), AFP-L3, and des-gamma-carboxy prothrombin (DCP), have been proposed as potential tools for the early detection of HCC.

Here, we introduce the laminin γ2 monomer (LG2m) as a potential biomarker for HCC surveillance in chronic viral hepatitis patients. In our previous multicenter prospective cohort study, we demonstrated the utility of serum LG2m measurement for predicting HCC in chronic hepatitis C patients who achieved sustained virological responses after treatment with direct-acting antivirals. Recently, we also observed the clinical utility of LG2m as a biomarker for HCC surveillance in patients with chronic HBV infection in a retrospective study. We also summarize the currents status of our recent multicenter prospective cohort study including about 5,800 patients with HBV/HCV infection and/or steatotic liver diseases.

Evening Seminar (Miyarisan Pharmaceutical Co., Ltd.)

Dr. Takanori Kanai
Division of Gastroenterology and Hepatology,
Department of Internal Medicine, Keio University School of Medicine,
Japan

Harnessing the Liver-Brain-Gut Axis: A Novel Vagal Stimulation Strategy for Intestinal Treg Regulation

The gastrointestinal tract is constantly challenged by antigens derived from the microbiota and diet, requiring a delicate balance between immune activation and tolerance to maintain intestinal homeostasis. Among the key immune players in this balance are peripheral regulatory T cells (pTregs), which produce anti-inflammatory cytokines and prevent excessive immune activation. Impaired pTreg function may be closely linked to the development and progression of inflammatory bowel disease (IBD). Despite intensive efforts to therapeutically enhance pTregs, clinically applicable strategies remain limited. We recently identified a non-canonical neural circuit, a liver-brain-gut vagal pathway mediated by the hepatic branch of the left vagus nerve, that is essential for the maintenance of intestinal pTregs. Building upon this discovery, we developed a novel vagal hepatic nerve stimulation (VHNS) approach as a potential means of promoting intestinal immune tolerance in mice. Rather than focusing on the direct expansion of pTregs alone, VHNS appears to operate through a dual mechanism: it enhances the induction of intestinal pTregs peripherally while also engaging central neural circuits that influence stress responses. In particular, VHNS was found to activate specific brain regions, including the central nucleus of the amygdala (CeA), which has long been implicated in the regulation of emotional and stress-related behaviors. This observation suggests that psychological stress and immune tolerance in the gut may be more tightly interconnected than previously recognized. Strikingly, modulation of this amygdala circuit altered intestinal pTreg dynamics and influenced the susceptibility to colitis, underscoring the relevance of brain–gut communication in shaping intestinal immunity. Taken together, these findings highlight VHNS as a paradigm-shifting therapeutic strategy for IBD. By simultaneously targeting pTreg function and central stress-related neural circuits, this approach offers a novel framework for restoring immune homeostasis in the intestine. More broadly, the work underscores the therapeutic potential of modulating neuro–immune crosstalk to address chronic inflammatory diseases of the gut.

Evening Seminar (Miyarisan Pharmaceutical Co., Ltd.)

Dr. Bernd Schnabl
Professor of Medicine
Director, San Diego Digestive Diseases Research Center
University of California San Diego,
Department of Medicine
USA

Targeting Goblet Cell Pathways to Prevent Microbial Translocation and Alcohol-Associated Liver Disease

Alcohol use disorder (AUD) and alcohol-associated liver disease (ALD) remain significant global health burdens, representing leading causes of liver-related morbidity, mortality, and the need for transplantation. A growing body of evidence implicates the gut-liver axis as a key driver of ALD pathogenesis, with microbial translocation from the intestine to the liver serving as a critical trigger of hepatic inflammation and injury. However, the mechanisms regulating this translocation are not fully understood. We identified a novel mechanism by which chronic alcohol exposure impairs gut immune surveillance, contributing to ALD development. We demonstrate that intestinal goblet cells (GCs), which play an immunomodulatory role by forming goblet cell-associated antigen passages (GAPs), are functionally suppressed in the context of chronic alcohol consumption. GAP formation is normally initiated via activation of the muscarinic acetylcholine receptor M4 (mAChR4), which allows luminal antigen sampling by lamina propria antigen-presenting cells (LP-APCs). Using both human samples and murine models, we show that chronic ethanol exposure significantly reduces mAChR4 expression in the small intestine, resulting in diminished GAP formation and compromised mucosal immunity. Importantly, we show that activation of the intestinal interleukin-6 signal transducer (IL6ST) pathway restores mAChR4 expression and GAP formation. This reactivation leads to enhanced type 3 innate lymphoid cell (ILC3)-derived IL-22 production and upregulation of antimicrobial Reg3 family proteins. These antimicrobial responses effectively block bacterial translocation to the liver and protect against ethanol-induced steatohepatitis. Furthermore, targeted activation of GC-specific mAChR4 alone was sufficient to prevent ALD, confirming the centrality of this pathway in gut-liver immune homeostasis. Our findings identified a previously unrecognized mechanism linking alcohol-induced disruption of GC-mediated antigen sampling to increased bacterial translocation and liver injury. They also highlight the therapeutic potential of mAChR4 and IL6ST agonists in restoring gut barrier function and preventing ALD progression. This work is the basis for novel interventions that modulate intestinal mucosal immunity to combat alcohol-related liver disease.

Morning Seminar 1 (Gilead Sciences K.K.)

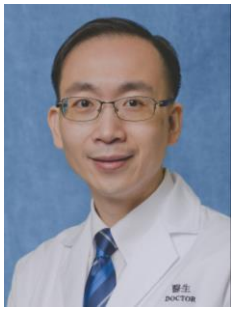
Dr. Takahiro Kodama
Assistant professor, Department of Gastroenterology and Hepatology,
Graduate School of Medicine, The University of Osaka
Japan

A New Era in the Management for Hepatitis B: Toward Treatment Optimization Based on Basic Research and Clinical Data

Chronic hepatitis B virus (HBV) infection remains a major global health challenge, with an estimated 296 million people infected worldwide. Despite the widespread use of nucleos(t)ide analogues (NAs), functional cure remains elusive in the majority of patients. As the therapeutic landscape continues to evolve, there is growing emphasis on long-term clinical outcomes and immune-based therapeutic strategies. In this seminar, we will explore how integrated insights from clinical cohorts and basic research are reshaping the future of HBV management.
We will begin by reviewing recent clinical data, including 8-year long-term efficacy and safety results of tenofovir alafenamide (TAF)(Buti M, et al., Aliment Pharmacol Ther. 2024), which underscore its durable viral suppression, renal and bone safety profiles, and potential implications for lifelong therapy. We will also present findings from our real-world observational study tracking long-term outcomes of NA-treated patients (Murai K et al., Hep Res in press). These data provide important perspectives on hepatocarcinogenesis, HBsAg kinetics, and risk stratification for treatment discontinuation or surveillance strategies.

The latter part of the seminar will shift focus to a novel immunocompetent mouse model of chronic hepatitis B, developed using a transposon-based system to deliver both the HBV genome and FAH cDNA into the liver (Shigeno S et al., Cell Mol Gastroenterol Hepatol, 2024). This model recapitulates key features of chronic infection, including persistent viremia and intrahepatic immune tolerance. Using this platform, we have begun to identify and validate immune-related therapeutic targets that may enhance HBV-specific immunity and promote viral clearance. This approach also enables the preclinical evaluation of combination therapies aiming to break immune exhaustion and achieve functional cure.
Through the integration of robust clinical datasets and innovative animal models, we are entering a new era of HBV therapeutics—one that moves beyond viral suppression toward immune modulation and personalized treatment strategies. This seminar will provide a comprehensive overview of emerging trends, translational research, and future directions for optimizing the management of chronic hepatitis B.

Morning Seminar 1 (Gilead Sciences K.K.)



Dr. Vincent Wai-Sun Wong
Professor
Department of Medicine and Therapeutics
The Chinese University of Hong Kong
Hong Kong SAR, China

Cardiometabolic Disease and Chronic Hepatitis B

Chronic hepatitis B remains a leading cause of hepatocellular carcinoma (HCC) and cirrhosis in Asia, despite evolving epidemiology. With aging populations, cardiometabolic diseases—including diabetes, obesity, and hypertension—are increasingly prevalent in patients with chronic hepatitis B, creating complex disease interactions. While chronic hepatitis B is associated with lower rates of hepatic steatosis and hypertriglyceridemia compared to the general population, concurrent steatosis correlates with higher hepatitis B surface antigen seroclearance. However, the causal relationship (e.g., viral suppression vs. metabolic pathways) remains unresolved.

Observational studies highlight that cardiometabolic diseases exacerbate liver outcomes in chronic hepatitis B. Diabetes and obesity independently increase risks of cirrhosis, HCC, and hepatic decompensation, with diabetes elevating HCC risk by 23–36%. The mechanism driving these risks -whether through direct metabolic dysfunction or steatosis-induced inflammation- is still unclear. Notably, glycemic control in diabetic patients correlates with reduced cirrhosis and HCC incidence, suggesting modifiable pathways.

Among cardiometabolic drugs, statins reduce HCC risk by 53–64% in patients with chronic hepatitis B, exhibiting dose-dependent efficacy. Antidiabetic agents (e.g., metformin, sodium-glucose co-transporter-2 inhibitors, glucagon-like peptide-1 receptor agonists) may lower HCC incidence through improved metabolic parameters. These drugs are generally safe in compensated liver disease but require caution in decompensated cirrhosis.

In conclusion, integrating cardiometabolic disease management into chronic hepatitis B care is crucial for improving outcomes. Prospective studies are needed to clarify causal mechanisms and optimize therapeutic strategies.

Morning Seminar 2 (Nobelpharma Co., Ltd)

Dr. Nobuhiro Nakamoto
Division of Gastroenterology and Hepatology,
Department of Internal Medicine, Keio University School of Medicine
Japan

Zinc Supplementation in the Treatment of Liver Cirrhosis

Zinc is an essential trace element that plays a pivotal role in nitrogen metabolism, primarily through its function as a cofactor for ornithine transcarbamylase in the urea cycle. In patients with liver cirrhosis, zinc deficiency is highly prevalent and contributes to impaired ammonia detoxification, increased reliance on the glutamine synthesis pathway, and increased utilization of branched-chain amino acids. These metabolic alterations are closely linked to sarcopenia, malnutrition, and the clinical spectrum of hepatic encephalopathy, ranging from minimal cognitive impairment to overt disorientation and coma.

Zinc supplementation has been shown to improve ammonia metabolism, enhance neuropsychological performance in covert hepatic encephalopathy, and support overall nutritional and metabolic status. Importantly, its efficacy is strongly dependent on adequate dosing, which should be tailored to body size and baseline nutritional condition. Inappropriate or insufficient supplementation may fail to achieve therapeutic benefits, while excessive administration may interfere with the absorption of other trace metals such as copper and iron. Therefore, careful dose adjustment and monitoring are essential in clinical practice.

We are particularly interested in the potential role of zinc as part of combination strategies rather than as monotherapy alone. Of note, concomitant administration with branched-chain amino acids has been hypothesized to enhance improvements in serum albumin levels by addressing both nitrogen balance and protein synthesis. Based on this hypothesis, our group has initiated clinical research to evaluate the additive benefits of zinc and BCAA therapy in patients with liver cirrhosis and hypoalbuminemia. This line of investigation reflects a broader effort to integrate nutritional and metabolic interventions into the standard care of cirrhosis.

In summary, zinc supplementation represents an important and often underrecognized therapeutic option in the comprehensive management of cirrhosis and hepatic encephalopathy. Its benefits extend beyond ammonia detoxification, influencing muscle metabolism, nutritional status, and possibly long-term prognosis. This lecture will provide an overview of the pathophysiological background of zinc deficiency in liver cirrhosis, summarize the current clinical evidence, and discuss future perspectives, with a particular focus on how zinc therapy may be optimized and combined with other interventions to improve outcomes for patients with chronic liver diseases.

Morning Seminar 2 (Nobelpharma Co., Ltd)

Dr. Ryosuke Tateishi
Associate Professor,
Department of Gastroenterology
The University of Tokyo Graduate School of Medicine
Japan

The Role of Zinc in the Management of Hepatocellular Carcinoma

Zinc is an essential trace element for hepatic function, serving as a cofactor for numerous enzymes and transcription factors. Zinc deficiency is frequently observed in advanced chronic liver disease, with serum zinc levels falling as cirrhosis progresses. Hepatocellular carcinoma (HCC) tissues often exhibit reduced zinc content and downregulation of zinc-dependent tumor suppressors compared to surrounding liver. Low zinc status has been linked to higher HCC risk and worse outcomes, as seen in viral hepatitis patients where zinc deficiency is associated with increased HCC incidence. Clinically, growing research suggests that optimizing zinc status may improve HCC management. Long-term zinc supplementation in patients with chronic liver disease has been shown to preserve liver function and significantly reduce the occurrence of HCC. In a cohort of hepatitis C patients who achieved viral clearance, those receiving oral zinc had a markedly lower 3-year HCC incidence compared to unsupplemented patients. In addition, low baseline zinc is now recognized as an independent prognostic factor for poor survival in early-stage HCC after curative therapy. This lecture will cover foundational knowledge and cutting-edge findings from high-impact studies to elucidate zinc's multifaceted role in hepatocarcinogenesis, tumor progression, immune regulation, and liver function in HCC.

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Plenary Session

Plenary Session

Dr. Minh Duc Pham
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Japan

Single Cell Fixed RNA-seq Revealed HSCs(LMCD1+) is a Driver of Liver Fibrosis by Modulating AKT-PRAS40-4EBP1

Background and Aims: This study aimed to leverage fixed single cell RNA sequencing technology (FLEX) to investigate experimental models of cirrhosis progression and regression, with the goal of identifying novel therapeutic mediators and regulated pathways.

Methods: Thioacetamide (TAA) was administered intraperitoneally to mice at escalating doses ranging from 50 to 400 mg/kg over a 10-week period to induce liver fibrosis, while control mice received saline. Regression of liver fibrosis was assessed two weeks after TAA cessation. Frozen liver tissues from mice samples were fixed, dissociated into single cells, and analyzed via single-cell RNA sequencing (scRNA-seq) following the 10X Genomics protocol.

Results: We identified 9 disctint HSCs subclusters with distinct signature genes and enrichment pathways in healthy control, fibrosis and regression. Notably, LIM-domain-related genes, including LIMA1, LIMK2, PDLIM2, PDLIM5, PDLIM7, FHL2, FHL3, and LMCD1, were significantly upregulated in cirrhotic HSCs from both mouse and public human database, but were downregulated during fibrosis regression. Functional studies demonstrated that silencing LMCD1 attenuated HSCs activation, whereas overexpression of LMCD1 strongly enhanced HSCs activation via the AKT-PRAS40-4EBP1 pathway. Specific inhibition using AZD8055 mitigated HSCs activation, both spontaneously and under TGFb1 stimulation, and significantly reduced the phosphorylation of 16/37 proteins, including CREB, c-JUN, WNK1, GSK3B, ERK1/2, P70S6K, and RSK1/2/3. LMCD1 highly expressed in fibrotic region and strongly correlated with MASLD-related fibrosis, with an area under the receiver operating characteristic (AUROC) curve of 0.92 (95% CI: 0.76-1; p=0.006) for predicting advanced MASLD-related fibrosis.

Conclusion: This study highlights previously unrecognized molecular dynamics of HSCs activation via LMCD1-AKT-PRAS40-4EBP1.

Plenary Session

Dr. Prihantini Prihantini
AI-Bio Medicine Research Group,
IMCDS-BioMed Research Foundation, Jakarta,
Indonesia

Mathematical Modeling of Stellate Cell-Macrophage Crosstalk Predicts Fibrotic Transition Dynamics in MASLD Using Patient-Derived Single-Cell Transcriptomic and Epigenomic Data

Background: Fibrosis in metabolic dysfunction-associated steatotic liver disease (MASLD) arises from hepatic stellate cell (HSC) activation driven by pro-inflammatory macrophage signaling. This study aimed to develop a predictive mathematical model simulating early fibrotic transitions by capturing dynamic crosstalk between HSCs and monocyte-derived macrophages (MdMs) using patient-derived single-cell data.

Methods: We utilized datasets from the Gene Expression Omnibus: GSE244832 for single-nucleus RNA-seq and ATAC-seq profiles of HSCs from normal, MASLD, and NASH liver tissue, and GSE235079 for scRNA-seq data of CD45+ macrophages from 21 MASLD patients. A hybrid system of non-linear ordinary differential equations and zonation-weighted partial differential equations was constructed to simulate TGFB1-RSPO3-COL1A1 signaling and α-SMA expression in HSCs. Macrophage cluster dynamics and transcription factor influence (RUNX1, SPI1) were modeled from expression and accessibility data. Simulations were conducted across 1,000 in silico liver microenvironments stratified by inflammatory burden.

Results: Fibrotic transition occurred when MdM1:HSC ratio exceeded 3.2:1 and TGFB1 flux surpassed 19.6 ng/mL/day, with progression from F0 to F2 within 9.3 months (95% CI: 8.7-10.0). Delayed RSPO3 feedback (>12.5 h) reduced fibrosis resolution probability by 62.1%, while SERPINE1 inhibition decreased α-SMA+ HSC activation by 47.6% ($p < 0.001$). Early RUNX1 overexpression in MdMs amplified TGFB1 signaling by 2.4-fold and accelerated fibrogenic loop convergence in spatially inflamed zones, particularly periportal fibrotic clusters. Model performance achieved AUROC = 0.79, precision = 0.81, and recall = 0.76.

Conclusion: This in silico fibrosis simulator captures patient-specific fibrotic dynamics and identifies therapeutic tipping points, offering a novel mechanistic framework for antifibrotic intervention timing in MASLD.

Plenary Session

Dr. Michitaka Matsuda
Department of Liver Diseases, Japan Institute for Health and Security
Japan

Fibrosis Microenvironment of Reduced HBsAg Area Enriches HCC Recurrence Risk Genes in Chronic Hepatitis B Patients

Background: Liver fibrosis is a precancerous microenvironment, the mechanisms of which have not been fully understood. The study aims to identify the risky microenvironment for future HCC development or recurrence in patients with chronic hepatitis B (CHB).
Methods: We used surgically resected HCC specimens from CHB patients for GeoMx spatial transcriptome and single-cell RNA sequencing (scRNA-seq). From the background non-cancerous liver tissue, stromal and parenchymal area-specific transcriptomes were acquired by GeoMx and deconvoluted with scRNA-seq data from the matched samples (spatial deconvolution). HCC recurrence risk genes were defined from the liver transcriptome data of the CHB cohort. The spatial distribution of HBsAg and HBV-DNA was histologically evaluated by immunofluorescent staining and in situ hybridization.
Results: HBsAg-dense and -sparse areas are randomly distributed across the tissue. HBV-DNA was located in hepatocyte cytosol at the HBsAg-dense area, indicating active viral replication. In contrast, HBV-DNA was located in hepatocyte nuclei at HBsAg-sparse areas, suggesting the presence of cccDNA at the site. The gene signature associated with HCC recurrence was more enriched at the HBsAg-sparse area than the HBsAg-dense area, suggesting that HBsAg reduction is associated with developing a precancerous microenvironment. Spatial deconvolution delineated the heterogeneous microenvironment of stromal and parenchymal areas. Compared to the HBsAg-dense area, the HBsAg-sparse area enriched more exhausted T cells and damage-associated hepatocytes.
Conclusion: Spatial transcriptome and scRNA-seq of CHB patients' liver tissue delineated the heterogeneous fibrosis microenvironment. The immunosuppressive microenvironment at the HBsAg-sparse area was associated with the recurrence of HCC after surgical resection in CHB patients.

Dr. Kai Oshima
Department of Gastroenterology, Graduate School of Medicine,
The University of Tokyo,
Japan

Development of a High-Accuracy Machine Learning Model for Predicting Pathological Cirrhosis in Patients with Steatotic Liver Disease

Background: Fibrosis stage is a key prognostic factor in steatotic liver disease (SLD), and accurate identification of cirrhosis (F4) is essential for clinical management. Non-invasive tools like liver stiffness measurement (LSM) are commonly used but can be limited by accessibility and diagnostic performance in certain populations. This study aimed to develop and validate a machine learning (ML) model using only routine clinical data to predict F4 cirrhosis, independent of LSM.

Methods: A total of 438 patients with biopsy-confirmed SLD were analyzed. The dataset was randomly divided into training (80%) and testing (20%) sets. Multiple ML algorithms-including deep learning, gradient boosting (GB), logistic regression, random forest, and support vector machine-were trained on baseline demographic, clinical, and laboratory variables. Model performance was assessed using the area under the receiver operating characteristic curve (AUC) and compared to Agile 4, LSM, and the Fibrosis-4 index (FIB-4). Hyperparameters were tuned via Bayesian optimization, and feature importance was evaluated using permutation methods.

Results: Of the 438 patients, 39 (8.9%) had F4 cirrhosis. The GB model achieved the highest AUC (0.9062; training AUC 0.9722) in the test set, outperforming Agile 4 (test AUC 0.8328), LSM (0.8273), and FIB-4 (0.7609). Key predictors included platelet count, alkaline phosphatase, albumin, BMI, and γ-glutamyl transferase. The final GB-based model is available as an easy-to-use application at "https://ai-basedf4predictionmodel.streamlit.app/".

Conclusion: The GB-based ML model showed high accuracy for identifying F4 using only routine clinical data. This non-invasive, cost-effective tool could complement or serve as an alternative to LSM-based methods, especially in resource-limited settings.

Plenary Session

Dr. Vaibhav Tiwari
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India

Endotoxin-Induced Metabolic Reprogramming in Liver Sinusoidal Endothelial Cells Drive Hepatic Microvascular Dysfunction and Portal Hypertension During Sepsis in Experimental Models of Liver Cirrhosis

Background: Liver sinusoidal endothelial cells (LSECs) are key hepatic sentinels, directly exposed to microbial toxins when gut barriers fail in cirrhosis. Sepsis further worsens vascular dysfunction and portal hypertension (PHT) in these patients. However, how LSEC metabolic changes contribute to this remains unclear. This study investigated the role of the glycolytic enzyme 6-phosphofructo-2-kinase (PFKFB3) in hepatic microvascular dysfunction during endotoxemia in cirrhosis and its impact on PHT.

Methods: Sepsis was induced through caecum ligation and puncture (CLP) in healthy rats and by lipopolysaccharide (LPS) injection in Carbon tetra chloride and Thioacetamide-induced cirrhotic rats. PFKFB3 was pharmacologically inhibited using 3PO. Study groups included controls, sepsis-induced, and PFKFB3-inhibited animals in both healthy and cirrhotic models. Hemodynamic measures, ex vivo microvascular function, and molecular, biochemical, and histological analyses were conducted. Lactate, reactive oxygen species (ROS), nitric oxide (NO), and monocyte adhesion to LSECs were assessed.

Results: Sepsis significantly increased portal pressure, portal blood flow, and arterial flow, all of which decreased with PFKFB3 inhibition. Higher ROS, lactate, and protein levels of PFKFB3, HK1, LDH1, ICAM1, and Claudin-5 confirmed metabolic shifts, which were reversed by treatment. Monocyte adhesion on LSECs reduced with PFKFB3 inhibition, restoring endothelial integrity. Inflammatory gene expression and liver enzymes also improved with treatment.

Conclusion: Endotoxin-driven metabolic reprogramming in LSECs via PFKFB3 promotes vascular dysfunction and PHT in cirrhosis. Targeting PFKFB3 restores LSEC function and may offer a therapeutic option to improve hemodynamics and limit sepsis-related vascular complications.

Dr. Pham Tuan Anh
Department of Global Education and Medical Sciences,
Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan

Macrophages and Hepatic Stellate Cells Interactions via Semaphorin 4D-PlexinB2 Axis Promote Liver Fibrosis

Background: Liver fibrosis remains a major unmet medical challenge due to the lack of effective treatments to reverse or halt disease progression. Advances in single-cell technologies have enabled detailed analysis of cell-cell interactions during fibrosis. Here, we employed Single-Cell Fixed RNA Profiling (FLEX) to investigate the cellular landscape of fibrosis progression and regression in a murine model, aiming to identify novel anti-fibrotic targets.
Methods: We integrated and annotated macrophages from fixed scRNAseq data using R for computational analysis. Molecular investigations included immunoblotting, immunofluorescence, immunohistochemistry, flow cytochemistry, as well as neutralizing antibody application to elucidate functional roles.
Results: Cirrhotic mouse livers exhibited increased macrophages compared to healthy control and fibrosis regression groups. Macrophages were further classified into resident Kupffer cells (KC1), activated Kupffer cells (KC2), proliferating Kupffer cells (KC3), and monocyte-derived macrophages (MoMacs). KC2 and MoMacs secreted higher levels of inflammatory cytokines than KC1. Sema4D was among the top transcripts in MoMacs and was implicated in their activation. Its expression was elevated at the mRNA, protein, and secreted levels. CellChat analysis showed Sema4D binding to Plexin B1/2 on hepatic stellate cells (HSCs) occurred only in fibrotic livers. MultiNicheNet ranked this as the top Macrophage-HSCs interaction. SEMA4D and its receptor were co-expressed in human and mouse fibrotic livers. SEMA4D promoted collagen synthesis in HHSteCs and was therapeutically targeted in vivo using VX15/2503, which suppressed fibrosis.
Conclusion: Sema4D-Plexin B1/2 signaling is a promising target for anti-fibrotic therapy.

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Abstracts

Late Breaking Oral Session

Late Breaking

LBO-1 #10242

Histologic Improvement and Sustained Benefit Across Hepatic and Metabolic Biomarkers with Pegozafermin Therapy: Results from a 48-week Multi-center, Randomized, Double-blind, Placebo-controlled Phase 2b trial (ENLIVEN)

Rohit Loomba[1], Vincent W. S. Wong[2], Shibao Feng[3], Mildred D. Gottwald[3], Hank Mansbach[3], Cynthia L. Hartsfield[3], Wenyan Wang[3], Maya Margalit[3]
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Background: Metabolic dysfunction-associated steatohepatitis (MASH) is often associated with common comorbidities. FGF21 analogs such as pegozafermin (PGZ) have potent anti-fibrotic effects as well as metabolic benefits in patients with MASH. The Phase 2b ENLIVEN trial was designed to evaluate the efficacy and safety of PGZ given weekly (QW) or every two weeks (Q2W) versus placebo in MASH patients with biopsy-proven F2/F3 fibrosis. Primary histology endpoints were assessed at week 24, followed by a blinded 24-week extension for a total of 48 weeks.
Methods: Patients were randomized to PGZ 15mg QW, 30mg QW, or 44mg Q2W or placebo for 24-weeks (histology-based primary endpoints). The full analysis set includes F2/F3 patients with NAFLD activity score (NAS) > 4 at baseline (n=192).
Results: Both primary histological endpoints were achieved in a significantly higher proportion of patients treated with PGZ 30mg QW or 44 mg Q2W compared to placebo. Additionally, PGZ treatment significantly improved liver fat content, biomarkers of fibrosis and liver injury at both week 24 and week 48. PGZ was generally safe and well tolerated with the most common treatment-emergent adverse events (TEAEs) being mild/moderate nausea and diarrhea.
Conclusions: Treatment with PGZ in MASH patients with F2/F3 fibrosis led to highly significant fibrosis regression and MASH resolution. Robust and sustained improvements in non-invasive biomarkers of liver fat and inflammation, fibrosis, and metabolic markers were also observed with a consistent and favorable safety and tolerability profile. Phase 3 studies in non-cirrhotic (ENLIGHTEN-Fibrosis) and cirrhotic (ENLIGHTEN-Cirrhosis) MASH are currently underway to confirm these results.

LBO-2 #10243

Insights from Phase 2 Study Results for Survodutide in People with MASH Fibrosis F1-F3

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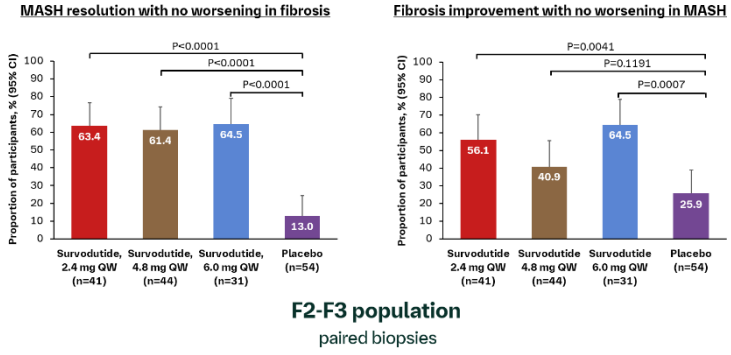
Background: Survodutide, a novel dual agonist of the glucagon receptor and GLP-1 receptor, is under investigation for MASH. We report phase 2 trial results for people living with MASH fibrosis (F1-F3).
Methods: In this multinational, double blind study (NCT04771273), 295 adults with biopsy proven MASH (NAS ≥4), fibrosis stage F1–F3, and BMI ≥25 kg/m² were randomised to weekly placebo or survodutide (2.4, 4.8, or 6.0 mg; titrated over ≤24 weeks) for 48 weeks. The primary endpoint was histological improvement of MASH without fibrosis worsening. Secondary and further endpoints included improvement in fibrosis (≥1 stage decrease) without worsening of NAS, absolute change in NAS, and change in ALT, AST.
Results: Baseline characteristics were balanced (mean age 50.8 years; BMI 35.8 kg/m²; NAS 5.2; 41% F2, 35% F3). The primary endpoint was achieved in 64.3%, 83.0%, and 65.9% of participants receiving 2.4, 4.8, and 6.0 mg survodutide, respectively, versus 18.2% with placebo (p<0.001, paired biopsies). NAS reductions were −2.80 to −3.30 with survodutide versus −0.40 with placebo; ALT and AST decreased markedly. In those with F2–F3 fibrosis and paired biopsies (n=170), ≥1 stage fibrosis improvement without MASH worsening occurred in up to 64.5% (6.0 mg) versus 25.9% with placebo (p<0.001). Survodutide also significantly led to MASH resolution without fibrosis worsening across doses (p<0.001). Adverse events were mainly gastrointestinal and consistent with the drug class; no unexpected safety concerns emerged.
Conclusions: Survodutide produced substantial histological benefits in MASH, including high rates of fibrosis regression in advanced stages. Phase 3 programmes in pre-cirrhotic/ cirrhotic MASH (LIVERAGE™, LIVERAGE™ Cirrhosis) and obesity (SYNCHRONIZE™) are ongoing.



Late Breaking

LBO-3 #10239

TMBIM5 Attenuates High-fat-mediated Liver Injury by Activating Fundc1-related Mitophagy and Suppressing Drp1-related Fission

Qi Shen, Tian Xia, Ruibing Li, Mianyang Li
The Chinese PLA General Hospital

Background and Aims: Metabolic dysfunction-associated fatty liver disease (MAFLD) is the most prevalent chronic liver disease worldwide, yet effective therapies remain lacking. TMBIM5 is known to preserve mitochondrial function in other diseases, but its role in MAFLD is unclear. This study aimed to investigate the role and molecular mechanism of TMBIM5 in MAFLD.

Methods: The role of TMBIM5 was investigated in both mouse and cell (AML12) models. Liver pathology was assessed by H&E, Masson, and Oil Red O staining. Liver function were measured using ELISA. Inflammation, apoptosis, and mitochondrial function were evaluated by qPCR, Western blotting, immunofluorescence, ROS production, ATP levels, JC-1 staining, MPTP opening, and oxygen consumption rate trials. LC-MS/MS was applied to explore downstream mechanisms.

Results: High-fat diet (HFD) markedly downregulated TMBIM5 expression in mouse liver. TMBIM5 deficiency further aggravated HFD-induced steatosis and liver injury, whereas overexpression alleviated these damage. LC-MS/MS analysis revealed that the differentially expressed proteins before and after TMBIM5 overexpression were predominantly enriched in mitochondria-related pathways, suggesting mitochondrial dysfunction as a major downstream event regulated by TMBIM5. We found that TMBIM5 overexpression attenuated PA-induced mitochondrial oxidative stress and preserved mitochondrial integrity, thereby improving mitochondrial function. Furthermore, we demonstrated that TMBIM5 restores mitochondrial homeostasis by activating Fundc1-mediated mitophagy and suppressing Drp1-dependent mitochondrial fission, with mitophagy acting upstream of fission in this regulatory cascade.

Conclusion: TMBIM5 is a therpeutic target for conferring protection against high-fat-mediated liver injury by activating Fundc1-realted mitophagy and suppressing Drp1-related fission to relieve MAFLD.

LBO-4 #10241

The Mechanism of TMBIM5 in Ameliorating Alcohol-related Liver Disease by Regulating Mitochondrial Dynamics

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The Chinese PLA General Hospital

Background and Aims: ALD is a group of metabolic disorders induced by prolonged and heavy alcohol consumption. However, there are many limitations in the treatment of ALD. TMBIM5 has been shown to maintain the normal function of mitochondria in other diseases, but its role in ALD is unclear. This study aimed to investigate its role and mechanism TMBIM5 in the development of ALD.

Methods: The mechanism was investigated TMBIM5 in alcohol-induced in vivo and in vitro models. The pathological changes were observed by H&E and Masson staining. Inflammation, apoptosis, and mitochondrial function were evaluated by qPCR, Western blotting, immunofluorescence, ROS production, ATP levels, JC-1 staining, MPTP opening, and oxygen consumption rate trials. And the CO-IP experiments and a series of mutant plasmids of TMBIM5 were constructed to further clarify the molecular mechanism.

Results: A significant decrease in TMBIM5 protein expression was observed in alcohol-induced groups, while no significant change is observed at the mRNA level. TMBIM5 deficiency further aggravated alcohol-induced liver injury, whereas overexpression alleviated these damage. In addition, we found that TMBIM5 overexpression attenuated alcohol-induced mitochondrial oxidative stress and preserved mitochondrial function. Furthermore, we elucidate alcohol induces post-transcriptional degradation of TMBIM5 by downregulating the expression of mitochondrial fission proteins, while upregulating fusion proteins, ensuring the stability of mitochondrial structure and function, thereby protecting hepatocytes from alcohol damage.

Conclusion: TMBIM5 can alleviate hepatocyte injury by regulating mitochondrial dynamics and can potentially be modulated as a therapeutic target to relieve ALD.

Late Breaking
LBO-5 #10246

Using a Human Liver-on-a-chip Model to Study Alcohol-associated Liver Disease by Targeting LSEC and ALDH2

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Background: Current research on alcohol-associated liver disease (ALD) has limitations due to insufficient expression and activity of alcohol-metabolizing enzymes in hepatocytes. We developed a liver-on-a-chip with human hepatocytes and liver sinusoidal endothelial cells (LSECs). We found that ALDH2 is expressed also in LSECs, downregulated in senescent LSECs, and relatively low in cirrhosis patients. We hypothesize that reduced ALDH2 in aging LSECs contributes to ALD development through hepatic acetaldehyde (AcH) accumulation.
Methods: The hepatocyte-containing chips with or without LSECs were treated with 0.2% ethanol. ALDH2 was silenced in LSECs or activated by Alda-1. AST, ALT, AcH and ethanol levels were measured. ALDH2 and senescence markers were examined by single-cell RNAseq of human alcoholic cirrhosis and cultured samples.
Results: Albumin, ADH1, ALDH2 and CYP2E1 levels were higher in our model. The ethanol-induced AST/ALT release in the LSEC-free chip was suppressed in the chip with LSECs, suggesting that LSECs protect hepatocyte damage. In LSECs, ALDH2 silencing raised AST/ALT enzyme release but ALDH2 activation lowered the release, underscoring the protective role of ALDH2 in LSECs. scRNA-seq data of cirrhosis showed reduced ALDH2 expression and senescence markers upregulation in LSECs. Long-term AcH exposure caused LSEC aging, with ALDH2 reduced and AST/ALT levels increased. Overall, these data suggest that cirrhosis causes LSEC aging and lowers ALDH2 expression, and that in cirrhosis excessive ethanol exposure induces severe liver damage due to AcH accumulation by downregulated ALDH2 in senescent LSECs, which might explain severe alcoholic hepatitis in cirrhosis.
Conclusion: We demonstrated the importance of LSEC ALDH2 in ALD.

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Abstracts

Parallel Sessions

Parallel Session 1
OF1-1 10174

Gender-Specific Body Composition Phenotypes Predict Advanced Fibrosis in Metabolic Dysfunction-Associated Steatohepatitis: A Cross-Sectional MRI-Based Clustering Analysis

Jordan Low[1], Jie Ning Yong[1], Hee Seung Yang[1], Mark Muthiah[2], Cheng Han Ng[2], Vigneshwaran Selvakumar[1]
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Background: Metabolic dysfunction-associated steatohepatitis (MASH) progression may be influenced by body composition phenotypes. This study aimed to identify distinct muscle-adipose tissue distribution patterns and their associations with disease severity in MASH patients.
Methods: Cross-sectional analysis of 132 patients using AMRA Profiler MRI to quantify anterior/posterior thigh muscle mass, abdominal adipose tissue, visceral adipose tissue, abdominal subcutaneous adipose tissue, and spinal erector muscle mass. Agglomerative hierarchical clustering with Ward's linkage was performed separately by gender. Associations between clusters and disease outcomes (at-risk MASH, advanced fibrosis, cirrhosis, clinically significant fibrosis) were analyzed using Fisher's exact test with False Discovery Rate correction.
Results: The cohort included 132 participants (median age 44.0 years, BMI 32.0 kg/m^2, 51.5% female). Three distinct phenotypic clusters emerged for each gender. In males, clustering showed no significant associations with disease outcomes. In females, clustering demonstrated significant association with advanced fibrosis ($p=0.006$, FDR $p=0.048$). Cluster 3 females exhibited the highest advanced fibrosis rate (52.2%) and were characterized by reduced thigh muscle mass and decreased abdominal subcutaneous adipose tissue compared to other clusters.
Conclusion: Body composition clustering reveals gender-specific associations with MASH progression. Female-specific muscle-adipose distribution patterns may serve as predictive markers for advanced fibrosis, suggesting sex-specific mechanisms in metabolic liver disease progression warrant further investigation.

OF1-2 10102

Pathological Classification of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) Based on Muscle Fatty Changes and Quantitative Changes Using MRI: A Cluster Analysis Study

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Background: Assessing muscle quality by MRI-PDFF has been possible, however, reports focusing on myosteatosis are scarce. This study aimed to classify the pathology of MASLD by cluster analysis using muscle fat content and nutritional indices, and to elucidate the relationship between liver function and muscle changes.
Methods: We retrospectively evaluated MRI scans of 120 patients with MASLD. We extracted the fat content of psoas and erector spinae muscles quantified by PDFF, GNRI, FIB-4, age, and ALBI score, and performed cluster analysis using the K-means method. The clusters were visualized by principal component analysis (PCA) and their characteristics were compared. Additionally, restricted cubic spline analysis was examined the relationship between the ALBI score and muscle quality (PDFF) and quantity (GNRI).
Results: Cluster analysis classified patients into four groups: Cluster 1: young, well-nourished, and low muscle fat; Cluster 2: moderate FIB4, low muscle fat, and well-nourished; Cluster 3: elderly, high FIB4, and malnutrition; Cluster 4: moderate FIB4, high muscle fat, and well-nourished. The PCA plot clearly separated Cluster 3, which showed a significant deterioration in both muscle quality and quantity. Spline analysis showed that muscle fat content began to increase at the point of ALBI -2.8 and to decrease when ALBI exceeded -2.5. GNRI showed to decrease rapidly when ALBI exceeded -2.3.
Conclusions: The progression pattern in which deterioration of muscle quality begins in the compensated stage and is followed by a decrease in muscle mass in the decompensated stage may be an important perspective for future prognosis prediction and nutritional intervention.

Parallel Session 1
OF1-3

Metabolic-associated Fatty Liver Disease: Research Advanced in Epidemiology, Risk Factors, and Precision Prevention and Control Strategies in China

Liu Jing, Department of Hepatology, Affiliated Hospital of Hangzhou Normal University, China

Metabolic associated fatty liver disease (MAFLD)has replaced viral hepatitis as the most common chronic liver disease globally and now affects 29.8% of Chinese. MAFLD is a manifestation of multisystem metabolic disorders involving the liver . If not intervened in a timely manner, it can eventually progress to liver cirrhosis, liver cancer, and liver failure. Due to the lack of typical histological manifestations of steatohepatitis and clinical features, NAFLD-related liver cirrhosis was once considered a cryptogenic liver cirrhosis accompanied by metabolic disorders. With the introduction of the new definition of MAFLD, even if there is a lack of typical histological manifestations of steatohepatitis (no or less than 5% hepatic steatosis), as long as it meets the new definition of MAFLD, it can be defined as MAFLD - related liver cirrhosis, indicating that MAFLD-related liver cirrhosis is no longer a cryptogenic liver cirrhosis. It has unique epidemiological characteristics, diagnostic criteria, adverse intra-hepatic and extra-hepatic outcomes, and treatment strategies. Research shows that the population with MAFLD in China will increase by 29.1% to 314.58 million cases from 2016 to 2030.
Meanwhile, decompensated liver cirrhosis and liver-related deaths secondary to MAFLD are expected to double. Patients with MAFLD-related liver cirrhosis have unique clinical and histopathological characteristics. Given that there are currently no drugs approved by the Center for Drug Evaluation (CDE) in China for the treatment of MAFLD. Therefore, further systematic research on the clinical characteristics and prognosis of MAFLD - related liver cirrhosis in China will be of great significance for formulating corresponding clinical prevention and treatment strategies.

Parallel Session 2

OF2-1 10078

Dynamic Changes in Steatotic Liver Disease Subtypes and Risk of Cardiovascular Disease: A Nationwide Cohort Study

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Background: With the global rise in obesity and type 2 diabetes, the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) has also increased. Although subtypes of steatotic liver disease (SLD), including MASLD, MASLD with increased alcohol intake (MetALD), and alcohol-related liver disease (ALD), are well known to increase cardiovascular disease (CVD) risk, most existing studies have evaluated SLD status at a single time point. Given that alcohol consumption can vary over time, such assessments may not reflect meaningful transitions between SLD subtypes. This study aimed to evaluate whether transitions between SLD subtypes affect incident CVD risk.
Methods: We analyzed data from 799,631 Korean adults aged 20 years or older who completed two national health screenings between 2009–2010 and 2011–2012. SLD was defined as fatty liver index ≥60. Transitions between MASLD, MetALD, and ALD were identified, and incident CVD, including coronary heart disease and stroke, was followed from January 1, 2013, to January 31, 2022. Subdistribution hazard ratios (SHRs) were estimated using Fine and Gray models, accounting for non-CVD death as a competing risk.
Results: Compared to sustained MASLD, both transition to MetALD (SHR, 0.89; 95% confidence interval [CI], 0.86–0.91) and sustained MetALD (SHR, 0.80; 95% CI, 0.78–0.83) were associated with lower CVD risk. In contrast, transition from MetALD to ALD increased stroke risk (SHR, 1.17; 95% CI, 1.07–1.28).
Conclusion: Dynamic changes in SLD subtypes, particularly those related to alcohol consumption, significantly impact CVD risk. Monitoring these transitions may enhance risk stratification and inform prevention strategies in patients with SLD.

OF2-2 10080

The Risk of Heart Failure in Patients with Atrial Fibrillation According to the Steatotic Liver Disease Subtype

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Background: South Korea is expected to enter a super-aged society, and the proportion of elderly patients with heart failure is projected to rise accordingly. Older adults with atrial fibrillation (Afib) are at a higher risk of HF, and metabolic related conditions, including steatotic liver disease (SLD), may contribute. This study explored the association between SLD subtypes and incident HF.
Methods: We conducted a cohort study using the Korean National Health Insurance Service (NHIS) database from 2002 to 2019. Elderly individuals diagnosed with Afib between 2002 and 2010 were followed until December 31, 2019. The primary outcome of interest was HF, and the secondary outcomes included stroke and ischemic heart disease (IHD). Individuals were categorized into non-SLD, metabolic dysfunction-associated SLD (MASLD), MASLD with increased alcohol intake (MetALD), and alcohol-related liver disease (ALD). Subdistribution hazard ratios (SHRs) were evaluated using the FineGray model, accounting for death as a competing risk.
Results: A total of 2,744, 1,979, 247, and 110 older adults with Afib were identified in the non-SLD, MASLD, MetALD, and ALD groups, respectively. Compared to no SLD, HF risk was higher in SLD groups: MetALD (aSHR 1.77; 95% CI 1.37 to 2.30), ALD (aSHR 1.55; 95% CI 1.05 to 2.29), and MASLD (aSHR 1.20; 95% CI 1.05 to 1.37). No significant associations were found for stroke or IHD.
Conclusion: We found that older adults with Afib had an increased risk of developing HF accoring to SLD subtypes. These findings indicate the need of management of SLD in elderly patients with Afib.

Parallel Session 2
OF2-3 10181

Risk Factors for Cardiovascular Disease Among Older Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Nationwide Cohort Study

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent in the elderly and is linked to elevated cardiovascular disease (CVD) risk. However, research focusing on this population remains limited. This study identified CVD risk factors in elderly individuals with MASLD and examined their representation in widely used clinical risk calculators.
Methods: This population-based cohort study utilized data from the Korean National Health Insurance Service and included 91,057 individuals aged 65 or older who were diagnosed with MASLD between 2011 and 2012. Participants were followed from January 1, 2013, to December 31, 2022, for the incidence of coronary heart disease (CHD), stroke, and total CVD. CVD risk factors were identified using Cox proportional hazards regression and machine learning models, including logistic regression and extreme gradient boosting.
Result: Serum creatinine, Charlson comorbidity index (CCI), and antiplatelet agents use were consistently identified as significant predictors of incident CVD, with some variations in relative importance across specific outcomes. For CHD, the Cox proportional hazards model identified serum creatinine as the strongest predictor (adjusted hazard ratio [aHR] 1.65; 95% CI: 1.39-1.95), followed by 1.47 (1.27-1.69) for CCI≥2 and 1.41 (1.28-1.56) for antiplatelet agents use. Extreme gradient boosting model ranked antiplatelet agent use highest (SHAP: 0.14), followed by CCI (0.12) and serum creatinine (0.09).
Conclusion: The identified covariates are not included in common CVD risk models such as the Framingham Risk Score and pooled ASCVD equations, which target younger populations. The findings support the need for tailored CVD risk stratification in elderly MASLD patients.

Parallel Session 3

OF3-1 10205

Association of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) with Angiographic Severity of Coronary Artery Disease in Acute Coronary Syndrome

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Background: Due to common cardio-metabolic risk factors, there may be association between MASLD and coronary artery disease (CAD). The objective was to evaluate the association between MASLD and angiographic severity of CAD by Gensini Score (GS) in Acute Coronary Syndrome (ACS).
Methods: This cross-sectional analytical study was conducted in a tertiary care hospital. A total of 110 ACS patients were enrolled. Coronary angiogram was performed and severity of CAD was assessed by GS. Fibroscan of liver was done. Patients were divided into two groups: GroupI: Patients with MASLD and GroupII: Patients without MASLD (55 patients in each group). Then the association of MASLD and severity of CAD was analyzed statistically.
Results: Mean age of the patients was 50.15±8.92 years. DM, BMI and waist circumference were statistically significantly higher in MASLD group than non-MASLD group(p&lt:0.05). MASLD patients had more severe CAD (Gensini score > 36) compared with non-MASLD patients (70.9% vs 40.0%, p = 0.001). The mean Gensini score was also statistically significantly higher in the MASLD group (47.75&plusmn20.94 vs 32.64&plusmn16.8; p<0.001). Double vessel disease and triple vessel disease was significantly higher in MASLD group than non-MASLD group (36.4% vs 25.5% and 38.2% vs 18.2% respectively). Multivariate logistic analysis regression revealed that only MASLD (Odds ratio:2.95) and dyslipidemia (OR:3.60) were independent predictor of severe CAD (GS >36).
Conclusion: In patients with ACS, presence of MASLD was associated with increased severity of coronary artery disease (CAD) and multi vessel disease. MASLD may be considered as an independent predictor for severe CAD.

OF3-2 10012

Potential Targets in Metabolic-Associated Steatohepatitis Based on Bioinformatics Analysis and Machine Learning Strategies

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Background: MASH poses significant threat to human health and is recognized as the leading contributor to HCC. In this study, we leveraged publicly accessible datasets to identify novel differentially expressed genes that may serve as potential targets in MASH or potentially MASH-induced HCC.
Method: The publicly available datasets were obtained from the GEO. Differential gene expression analysis and enrichment analysis was performed. Subsequently, WGCNA and PPI network was constructed. Lastly, machine learning were employed to identify key feature genes.
Results: Utilizing integrated GEO database, we identified 446 genes exhibiting differential expression. Enrichment analysis indicated that these genes are predominantly associated with glucose and lipid metabolism and inflammatory processes. Through WGCNA, three modules were identified that demonstrated significant correlation with MASH. Furthermore, core genes among the differentially expressed genes were extracted via PPI. Ultimately, machine learning techniques were employed, leading to the identification of three genes: FosB, Fos, and SOCS3. Notably, FosB exhibited consistent expression across various datasets, demonstrated strong predictive capabilities for MASH, and was associated with improved prognostic outcomes in HCC by data from TCGA. Additionally, in vitro immunohistochemistry experiments revealed significant reduction in FosB expression in MASH.
Conclusion: Bioinformatics analyses conducted on various datasets, along with in vitro immunohistochemistry experiments, revealed significant downregulation of FosB in MASH. It indicates that FosB plays critical role in the pathogenesis of MASH, and its expression is associated with the prognosis of patients with HCC.Further experimental studies are required to investigate the potential targeting of FosB in MASH and MASH-induced HCC.

Parallel Session 3
OF3-3 10091

Gut Microbiota Dysbiosis and Its Role in the Pathogenesis of Metabolic Dysfunction-Associated Steatotic Liver Disease

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Background and Aim: Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most prevalent chronic liver disease in the world. An increasing number of studies have indicated a close relationship between dysbiosis and MASLD. Hence, there is an interest in exploring the fatty infiltration as the result of the dysbiosis, that includes bacterial composition disturbance, with profound analysis of preventive and aggressive factors. The aim of this study was to analyze the gut microbiota composition in patients with MASLD.
Methods: This study involved 123 subjects divided in two groups (83 MASLD and 40 healthy individuals in control group) diagnosed with MASH/MASLD based on ultrasound and biochemical tests. Biochemical evaluation included liver functional tests and lipid profile. Dysbiosis was assessed with stool bacteriological test and stool test for dysbiosis.
Results: Genus Enterococcus like Streptococcus were increased in patients with MASLD/MASH compared with controls, also uncultured Clostridiales as well as entero-hemolytic Escherichia Coli were increased, whereas genus Bifidobacterium, and Lactobacillaceae were decreased in patients with MASLD/MASH. Significant loss of beneficial bacteria for intestinal barrier function like Faecalibacterium was observed. The diversity of the microbiota was decreased in patients compared with controls.
Conclusion: our study revealed an association between Bacteroides abundance in the gut and MASLD/MASH. These results show that gut microbiota analysis adds prognostic information to the classical risk factors for MASLD severity, and strongly suggests that the gut microbiota has a significant role in the pathogenesis of MASLD. Patients with MASLD should be tested for dysbiosis, and vice versa.

Parallel Session 4
OF4-1 10213

Association of Combustible Cigarette and Noncombustible Tobacco Product Use with Mental Health Outcomes in Subtypes of Fatty Liver Disease: A Nationwide Cohort Study from Korea

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Background: We investigated the association between Combustible Cigarette(CC) and Noncombustible Nicotine/Tobacco Product(NNTP) use and the risk of mental disorders across subtypes of Fatty Liver Disease(FLD), using data from the Korean National Health Insurance Service.
Methods: Among 1,113,795 individuals without a prior history of mental disorders, we estimated adjusted Subdistribution Hazard Ratio(aSHR) for incident mental disorders. Smoking status was classified into 12 groups by combining six categories of CC smoking trajectory–Never CC smokers, Recent(<5years) CC quitters, Long-term(≥5years) CC quitters, Recent(<5years) CC initiators, Recent(<5years) relapsed CC smokers, and Continuous CC smokers–with concurrent NNTP use (Yes/No). Participants were classified into four mutually exclusive categories based on Hepatic Steatosis(HS), CardioMetabolic Risk Factors(CMRFs), and alcohol intake: nonSLD for HS=False, MASLD for HS=True, CMRFs≥1, and Mild or No alcohol intake, MetALD for HS=True, CMRFs≥1 and Moderate alcohol intake, ALD for (HS=True, CMRFs≥1, and Moderate or Heavy alcohol intake) or (HS=False, CMRFs=0, and Moderate or Heavy alcohol intake)
Results: In MASLD, Recent CC quitters with NNTP use had elevated risks of depressive disorder (aSHR=1.28; 95% CI [1.11–1.47]; p<0.001), and Continuous CC smokers with NNTP use also showed a significantly increased risk (aSHR=1.38; 95% CI [1.17–1.63]; p<0.001).Among individuals with MASLD, Recent CC quitters with NNTP use demonstrated higher risk of anxiety disorders (aSHR=1.13; 95% CI [1.01–1.27]; p=0.033) and Continuous CC smokers with NNTP use showed a similarly elevated risk (aSHR=1.21; 95% CI [1.05–1.39]; p=0.007).
Conclusion: Among individuals with MASLD, concurrent NNTP use was associated with significantly increased psychiatric risks, warranting integrated hepatic-mental health strategies.

OF4-2 10111

Handgrip Strength Estimation as a Predictor of Liver-Related Outcomes in Patients with Steatotic Liver Disease

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Background: This study aimed to investigate whether estimated handgrip strength (eHGS) serves as a prognostic biomarker for liver-related outcomes in patients with steatotic liver disease (SLD).
Methods: We conducted a nationwide cohort study using Korean National Health Insurance Service database, including 3,608,814 Korean adults with SLD from 2015, followed until January 31, 2022. The SLD was defined as a fatty liver index 30 or higher. The eHGS was calculated using a multiple linear regression incorporating demographic and anthropometric variables with both internal and external tests. The risk of liver-related outcomes, including primary liver cancer, hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA), liver cirrhosis, and decompensated cirrhosis, was compared across eHGS quartiles. The subdistribution hazard ratio (SHR) was calculated using the Fine-Gray model regarding competing risks.
Results: During a mean follow-up period of 6.92 years, patients in higher eHGS quartiles demonstrated progressively lower risks across all liver-related outcomes. Liver-related events occurred with incidence rates of 3.19, 2.26, 1.94, and 1.87 per 1,000 person-years across eHGS quartiles 1-4, respectively. Compared with the lowest quartile, the highest quartile showed significantly reduced risks of liver-related events (adjusted SHR: 0.66, 95% confidence interval [CI]: 0.64-0.67), primary liver cancer (0.70, 0.67-0.73), HCC (0.74, 0.70-0.77), and iCCA (0.58, 0.54-0.62). The risk of incident cirrhosis and decompensated cirrhosis decreased progressively across increasing eHGS quartiles.
Conclusion: Higher eHGS is independently associated with reduced liver-related outcome risks in patients with SLD. These findings support eHGS as a scalable prognostic biomarker for risk stratification for incident liver-related outcomes and personalized management strategies.

Parallel Session 4
OF4-3 10112

Differential Effects of Antihypertensive Drug Classes on Liver-related Outcomes in MASLD/MetALD Patients with Hypertension

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Background: Patients with metabolic dysfunction-associated steatotic liver disease (MASLD) or MASLD with increased alcohol intake (MetALD) frequently develop hypertension, requiring antihypertensive therapy. However, comparative effects of antihypertensive drug classes on liver outcomes remain unclear. This study aimed to evaluate liver-related events among antihypertensive drug classes in patients with MASLD or MetALD and hypertension.
Methods: From the Korean National Health Insurance Service database, we identified 537,372 adults with MASLD or MetALD who underwent health screening (2013-2014), had hypertension between 2012-2014, and were prescribed a single class of antihypertensive medication (angiotensin-converting enzyme inhibitors [ACEis], angiotensin II receptor blockers [ARBs], beta-blockers [BBs], or calcium channel blockers [CCBs]) for 90 or more days in 2014. Individuals prescribed multiple drug classes, with pre-existing liver disease, or who died before follow-up were excluded. The primary outcome was liver-related events, including primary liver cancer, liver cirrhosis, and decompensated cirrhosis. Baseline characteristics were balanced using inverse probability of treatment weighting, and subdistribution hazard ratios calculated using Fine-Gray models to account for competing risk of death.
Results: During 3.67 million person-years, 11,313 liver-related events occurred. Compared with ACEis, ARBs reduced liver-related events (subdistribution hazard ratio 0.93; 95% confidence interval 0.91-0.96), primary liver cancer (0.95; 0.91-0.99), and liver cirrhosis (0.92; 0.90-0.95). Other antihypertensive classes showed mixed effects.
Conclusion: Antihypertensive drug classes exhibited differential effects on liver-related outcomes. ARBs showed the most consistent hepatoprotective effects across liver-related outcomes, while other classes exhibited variable results. These findings highlight the importance of considering liver-specific effects when selecting antihypertensive therapy in high-risk populations.

Parallel Session 5

OF5-1 10148

AI-Integrated Biosensor Wearables for Monitoring Metabolic Dysfunction-Associated Steatotic Liver Disease in Adolescents with Type 1 Diabetes

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Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is an emerging complication in adolescents with Type 1 Diabetes Mellitus (T1DM), driven by chronic hyperglycemia, insulin resistance, and sedentary behavior. Objective:This study assesses the impact of AI-powered wearable biosensor technology in detecting early physiological changes associated with MASLD and promoting personalized lifestyle education in adolescents with T1DM.
Methods: A 30-day observational study was conducted in Gurugram City with 260 adolescents diagnosed with both T1DM and MASLD. Participants used wearable devices equipped with biosensors measuring photoplethysmography (PPG), electrodermal activity (EDA), skin temperature, and accelerometry to track activity levels, sleep stages, heart rate variability (HRV), and blood pressure. AI algorithms analyzed trends and deviations linked to MASLD progression, triggering alerts for key markers such as reduced activity, elevated BMI (>5% from baseline), and disrupted sleep. Personalized educational feedback was provided in real-time to guide nutrition, exercise, and stress management.
Results: The wearable system effectively identified early signs of MASLD, including reduced HRV, high blood pressure, and poor sleep quality. Participants receiving AI guided feedback showed notable improvements in physical activity, sleep consistency, and adherence to dietary recommendations. Liver-related outcomes improved with increased patient engagement and awareness. AI driven education also supported better dietary choices and stress reduction strategies.
Conclusion: AI-integrated wearable biosensors offer a novel approach to managing MASLD in adolescents with T1DM by enabling early detection, personalized intervention, and continuous education. This technology holds promise for slowing disease progression and enhancing metabolic and liver health outcomes.

OF5-2 10149

The Role of Wearable Technology and Geo-Fencing in Physiological Monitoring and Pre-Transplant Optimization for Adolescents with NAFLD Undergoing Bariatric Surgery

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Background: This study investigates the utility of wearable technology integrated with geo-fencing in improving physiological monitoring, lifestyle adherence, and quality of life among obese adolescents undergoing bariatric surgery for non-alcoholic fatty liver disease (NAFLD) in Gurugram, India potentially delaying or reducing the need for future liver transplantation (LT).
Methods: A total of 840 obese adolescents with NAFLD (balanced by gender) scheduled for bariatric surgery were enrolled. Participants used the Fire-Boltt Quantum smartwatch integrated with geo-fencing alerts for 30 days postsurgery. The wearable devices monitored vital metrics including weight, blood pressure, blood glucose, step count, calorie balance, sleep patterns, motion time, and heart rate. Geo-fencing triggered real-time alerts if participants left their prescribed activity zones. Participants also completed symptom questionnaires and weekly interviews evaluating gastrointestinal health, cognitive focus, and medication reliance.
Results: Significant metabolic improvements were observed in physically active adolescents using the wearable technology. These included normalization of heart rate ($p < 0.05$), enhanced calorie expenditure, and significant reductions in blood glucose and blood pressure ($p < 0.01$). Improvements in sleep patterns and metabolic markers were also documented by physiotherapists. Additionally, less active participants demonstrated cognitive benefits, including improved memory and reduced episodes of wandering, leading to decreased medication usage. Geofencing reinforced adherence to activity recommendations, providing real-time behavioral nudges critical in the pretransplant setting.
Conclusions: Wearable technology combined with geo-fencing offers a promising tool for real-time physiological monitoring in adolescents with NAFLD undergoing bariatric surgery.

Parallel Session 5
OF5-3 10008

Sex and Menopausal Differences in the Association between Visceral Adipose Tissue and Metabolic Dysfunction-associated Steatotic Liver Disease: A Cross-sectional and Mendelian Randomization Study

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Background: Visceral adipose tissue (VAT) is recognized as a risk factor for metabolic dysfunction-associated steatotic liver disease (MASLD). The study aimed to investigate the causal relationship between VAT and MASLD.
Methods: The study comprised two parts: (1) A cross-sectional analysis of 7,596 Chinese adults assesses the relationship between visceral fat area (VFA)-quantified VAT and MASLD severity (steatosis grades S0-S3), stratified by sex/menopausal status and adjusted for confounders. (2) Mendelian randomization (MR) analyses utilize summary-level genome-wide association study (GWAS) data (MASLD, n=797,878 Europeans; VAT-related sex-specific variants, n=325,153 Europeans). Two-sample MR tests causality, while two-step MR assesses VAT's mediating role between sex hormones and MASLD.
Results: (1) In the cross-sectional study, VFA showed a graded positive association with MASLD severity, with significant interaction by sex (P=0.03) and menopausal status (P<0.001). Adjusted models revealed higher odds ratios (ORs) of severe MASLD in men (Q2=1.64; Q3=2.26; Q4=2.19 vs. Q1) and markedly elevated risks in premenopausal women (Q2=3.73; Q3=5.52; Q4=9.83 vs. Q1), particularly postmenopausal women (Q2=6.47; Q3=22.00; Q4=39.13 vs. Q1) (all p<0.001). (2) MR confirms a causal VAT-MASLD association exclusively in females (OR1=1.77, P1=2.22×10^{-6}; OR2=3.42, P2=1.25×10^{-6}) in two independent MASLD datasets. Moreover, female VAT mediated the effects of elevated bioavailable testosterone (BT) and reduced sex hormone-binding globulin (SHBG) on MASLD risk.
Conclusions: Women, especially postmenopausal, show a stronger VAT-MASLD correlation than men, with causality exclusive to women. Increasing SHBG and anti-androgen therapies may be strategies to reduce VAT accumulation and MASLD risk in women.

Parallel Session 6

OF6-1 10153

Neutrophil Elastase Undergoes Endocytosis into Hepatocytes and Contributes to Liver Injury in Alcoholic Hepatitis

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A hallmark of alcoholic hepatitis (AH) is extensive neutrophil infiltration into the hepatic parenchyma, suggesting direct interactions between neutrophils and hepatocytes. To investigate this, we performed immunohistochemistry for neutrophil-specific granule proteins, myeloperoxidase (MPO) and neutrophil elastase (NE), in liver explants from AH patients and normal human livers. In AH samples, both proteins were frequently detected within hepatocytes. Triple immunofluorescence staining using hepatocyte marker (Keratin 18) and neutrophil proteins (MPO and NE) confirmed a significantly increased number of NE-positive puncta within hepatocytes in AH livers compared to controls. This was recapitulated in an in vitro co-culture of human neutrophils and hepatocytes. Electron microscopy revealed punctate MPO signals within lipid bilayer structures in hepatocytes. Co-localization with lysosomal markers (Lamp1&2, Lysotracker) suggested that MPO is internalized via endocytosis and transported intracellularly to the lysosome-mediated degradation pathway. Among several endocytosis inhibitors tested, PI3K inhibitors (Wortmannin and Ly294002) significantly suppressed MPO uptake, suggesting a PI3K-dependent endocytosis pathway. RNA sequencing of hepatocytes following granule treatment or neutrophil co-culture showed upregulation of SERPIN E2 and A3, protease inhibitors that counteract NE activity. Proteomic analysis revealed selective degradation of hepatocyte proteins by NE, supporting its intracellular proteolytic activity post-endocytosis. In murine AH models, both NE inhibition and NE gene knockout significantly alleviated liver injury.These findings reveal that neutrophil elastase enters hepatocytes via endocytosis and promotes liver injury through proteolytic mechanisms, identifying NE as a potential therapeutic target in AH (Ethical Approval Code; HIC-2000025846, HIC-1304011763).

OF6-2 10206

IL-1R1 Deficiency Attenuates Hepatic Ischemia-Reperfusion Injury by Coordinating Oxidative Stress Control, Hepatocyte Regeneration, and Immune Rebalancing

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Background: Interleukin-1 receptor type 1 (IL-1R1) mediates sterile inflammatory pathways, yet its role in hepatic ischemia-reperfusion injury (HIRI) remains poorly defined. We investigated the impact of IL-1R1 deficiency on liver damage, regeneration, oxidative stress, and immune remodeling during HIRI.

Methods: HIRI was induced in wild-type (WT) and IL-1R1 knockout (KO) mice via 60 minutes of partial warm ischemia. Liver injury was assessed by serum ALT/AST, histology, TUNEL staining, and mitochondrial ROS (MitoSOX). Hepatocyte proliferation (Pan-Keratin$^+$Ki67$^+$), AhR expression, and inflammatory cytokines (qRT-PCR) were evaluated. Flow cytometry was used to analyze liver and splenic immune compartments, including macrophages, myeloid cells, and T/B lymphocytes.

Results: IL-1R1 KO mice exhibited significantly reduced ALT/AST levels, hepatocellular necrosis, and apoptosis compared to WT mice. Proinflammatory cytokine expression was markedly downregulated in KO livers. Hepatocyte proliferation was preserved in KO mice post-HIRI, and mitochondrial ROS levels were significantly lower, indicating protection from oxidative stress. Notably, KO mice maintained higher AhR expression in hepatocytes, suggesting preserved anti-inflammatory and detoxification signaling. Immune profiling revealed substantial remodeling in IL-1R1 KO mice, including increased retention of Kupffer cells, reduced monocyte-derived macrophages, and decreased Ly6C$^+$ monocytes and neutrophils. In the adaptive compartment, IL-1R1 KO mice retained significantly more hepatic CD19$^+$ B cells and CD3$^+$ T cells post-HIRI, including expanded CD8$^+$ T cells and attenuated CD4$^+$ T cell loss compared to WT.

Conclusions: IL-1R1 deficiency confers protection against HIRI by limiting hepatocellular damage and oxidative stress, sustaining regenerative and stress-responsive signaling, and reshaping both hepatic and systemic immune responses.

Parallel Session 6

OF6-3 10058

Role of Recombinant Human Cytoglobin against Acetaminophen-induced Liver Injury

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Background and Aims: Cytoglobin (CYGB), a gas-binding hexacoordinated globin, exhibits protective effects against chronic liver diseases, including fibrosis and cancer. This study investigates the preventive and therapeutic efficacy of recombinant human cytoglobin (rhCYGB) in a murine model of acetaminophen (APAP)-induced liver injury (AILI).
Methods: A total of 50 male C57BL/6 wild-type mice was used in this study. APAP injection was at the dose of 300 mg/kg body weight. Intravenous injections of rhCYGB in a time- and dose-dependent manner were performed to evaluate its preventive and therapeutic effects against AILI. Mice were euthanized 6 hours after APAP injection in all treatment groups to assess early liver injury. RNA sequencing was performed to identify downstream pathways and gene expression alterations.
Results: Time-dependent analysis indicated that rhCYGB administration 12 hours before APAP injection significantly reduced liver necrosis (-80%, H&E staining), apoptosis (-78%, TUNEL), and serum AST (-87%) and ALT (-94%) levels. In the dose-dependent study, a dose of 10 mg/kg rhCYGB yielded the most substantial therapeutic benefits, with reductions in necrosis (-62%), apoptosis (-44%), AST (-45%), and ALT (-83%). RNA sequencing revealed downregulation of inflammatory pathway genes, including Il1a, Tnfrsf10b, Cox16, and Cox20, alongside upregulation of anti-apoptotic genes (Bag3, Bcl2l1, Bcl3, Bcl2a1a) and autophagy-related genes (Atg2a, Atg16l2, Vps18) in rhCYGB-treated mice compared to controls, confirmed by quantitative RT-PCR. Immunoblotting demonstrated a significant upregulation of Bcl-2 expression (+134%) following rhCYGB treatment.
Conclusions: These findings demonstrate that rhCYGB confers significant hepatoprotection against APAP-induced liver injury.

OF6-4 10036

Engineering Vesicle-Mediated Metabolic Regulation and Immune Targeting for the Treatment of Autoimmune Hepatitis

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Background and Aims: Metabolic disorder promotes CD4+ T-cell activation and associated inflammatory liver injury in autoimmune hepatitis (AIH). Strategies that target CD4+ T-cell metabolism hold great prospects for treatment. Here, we investigated the energy metabolic changes of CD4+ T cells in AIH patients and mice. Furthermore, we constructed a novel targeted delivery nanosystem, that is, a hybrid vesicle (Hy-EV) of metformin engineered extracellular vesicle (Met-EV) and dendritic cell membrane vesicle (DCMV), for the treatment of AIH.
Methods: The metabolic profiles of CD4+ T cells were characterized in human AIH and mouse hepatitis models. The liver protective effect of Hy-EV was evaluated by transaminase levels, histopathology, and inflammation. The targeting ability of Hy-EV was quantitatively detected using an IVIS imaging system and a confocal microscopy.
Results: Significant differences were found in the glycolysis and OXPHOS-related gene expression in CD4+ T cells between normal control and AIH group. Hy-EV treatment effectively rescued liver injury in AIH mice. In-depth exploration found that MDV inherited Met-EV's ability to reduce CD4+ T-cell activation and cytokine release by reducing glycolysis while enhancing mitochondrial oxidative phosphorylation in such cells. In addition, DCMV component of Hy-EV displayed enhanced targeting potency for hepatic CD4+ T cells due to the overexpression of the key molecules which mediated DC-T cell contact. Lastly, multiple long-term administration of Hy-EV showed no systemic toxicity.
Conclusion: Hy-EV exploits a synthetic effect in enhancing efficacy and targeting in the treatment of AIH, which is of high value to serve as a viable strategy in clinical practice.

Parallel Session 7

OF7-1 10163

Pharmacological Inhibition of Hepatic DGAT2 Reduces Triglyceride Synthesis and Attenuates MAFLD Progression in Mice

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Background: This study primarily aimed to explore whether superadded inflammation in MAFLD increases the expression of TG synthesizing enzymes acyl-CoA: diacylglycerol acyltransferase (DGAT) 1&2 expression and associated TG synthesis in the hepatic and adipose tissues. Secondly, we investigated the effects of the FXR agonist INT-747 and the DGAT2 inhibitor (DGAT2i) on the regulation of the hepatic DGAT-TG pathway in MAFLD (with or without LPS).
Methods: After 90 days of feeding with either a high-fat diet (HFD) or chow, mice were orally administered INT-747 or a DGAT2 inhibitor (DGAT2i) for 7 days. Additionally, treatment groups were given lipopolysaccharide (LPS) to assess the effect of superadded inflammation in the context of fatty liver.
Results: HFD-induced MAFLD mice exhibited significantly elevated DGAT1 and DGAT2 mRNA and protein expressions in hepatic and adipose tissues compared to chow-fed mice. LPS administration to MAFLD mice led to a further marked increase in hepatic DGAT2 expression and associated hepatic TG levels, while hepatic DGAT1 and adipose tissue DGAT1 and DGAT2 expression remained unchanged, consistent with immunohistochemical findings. Treatment with either INT-747 or DGAT2i in MAFLD mice, with or without LPS challenge, resulted in a reduction of hepatic and circulating plasma TG levels, along with decreased DGAT 1 and DGAT 2 expression.
Conclusion: Our novel findings strengthen the link between dramatically elevated hepatic but not adipose tissue DGAT2 expression and associated TG synthesis in MAFLD mice with superimposed inflammation. INT-747 and DGAT2i treatments ameliorate MAFLD progression by inhibiting hepatic DGAT2 over-expression and associated TG synthesis.

OF7-2 10071

Deficiency of Hepatic Protein Tyrosine Phosphatase 1B is Protective in a Mouse Model of MASH

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Metabolic dysfunction-associated steatohepatitis (MASH) is a leading cause of liver-related morbidity and mortality. The current interventions are limited, underscoring the need for novel mechanism-based pharmacotherapies. Protein tyrosine phosphatase 1B (PTP1B) regulates phosphotyrosine signaling and hepatic metabolism, but its role in MASH remains incompletely understood. In this study, we observed elevated hepatic PTP1B expression in the fast food diet (FFD) dietary mouse model of MASH and, notably, in liver biopsies from MASH patients. To elucidate the impact of modulating PTP1B expression in MASH, we used mice with liver-specific PTP1B disruption in the FFD model of the disease and then monitored alterations in inflammation, steatosis, and fibrosis. PTP1B deficiency ameliorated FFD-induced hepatic injury and inflammation as evidenced by lower alanine aminotransferase, TNF and IL1B, and NFkB phosphorylation. Additionally, PTP1B deficiency partially rebalanced the hepatic and systemic lipid dysregulation under the FFD-fed state. Notably, PTP1B deficiency alleviated the hepatic fibrosis induced by the prolonged FFD regimen. Moreover, mice with hepatic PTP1B deficiency exhibited improved glucose control under FFD independently of body weight changes. Mechanistically, PTP1B deficiency was associated with enhanced hepatic insulin signaling and decreased oxidative stress. Collectively, these findings establish that hepatic PTP1B deficiency modulates several pathways implicated in MASH and manifests improvements that will curtail the progression of the disease. Further investigation is warranted into targeting this phosphatase as part of the armamentarium in the therapeutic landscape for MASH.

Parallel Session 7

OF7-3 10025

Development and Characterization of a Murine Model of Anorexia Nervosa-Associated Microvesicular Steatosis

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Background: Anorexia nervosa (AN), prevalent among young women, is often associated with hepatic microvesicular steatosis. While hypoalbuminemia and impaired lipid transport are suspected contributors, the underlying mechanisms remain unclear. Moreover, hepatic lipid metabolism in AN may differ fundamentally from that in simple starvation. This study aimed to establish a murine model of AN-associated microvesicular steatosis and to compare it with models of caloric restriction and diet-induced obesity.
Methods: Female C57BL/6 mice (5 weeks old) were assigned to four groups (n=8): food-restricted (FR), AN-like, high-fat diet (HFD), and control (Ctr). FR and AN mice underwent progressive time-restricted feeding; after 7 days of acclimatization, FR and AN mice underwent progressive time-restricted feeding (6 h/day on Day 6 to 3 h/day from Day 9 onward). On Day 17, animals were euthanized; serum and liver tissues were collected. Serum biochemistry (ALT, TG, T-CHO), liver histology (H&E, Oil Red O, EM), Adipophilin immunostaining, and RNA sequencing.
Results: FR and AN groups showed significant weight loss (~70%). Macrovesicular steatosis was evident in HFD mice. While H&E staining revealed minimal lipid accumulation in FR and AN groups, Oil Red O identified microvesicular fat in 37.5% of AN mice. Adipophilin-positive areas were significantly higher in AN and HFD groups ($p<0.05$). Serum TG levels were lower in FR and AN groups. RNA-seq demonstrated AN and FR mice shared similar profiles, distinct from HFD and controls.
Conclusions: This novel murine model reveals unique features of AN-associated steatosis, not predicted by serum markers. Further studies on hepatic autonomic regulation are warranted.

OF7-4 10065

Deregulation of FTO Isoforms in the Progression of Nonalcoholic Fatty Liver Disease to Nonalcoholic Steatohepatitis and its Amelioration with Entacapone

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Background and Aim: The increasing incidence of obesity, metabolic syndrome, and MASLD emphasizes the need for new management approaches. Fat mass and obesity-associated (FTO) protein is associated with obesity. Here, we aimed to examine the expression and progression of FTO isoforms in MASLD. Furthermore, we repurposed entacapone, a known FTO inhibitor, for the amelioration of MASLD.
Methods: A retrospective study included 75 adults with biopsy-proven MASLD (n=25), MASH (n=25), and cirrhosis (n=25), and a healthy group (n=5)(age, 36 ± 19 years; body mass index [BMI], > 28 kg/m2). Liver histology was assessed by microscopy, whereas ALT, AST, leptin, and adiponectin levels were measured (ELISA). FTO isoform expression (1, 3, 5, 12) was assessed via RT-qPCR, IHC, and WB. Validation in primary human hepatocytes involved FFA and entacapone treatment, assessed by Oil Red O staining and MTT assay.
Results: The expression of FTO isoforms (1,3, and 5) was relatively higher in MASLD and MASH patients (p&It;0.05). In contrast, FTO-12 expression was higher in cirrhotic patients. Interestingly, isoforms 1, 3, and 5 positively correlated with MASLD progression. In vitro studies corroborated the clinical observations showing elevated expression (p&It;0.01) of isoforms 1, 3, and 5 and decreased expression of isoform 12. Interestingly, treatment with entacapone downregulated the expression of FTO isoforms, except isoform 5.
Conclusion: FTO expression is deregulated during MASLD progression, with isoform 12 overexpressed in cirrhosis and 1, 3, and 5 elevated in MASLD and MASH. Entacapone normalized FTO isoform expression in a primary human hepatocyte MASLD model, indicating therapeutic potential.

Parallel Session 8

OF8-1 10007

Xietu Hemu Prescription Suppresses Adipocytogenesis and Alleviates Dysregulation of Lipid Metabolism in Vitro through LEP/AMPK/PPARG Axis

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Background: Xietu Hemu prescription (XHP) is a Chinese patent formula optimized based on the theory of phlegm-dampness, which has been clinically proven to be effective against obesity and related MASLD, but its molecular mechanism has not yet been clarified.
Objective: To elucidate the mechanism of XHP inhibits adipocyte differentiation and regulating lipid metabolism.
Methods: The main therapeutic direction of XHP in metabolic-related diseases was analyzed by 3T3-L1 cell differentiation model combined with RNA-seq analysis of gene expression changes during white adipogenesis. Network pharmacology analysis was used to predict therapeutic targets. The accumulation of lipid droplets and the expression of related proteins was verified by Oil Red O staining and Western blot. Bioinformatics analysis and molecular docking identified core targets and signaling pathways, which were further validated via immunofluorescence and siRNA interference.
Results: XHP serum significantly inhibited 3T3-L1 cell differentiation, decreased lipid droplet accumulation and TC/TG levels, and down-regulated PPARg, C/EBPa, and FABP4 expression. RNA-seq and network pharmacological intersectionality analyses identified 23 core targets enriched in the AMPK signaling pathway. Molecular docking confirmed the strong binding ability of XHP compounds to targets such as LEP (-34.405 kcal/mol) and FASN (-9.807 kcal/mol). The Elisa assay demonstrated that XHP serum enhanced leptin autocrine secretion and subsequently activated the AMPK signaling pathway, while LEPR knockdown abolished this effect.
Conclusions: XHP inhibits adipogenesis and improves lipid metabolism homeostasis via the LEP/AMPK/PPARG pathway, offering a promising multi-target strategy for obesity-related metabolic disorders.

OF8-2 10014

Myricetin Ameliorates MASLD by Enhancing Mitochondrial Function and Promoting PINK1/Parkin-dependent Mitophagy

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), particularly its severe form metabolic dysfunction-associated steatohepatitis (MASH), poses significant health risks, leading to liver fibrosis and cirrhosis. While traditional Chinese medicine has shown potential in treating MASLD, the mechanisms and efficacy of specific compounds like myricetin remain under-explored. This study aims to investigate the effects of myricetin on liver steatosis, mitochondrial function, and mitophagy in MASLD models, hypothesizing that myricetin could serve as a therapeutic agent by enhancing mitochondrial function and promoting PINK1/Parkin-dependent mitophagy.
Methods: Using a high-fat diet (HFD) and choline-deficient high-fat diet (CD-HFD)-induced mouse models, we evaluated the impact of myricetin on MASLD. Hepatic steatosis, inflammation, and systemic insulin resistance were assessed through various biochemical and histological analyses. RNA sequencing (RNA-seq) was conducted to elucidate underlying molecular mechanisms, focusing on fatty acid oxidation and mitophagy pathways.
Results: Myricetin treatment significantly reduced hepatic triglyceride accumulation, lowered serum AST and ALT levels, and improved insulin sensitivity in HFD- and CD-HFD-induced mice. RNA-seq analysis revealed an upregulation of genes involved in fatty acid beta-oxidation and mitochondrial function. Additionally, myricetin promoted mitophagy as evidenced by increased PINK1 and Parkin protein levels and enhanced mitophagy marker expression.
Conclusion: Myricetin effectively ameliorates MASLD by enhancing fatty acid beta-oxidation and mitochondrial function, offering a promising therapeutic strategy for MASH. The promotion of PINK1/Parkin-dependent mitophagy further supports its role in protecting hepatic cells, suggesting broader implications for metabolic disease treatment.

Parallel Session 8
OF8-3 10122

A Novel PEX13 Knockout Liver Cell Line Generated Using CRISPR Prime Editing Provides New Insights into Steatotic Liver Disease

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Background: Peroxisomes are important cellular organelles involved in fatty acid synthesis and oxidation. Peroxisome disorders are caused by major peroxisome dysfunction and have been associated with liver disease in some patients. Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common liver disease affecting up to 38% of adults, globally. Extensive research on MASLD is aimed at identifying the molecules and mechanisms involved in development of disease. We generated and characterized a novel PEX13 knock-out cell line model using CRISPR prime-editing to help understand the role of peroxisomes in the development of MASLD.
Methods: A novel cell line with the mutation PEX13 p.Arg16Ter was created in a healthy derived immortalised human hepatocyte (IHH) cell line using CRISPR prime editing. These cells were treated with or without free fatty acids to reflect steatosis. The gene expression of lipid metabolism genes was analysed using qRT-PCR.
Results: The insertion of the mutation PEX13 p.Arg16Ter, which creates a non-functional protein, was confirmed by Sanger sequencing. Our studies indicate that the PEX13knockout cell line had significantly reduced the expression of PEX13 and key lipid metabolism genes SREBF1, CD36, PPARG. This suggests a disruption in fatty acid synthesis, uptake, and insulin sensitivity.
Conclusion: We have generated a novel PEX13 knockout model of hepatic steatosis that can be used to understand lipid dysregulation in MASLD. Our results indicate that defects in the peroxisomal membrane protein encoding gene, PEX13 and thus peroxisomes themselves, significantly impact lipid metabolism in the liver.

Parallel Session 9

OF9-1 10207

A Proof of Concept for Ultrasound Based Artificial Intelligence Quantification of Liver Steatosis and Fibrosis

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Background: Early detection of patients with at-risk MASH is vital due to the heightened risk of disease progression. Current FibroScan diagnostics are costly, highlighting the importance for risk stratification to guide early clinical decision-making.
Methods: Analysis was done on a multi-ancestral Asian cohort, in which a subset underwent liver biopsy for suspected MASH. Histological activity was assessed using the CRN NAS and FibroScan data is available for liver stiffness estimation. Clinical profiling included metabolic comorbidities (T2–diabetes, hypertension, and dyslipidemia) and adjustments for age, ethnicity, smoking, alcohol use, and other relevant covariates. A pipeline will be constructed to analyze initial ultrasound images, focusing on key annotated features (Liver, gallbladder, abdominal wall, etc.) to differentiate patients meeting criteria for potential MASH (defined by FAST score ≥ 0.35) through a CNN model.
Results: n=454 patients (M:F = 234:220, median BMI 26.5 [IQR 20.2–32.8]) were analyzed at the time of writing. Using YOLOv11, we achieved mAP of 0.549 at 0.5 recall across all classes, and 0.892 specifically for liver masks. Metrics derived from the segmented masks (Echogenicity, mask shape, segmentation area) were integrated with biopsy and FibroScan data. A convolutional neural network (CNN) model trained on ultrasound images achieved 80.0% test accuracy for identifying at-risk MASH patients. The model demonstrated high specificity, correctly identifying 85% of all non-at-risk patients.
Conclusions: The ongoing development demonstrates potential for greater efficiency in early intervention. Data from additional patients (n=827) will be used to refine the model, with full results to be shared at the meeting.

OF9-2 10161

A Novel Fibrosis NIT that Uses the Myofibroblast Marker Fibroblast Activation Protein (FAP) and FIB4 in Metabolic Associated Steatotic Liver Disease

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Background: Fibrosis is a key driver of pathogenesis in metabolic dysfunction associated steatotic liver disease (MASLD). Fibroblast activation protein (FAP) is an extracellular gelatinase that is a marker of activated mesenchymal fibrogenic cells. This study created a diagnostic model, FAP–Index, utilising circulating FAP (cFAP) for triage of patients at risk of advanced fibrosis associated with diabetes mellitus or MASLD.
Method: Retrospective training (n=160) and external validation cohorts (n=332), with prevalence of histologic advanced fibrosis of 20% and 11%, were recruited from tertiary care centres. Our inhouse onestep FAP specific enzyme assay measured cFAP. The enzyme DPP4 was also quantified in sera. FIB4 and NAFLD fibrosis score (NFS) were calculated.
Results: A statistical model, FAP–Index, containing age, type 2 diabetes, ALT and ordinal cFAP, was developed using logistic regression. FAP–Index AUROC for advanced fibrosis was 0.875 (95% CI 0.813–0.938) and 0.841 (95% CI 0.776–0.906) in the training and validation cohorts. Low cutoff (Sensitivity 84.3%, negative predictive value (NPV) 95%) and high cutoff (Specificity 99.2%, positive predictive value 92.9%) for advanced fibrosis minimised indeterminates. FAP–Index following FIB4 reduced the frequency of indeterminate results by one-third to half compared to FIB4 alone. FAP–Index was comparable with FIB4 and superior to NFS, but cDPP4 instead associated with steatosis.
Conclusion: FAP–Index is a novel, rapid, robust, inexpensive diagnostic tool for advanced fibrosis in MASLD. Applying FAP–Index following FIB4 facilitates accurate risk-stratification of patients by greatly reducing the frequency of indeterminate results compared to FIB4 or NFS alone, without compromising NPV.

Parallel Session 9
OF9-3 10177

Development of Overt Hepatic Encephalopathy Increases Mortality in Patients with Cirrhosis: A Multicenter Retrospective Cohort Study

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Background: Overt hepatic encephalopathy (OHE) is a severe complication of liver cirrhosis. However, data on its incidence, prognostic significance, and associated risk factors in patients without OHE at baseline remain limited.
Methods: A multicenter retrospective cohort study was conducted by reviewing records of hospitalized patients with cirrhosis at three institutions in Japan. OHE was defined as West Haven grade >= 2 and its incidence during the follow-up was estimated using the cumulative incidence function. Prognostic factors were assessed using Cox proportional hazards regression analysis, with the development of OHE and hepatocellular carcinoma (HCC) treated as time-dependent covariates. Independent predictors for OHE development were analyzed using Fine-Gray proportional hazards regression analysis.
Results: Among 652 patients, the median age was 67 years, and 53% were male. The median model for end-stage liver disease (MELD) score was 9. During a median follow-up period of 3.2 years, 136 patients (21%) developed OHE and 183 patients (28%) died. The cumulative incidence of OHE at 1, 3, and 5 years was 8%, 16%, and 20%, respectively. Multivariable analysis demonstrated that OHE development (hazard ratio [HR], 3.07; 95% confidence interval [CI], 1.99-4.75) was a significant independent prognostic factor, regardless of age, sex, liver functional reserve, and HCC development. Furthermore, multivariable analysis identified lower body mass index, higher MELD score, lower albumin levels, and higher ammonia levels as independent predictors for OHE development.
Conclusions: OHE development is common and increases mortality among patients with cirrhosis. Therefore, close monitoring of high-risk populations is warranted to improve outcomes.

Parallel Session 10

OF10-1 10119

Wilms Tumor 1 Induces Hepatic Stellate Cell Invasion that Develops Bridging Fibrosis in Chronic Liver Injury

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Background: Chronic liver injury increases the extracellular matrix (ECM) deposition, and its further remodeling develops Bridging fibrosis (BF). We investigated the mechanistic role of hepatic stellate cells (HSCs) in BF formation by focusing on Wilms Tumor 1 (WT1).
Methods: Single-cell RNA-seq and GeoMx spatial transcriptomics were used to resolve cellular phenotypes and their location during BF formation (Spatio-temporal single-cell analysis).To examine the migration and ECM remodeling (i.e. invasion) capacity of HSCs, a 3D collagen-gel invasion assay was used. Transcriptomic change of HSCs during invasion were analyzed. HSC-specific WT1 KO mice were generated and subjected to bile duct ligation (BDL) to induce BF in mouse livers.
Results: Spatio-temporal single-cell analysis revealed a dynamic change in migration, invasion, and ECM production in fibrotic cell populations. ECM-producing myofibroblastic HSCs were enriched in Zone 1 while migrative and proliferative invasive HSCs emerged in Zone 2. Collagen-gel invasion assay indicated that HSCs invasion is required for full activation of HSCs that produce robust ECM. Transcription factor (TF) enrichment analysis identified WT1 as the most enriched TF in invasive HSCs. WT1 knockdown inhibited HSC invasion in vitro. HSC-specific WT1 mice failed to develop BF after the BDL. Transcriptomic analysis further indicated Cathepsin K (Ctsk) as a downstream effector of WT1. Ctsk inhibitor Odanacatib prevented BF formation after the BDL.
Conclusion: Spatio-temporal single cell analysis of BF liver and functional assay of HSC defined a unique invasive phenotype of HSCs regulated by WT1. WT1 and Ctsk can be a promising therapeutic target for liver fibrosis.

OF10-2 10159

Effects of Hydroxynonenal on Hepatic Macrophages in the Pathogenesis of MASLD

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Background: Hepatic macrophages play an important role in the development of liver fibrosis in MASLD by producing inflammatory cytokines and fibrosis-promoting factors. We analyzed the effects of hydroxynonenal (HNE) on hepatic macrophages in the development of MASLD.
Methods: (1) CD68, F4/80, and HNE staining of liver tissues from MASH patients and MASH model mice were performed. (2) The association between the degree of HNE deposition and the number of hepatic macrophage aggregates (HMA) was evaluated in 60 MASLD patients. (3) NC-fed mice were divided into HNE-treated and non-treated groups. HNE was administered intraperitoneally daily to the treated group. At 8 weeks, the presence of HMA and the degree of liver fibrosis was evaluated. (4) CDAA diet-fed mice were divided into Alda-1 (ALDH2 agonist) treated and non-treated groups. Alda-1 was administered intraperitoneally to the treated group for 8 weeks. The effects of HNE detoxification on HMA formation and liver fibrosis were evaluated.
Results: (1) Numbers of HMA were observed in the liver tissues of MASH patients and MASH model mice, and strong HNE deposition was observed in the HMAs. (2) Liver tissues with high HNE deposition showed significantly more HMAs and higher liver fibrosis. (3) Liver tissues of the HNE-treated group showed significantly more HMAs and higher liver fibrosis than the non-treated group. (4) Alda-1 treatment significantly reduced the number of HMA and the degree of liver fibrosis.
Conclusions: HNE may be involved in the formation of HMA and the development of liver fibrosis in the pathogenesis of MASLD.

Parallel Session 10
OF10-3 10010

DHX9 Loads Hepatocyte-derived Exosomal miR-106b to Activate Hepatic Stellate Cells via Actin Cytoskeleton in MASLD

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Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MAFLD) has emerged as the most prevalent chronic liver disease worldwide. The key point of MASLD is metabolic dysfunction-associated steatohepatitis (MASH) stage. Exosomes are membrane-bound vesicles containing proteins, lipids, RNAs and DNAs. MiRNAs are abundant molecules in exosomes, which exert effects by targeting genes in exosome recipient cells.
Method: MASLD patients and healthy people were recruited and collected plasma to extract exosomes to identify the miR-106b level. DIR dye was used to track the uptake of exosome in vivo and in vitro. RNA-sequencing was conducted to explore the downstream pathway of silencing DAB2 in hepatic stellate cells (HSCs). MiRNA pull down and mass spectrometry analysis were conducted to seek the binding protein of miR-106b. Methionine-choline deficient (MCD) diet was utilized to feed C57BL/6J mice for 8 weeks to construct a MASH model.
Result: MiR-106b was upregulated in exosomes derived from hepatocytes treated with PA (PA-exo) and exosomes derived from hepatocytes treated with corresponding BSA (Con-exo). Adding PA-exo and miR-106b induced the activation of HSCs. Injecting PA-exo aggravated the liver fibrosis in MCD mice. AAV-anti-miR-106b could relieve the degree of liver fibrosis in MCD mice. DAB2 expression was inhibited by miR-106b in HSCs. Silencing DAB2 activated HSCs via actin cytoskeleton pathway. In mass spectrometry analysis, DHX9 was found to bind miR-106b.
Conclusion: In MASLD patients and mice, hepatocyte-derived exosomal miR-106b were upregulated, and exerted a pro-fibrogenic effect via targeting DAB2 and actin cytoskeleton pathway. Under lipotoxic stress, DHX9 selectively loads miR-106b into exosomes.

Parallel Session 11

OF11-1 10009

Mechanism of TRPML1 in MAFLD: AMPK-Mediated Regulation of Autophagy and Lipid Metabolism

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD), formerly NAFLD, lacks clear pathogenesis and effective therapies. TRPML1, a lysosomal cation channel, is implicated in diseases but its role in hepatic lipid metabolism and MAFLD is unknown. This study explored TRPML1's mechanism and therapeutic potential.
Methods: TRPML1 expression was analyzed in MAFLD patient liver tissues (GEO database), validated in clinical samples, high-fat diet-fed TRPML1-knockout mice, and palmitic acid (PA)-treated HepG2 cells. Pharmacological activation/inhibition of TRPML1 assessed lipid deposition, ROS, and transcriptomic changes. Pathway analysis focused on AMPK/SQLE signaling and autophagy.
Results: TRPML1 was upregulated in MAFLD patients, animal models, and cells. TRPML1-knockout mice showed worsened lipid metabolism under high-fat diet. Activating TRPML1 reduced PA-induced lipid accumulation and ROS in HepG2 cells, while inhibition exacerbated these effects. Transcriptomics linked TRPML1 to AMPK/SQLE pathway activation and enhanced autophagy, which improved lipid homeostasis.
Conclusion: TRPML1 is compensatorily elevated in MAFLD and regulates lipid metabolism via AMPK/SQLE signaling and autophagy, highlighting its potential as a therapeutic target. Pharmacological TRPML1 activation may alleviate MAFLD progression. Further studies should prioritize clinical translation.

OF11-2 10221

Noninvasive Initiation and Monitoring of the Therapy with TNR-beta Agonist Resmetirom (RT) Using LIVERFASt (LFAST), FIB-4 and Vibration-controlled Transient Elastography (VCTE, Fibroscan) in Patients with MASH

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Background: LFAST is a new blood-based NIT that assess fibrosis, activity, and steatosis. Aims. to assess the dynamic of LFAST, FIB-4 and VCTE in monitoring patients on-RT (mean-change and fibrosis progression rate (PR) from baseline to repeated NIT).
Method: On-RT patients with baseline (t0) and repeated (t1) NITs have been included retrospectively. Statistics included Kaplan Meier non-parametric censored at -10% PR from t0, Tukey-Kramer Multiple-Comparison Test and subgroup analysis for dose/GLP-1 receptor agonists (GLP-1RA) analysis.
Results: Eligible patients without RT discontinuation: n=86, 61.4% 80mg-dose, 39%-male, 47%-T2D, 40% GLP-1RA, mean(se) age 61.5(1.3), BMI 32.6(0.7), ALT 45(3), FIB4 1.78(0.14). T0-prevalence of F2F3 were 63%(LFAST) and 44%(VCTE). Median(max) delays(mths) t0-to-t1 were 3.4(LFAST,VCTE) and 2.23(FIB4). 50pts. with t0-FIB4 1.3(2.0) or more had no change at t1, (1.75vs1.60, Fig.1b), ALT (45vs41) or AST (40vs36), platelets count (232vs241), all p=ns. 9pts had repeated VCTE (median t0-9.2 vs t1-10.7Kpa). 40pts achieved t1-LFAST with median scores (t0vst1): fibrosis (0.49vs0.39,p&It;0.05, Fig 1a), steatosis (0.48vs0.40,p&It;0.001, Fig. 1c), activity (0.42vs0.44,p=ns). Median(range) PR t0-to-t1 per month were: FIB4 -0.0007 (-9.8;1.5), LFAST-fibrosis -0.02 (-0.79;0.23) and steatosis -0.005 (-1.33;0.17). After 3.6mths of RT, LFAST-fibrosis PR of -10% or lower from t0 has been achieved more within 80mg-RT group than within 100mg-RT (54.6%vs27.3%, Cox Mantel p&It;0.05).(Fig 1d) The significant decrease t0-to-t1 in the total cholesterol has neither impacted the ApolipoproteinA1 [132 vs 147mg/dl] or LFAST-fibrosis score.
Conclusion: RT-Initiation based on NITs is efficient and allows further non-invasive monitoring. A rapid trend in fibrosis and steatosis improvement was observed, mainly in the 80mg-RT group.

Parallel Session 11
OF11-3 10006

Non-targeted Metabolomics Sequencing Combined with 101 Machine Learning Algorithms to Analyse Key Metabolites in Varying Degrees of Non-alcoholic Fatty Liver Disease

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Background: We are committed to investigating the key metabolites in NAFLD disease progression through metabolomic sequencing.
Methods: Forty plasma samples from each of the normal group (N), and low (L), medium (M) and high (H) NAFLD group patients were collected for untargeted metabolomic sequencing. Sample correlation, principal component analysis, and OPLS-DA revealed different metabolic profiles between normal controls and different degrees of NAFLD. Further clustering identified candidate metabolites that showed gradient changes in NAFLD process and their related pathways were explored. Then 101 machine learning combinations were used to screen the characteristic metabolites in the optimal model. Metabolite content level analyses were performed to obtain key metabolites with consistent and differential content trends in different degrees of NAFLD. Finally, a nomogram diagnostic model was constructed and evaluated based on key metabolites.
Results: The total number of differential metabolites 1 was 130 in groups L versus N, 136 in groups M versus N, and 162 in groups H versus N. 18 were candidate metabolites common to all stages of NAFLD progression, which were mainly involved in arachidonic acid metabolism. Nine characteristic metabolites were extracted from the optimal model LASSO+LDA, of which norleucine, myristic amide, 17-hydroxy-4-hydroperoxydocosahexaenoate, and prostaglandin H2 were further regarded as key metabolites. Nomogram model constructed from four key metabolites with strong diagnostic power for NAFLD.
Conclusion: The present study identified four key metabolites that were valuable for the diagnosis and progression of NAFLD, and was expected to provide theoretical support for the optimisation of precise diagnostic and therapeutic strategies.

Parallel Session 12

OF12-1 10182

Natural Killer Activating Receptor Ligands are Promising Biomarkers to Predict the Pathogenesis of At-risk MASH

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Aim: Patients with a NAFLD activity score ≥4 and significant fibrosis (≥F2) are defined as at-risk MASH, who are at increased risk for disease progression and may benefit from therapeutic strategies. The degree of intrahepatic natural killer (NK) cell infiltration has been reported to correlate with MASLD progression. The objective of this study is to evaluate the predictive utility of NK cell-activating receptor ligands for identifying at-risk MASH.
Methods: This study cohort comprised 69 patients with biopsy-proven MASLD. Serum levels of MHC class I polypeptide-related sequences A and B (MICA and MICB), and B7H6 were measured. Patients were categorized into MASL (n=25), non-at-risk MASH (n=19), and at-risk MASH (n=25) groups. Ligand levels were statistically compared among groups, and clinical characteristics related to their elevation were investigated. Additionally, logistic regression analysis was performed to identify predictors of at-risk MASH.
Results: MASH patients had higher ligand levels than MASL patients. B7H6 levels significantly correlated with portal inflammation ($p < 0.001$) and fibrosis stage ($p < 0.001$), and showed a trend with NAS score ($p < 0.05$). MICB showed a marginal correlation with fibrosis ($p=0.075$). B7H6 levels were highest in the at-risk MASH group. Logistic regression revealed that B7H6 was a significant predictor of at-risk MASH in both univariate ($p=0.024$) and multivariate models adjusted for sex, age, and BMI ($p < 0.001$).
Conclusion: Elevated serum B7H6 levels are associated with portal inflammation, advanced fibrosis, and increased risk of at-risk MASH, suggesting its potential as a predictive biomarker.

OF12-2 10162

Understanding the Microenvironment and Progression of Liver Fibrosis to Cancer for Developing Novel Precision Therapy

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Background: Protein kinases are critical therapeutic targets for curing hepatocellular carcinoma (HCC). As a serine/threonine kinase, the potential roles of STK39 in liver fibrosis and cancer remain to be explored.
Methods: We profile the whole kinome expression in clinical liver cancer samples and identify the overexpression of STK39. We then established STK39 knockout mice using CRISPR/Cas9 technology and investigated the role of STK39 in various liver fibrosis and cancer models.
Results: We firstly report that STK39 is highly overexpressed in clinical HCC tissues compared with adjacent tissues, high expression of STK39 was induced by transcription factor SP1 and correlates with a poor patient's survival. Gain and loss of function assays revealed that overexpression of STK39 promotes HCC cell proliferation, migration and invasion. In contrast, the depletion of STK39 attenuated the growth and metastasis of HCC cells. Moreover, knockdown of STK39 induces the HCC cell cycle arrest in the G2/M phase and promotes apoptosis. In mechanistic studies, RNA-seq revealed that STK39 positively regulates the ERK signaling pathway. Mass spectrometry identified that STK39 binds to PLK1. STK39 promotes HCC progression and activates the ERK signaling pathway that is dependent on PLK1. In the STK39 knockout mice model, we found the critical role of STK39 in viral infection and the progression of liver fibrosis and cancer.
Conclusion: Our study uncovers a novel role of STK39 in viral infection and the progression of liver fibrosis and cancer and suggests STK39 as a prognosis biomarker and a promising drug target of liver fibrosis and cancer.

Parallel Session 12
OF12-3 10160

Single Nuclei RNA Sequencing Shows the Engagement of PPARD Target Genes Primarily in Hepatocytes and Cholangiocytes by the Selective PPAR-delta Agonist Seladelpar

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Background and Aims: The selective Peroxisome proliferator-activated receptor delta (PPARD) agonist seladelpar reduces liver injury and modulates bile acid metabolism in preclinical models. Seladelpar was recently approved for the secondary treatment of primary biliary cholangitis (PBC). Despite its beneficial effects for liver diseases, the target cells of seladelpar on a single cell level remain unknown. This study aimed to investigate the effect of seladelpar on single liver cells.
Methods and Results: CD-1 mice were gavaged with vehicle or seladelpar (10 mg/kg body weight), and liver was harvested 6 hrs later. Single nuclei RNA sequencing (snRNA-seq) analysis showed the engagement of PPARD target genes primarily in hepatocytes and cholangiocytes by seladelpar. The top two upregulated genes, Ehhadh and Cyp4a14 are related to fatty acid metabolism and were increased in hepatocytes, cholangiocytes and Kupffer cells. Abcb4, an important canalicular transporter with hepatoprotective effects, was significantly upregulated in hepatocytes. We confirmed upregulated Abcb4 gene expression in seladelpar-treated primary mouse hepatocytes isolated from C57BL/6 mice. We further incubated nonparenchymal liver cells with seladelpar. Although there was a significant increase in the PPARD responsive genes Pdk4 and Angptl4 in cholangiocytes, Kupffer cells, and hepatic stellate cells, seladelpar did not exert specific liver protective effects in these cell types.
Conclusion: The selective PPARD agonist seladelpar induced PPARD-responsive genes primarily in hepatocytes and cholangiocytes. Seladelpar upregulated Abcb4 in hepatocytes, which might contribute to its beneficial effects in cholestatic liver disorders.

Parallel Session 13

OF13-1 10095

Clinical Significance of Leptin Receptors and Promoting Roles of Leptin in Hepatocellular Carcinoma

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Background: Obesity is a well-established risk factor for cancer development in various organs, including the liver. Leptin, an adipokine produced by adipose tissue in obesity, has been proposed as a key mediator linking adiposity to cancer. In hepatocellular carcinoma (HCC), however, the role of leptin remains inconclusive. This study thus aims to investigate roles of leptin and its receptor in the progression of HCC.
Methods: Leptin receptor (LEP-R) expressions in HCC tissue were investigated using immunohistochemistry. Roles of leptin on cell proliferation was examined using MTT assay. Effects of leptin on migration and invasion were assessed using wound healing assay and Boyden chamber Transwell assay. Molecular mechanisms underlying the effects of leptin on HCC progression were determined by Western blot analysis.
Results: HCC patients with high LEP-R expressions had significantly elevated alanine aminotransferase levels ($P<0.05$). However, low LEP-R is marginally associated with cirrhotic status of the patients ($P=0.08$). HCC cells treated with leptin did not show a different proliferation rate compared with the vehicle control. In contrast, leptin significantly promoted migration and invasion of HCC cells ($P<0.05$). Western blots revealed that HCC cells with leptin treatment had increased the phosphorylation of focal adhesion kinase and signal transducer and activator of transcription 3, resulting in the increased epithelial-mesenchymal transition markers.
Conclusion: The increased LEP-R expression was associated with hepatocellular damage markers. While leptin exerted promoting roles on HCC progression. These findings suggested that leptin-LEP-R axis play a significant role in obesity-associated HCC.

OF13-2 10221

The Risk of Decompensation in Steatotic Liver Disease-related Hepatocellular Carcinoma after Curative Treatment

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Background and Aims: Treatment options for steatotic liver disease (SLD) remain limited compared to viral hepatitis, potentially affecting the prognosis of patients with hepatocellular carcinoma (HCC). This study aimed to compare clinical outcomes between patients with SLD-related and viral-controlled HCC following curative treatment.
Methods: We retrospectively analyzed 380 patients undergoing radiofrequency ablation (RFA) for primary HCC (maximum diameter ≤3cm, ≤3 tumors): 255 with SLD-related HCC and 125 with viral-controlled HCC. Viral control was defined as sustained virological response for hepatitis C (n=80) or undetectable hepatitis B viral level during nucleos(t)ide analog therapy (n=45) before HCC diagnosis. We evaluated overall survival, recurrence, and hepatic decompensation using Kaplan-Meier method and multivariable Cox proportional hazards models. The findings were validated in a surgical cohort of 120 patients (70 SLD-related, 50 viral-controlled).
Results: The 3- and 5-year survival rates were 81% and 62% for SLD-related HCC and 94% and 89% for viral-controlled HCC, respectively ($p<0.001$, log-rank test). Multivariable analysis revealed no significant difference in recurrence rates between the two groups (adjusted hazard ratio [aHR]=1.06, 95% CI 0.75-1.48, $p=0.75$). However, SLD-related HCC demonstrated significantly higher hepatic decompensation risk (aHR=6.17, 95% CI 2.39-15.9, $p<0.001$) and worse overall survival (aHR=2.04, 95% CI 1.28-3.23, $p=0.003$). Similar results were observed in the surgical validation cohort.
Conclusions: Patients with SLD-related HCC have significantly higher hepatic decompensation risk than those with viral-controlled HCC, leading to poorer overall survival despite similar recurrence rates. These findings underscore the need for effective therapies targeting the underlying liver disease in SLD, including metabolic dysfunction.

Parallel Session 13
OF13-3 10130

Micro-RNA Gene Polymorphisms and Development of Hepatocellular Carcinoma in Egyptian Patients with Chronic Viral Hepatitis

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Background: The development and progression of hepatocellular carcinoma (HCC) is a multistage process involving the deregulation of genes that are crucial to cellular processes. Multiple risk factors are correlated with HCC. MicroRNA is differentially expressed in development of different types of malignancies, including hepatic malignancy. Single nucleotide polymorphisms (SNPs) are the most common sequence variation in human genome. SNPs in miRNAs may affect transcription, processing or target recognition and result in malignant diseases.
Aim: To determine the association between micro-RNA gene polymorphisms and development of HCC in Egyptian Patients.
Methods: This study included 200 individual who were matched in age and sex. Tumor staging was done using BCLC staging system. Quantification and genotyping of Micro-RNA were performed.
Results: Among the 200 patients, 2 groups were described: group I included 90 HCC patients with a male majority (72.2%) and 110 controls in group II. Three microRNA SNPs were assayed in both patients and controls. There was a significant association between rs10061133 miR-499b and the risk of HCC. The genotypes GG or G allele were associated significantly to an increased risk of HCC (GG: OR (95% CI) = 2.91 (1.23-4.22), p = 0.013; G allele: OR (95% CI) = 1.79 (1.12- 2.15), p = 0.026) compared with the genotype of AA or AG or A allele.
Conclusion: There is an association between the miRNA SNPs and the susceptibility to HCC, aiming to explore some roles and mechanisms of SNPs within miRNAs in the occurrence and development of HCC.

APASL STC 2025 Tokyo

"New Horizons for Steatotic Liver Disease: Cutting Edge Research and Emerging Therapeutics"

Abstracts

Poster Sessions

Poster Session 1
PF1-1 10236

Drug Induced Liver Injury Secondary to Anabolic Steroid Use in a Young Filipino Male: A Case Report and Therapeutic Challenge

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Background: Drug-induced liver injury (DILI) is a major cause of acute liver dysfunction, with anabolic androgenic steroids (AAS) emerging as an underrecognized etiology, especially in Southeast Asia. This case illustrates hepatocellular liver injury with cholestatic features secondary to prolonged anabolic steroid use, successfully managed with medical and extracorporeal therapies.
Case: PresentationA 26-year-old previously healthy, non-alcoholic, Filipino male presented with a one-week history of generalized jaundice and icteric sclerae. He reported an 8-month history of unsupervised use of oral anabolic steroids, oxandrolone, stanozolol, and mesterolone, alongside protein supplements. Laboratory results showed elevated liver enzymes with a hepatocellular pattern (R factor), and a RUCAM score supporting drug-induced liver injury. Liver biopsy demonstrated features consistent with chronic hepatitis secondary to DILI, with a Knodell Score of 4, indicating mild parenchymal injury. Management included intravenous Glycyrrhizic acid, N-acetylcysteine infusion, oral hepatoprotectives (UDCA, ademetionine, carnitine orotate), and subsequent hemoperfusion with hemodiafiltration due to worsening cholestasis. The patient demonstrated gradual clinical and biochemical improvement.
Conclusion: This case underscores the hepatotoxic potential of anabolic steroids, particularly 17 α-alkylated agents, in young adults. Prompt recognition, cessation of the offending agents, and initiation of hepatoprotective and extracorporeal therapies can prevent progression to fulminant liver failure. Greater awareness of AAS-related DILI is needed in regions where supplement misuse is rising.

PF1-2 10237

Acute Liver Failure Due to Anti-Tuberculosis Drug-Induced Liver Injury: A Case Report from Indonesia

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Background: Acute liver failure (ALF) is a life-threatening syndrome defined by coagulopathy and hepatic encephalopathy in patients without prior liver disease. Anti-tuberculosis drug (ATD)-induced ALF is rare but highly fatal, particularly in tuberculosis-endemic, resource-limited countries like Indonesia.
Case Description: A 26-year-old male, on 8 weeks of HRZE therapy for pulmonary tuberculosis, presented with altered consciousness (Glasgow Coma Scale [GCS] 9) and jaundice.
Laboratory results: AST 1453 U/L, ALT 2200 U/L, total bilirubin 22.6 mg/dL, INR 15.2; viral hepatitis serologies were negative. Hypoglycemia was corrected without neurological recovery. Abdominal ultrasound showed no chronic liver disease. ATDs were discontinued. Lactulose was titrated, with bowel movement achieved by day 4. Rifaximin was planned but unavailable; L-ornithine L-aspartate (LOLA) was initiated but stopped after one day due to limited supply. Gastrointestinal bleeding was managed with gastric lavage and temporary bowel rest (D5 via NGT). Antibiotics were escalated (ceftriaxone to ceftazidime plus levofloxacin). Despite supportive therapy, the patient's neurological status remained poor (GCS 9). After 5 days in ICU, he was transferred to the general ward but suffered sudden cardiac arrest the following day; resuscitation was unsuccessful.
Conclusion: This case illustrates severe ATD-induced ALF complicated by hepatic encephalopathy and gastrointestinal bleeding. Prognosis remained poor despite drug withdrawal and guideline-based supportive therapy. The absence of rifaximin and sustained LOLA highlighted treatment limitations in low-resource settings. The rapid progression from jaundice to encephalopathy within 5 days fulfilled criteria for fulminant presentation. Early recognition, immediate drug withdrawal, and timely access to liver transplantation remain essential to improving outcomes.

Poster Session 1
PF1-3 10238

Zonal Differences in Hepatocellular Mitochondrial Depolarization, Mitophagy, and Respiration after Acute Ethanol

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Background: Hepatocellular mitochondrial depolarization (mtDepo) after acute ethanol (EtOH) increases respiration for detoxifying EtOH metabolism. mtDepo also triggers mitophagy, which may become dysregulated and contribute to alcohol-associated liver disease (ALD) chronically. This study characterized the sublobular distribution of mtDepo, mitophagy and zonal mitochondrial metabolism after acute EtOH.
Methods: C57BL/6J and GFP-LC3 mice were gavaged with 6g/kg EtOH and administered intravenously MitoTracker Red (MTR) prior to liver fixation or hepatocyte isolation. Hepatocytes were zonally sorted based on MTR fluorescence. Cytochrome P4502E1 (CYP2E1) immunolabeling identified pericentral (PC) regions. Oxygen consumption rates (OCR) were assessed using Seahorse respirometry.
Results: Confocal imaging showed MTR fluorescence declined from periportal (PP) to PC zones in both groups due to flow-dependent cellular uptake of MTR as blood flowed through liver lobules. In controls, MTR localized to mitochondria in both zones, indicating polarization. After EtOH, diffuse MTR distribution in CYP2E1-positive PC hepatocytes indicated mtDepo, which was absent in PP zones. GFP-LC3 puncta marking mitophagy were also confined to PC zones. mtDepo reversed in freshly isolated PC hepatocytes as shown by rhodamine 123 uptake. Six hours after EtOH, OCRs increased ~2-fold in both PP and PC hepatocytes, returning to baseline by 24h. PP hepatocytes showed higher absolute OCRs, while PC hepatocytes showed greater proportional increases.
Conclusions: After acute EtOH, mtDepo and mitophagy are restricted to PC halves of liver lobules with preserved mitochondrial polarization in PP zones. Repolarization occurs after isolation, but elevated respiratory capacity persists, highlighting zonal differences in hepatic adaptation to EtOH that may underlie ALD progression.

PF1-4 10240

Once-monthly Efimosfermin Alfa (BOS-580) in Metabolic Dysfunction-Associated Steatohepatitis with F2/F3 Fibrosis: Results from A 24 Week, Randomized, Double-blind, Placebo-controlled, Phase 2 Trial

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Background: A Phase 2a study, efimosfermin alfa (BOS-580), an FGF21 analogue, significantly improved liver-steatosis, markers of liver-injury, and fibrosis in patients with phenotypic-MASH. A Phase 2, randomized, double-blind, placebo-controlled study was conducted in patients with biopsy-confirmed MASH, F2/F3-fibrosis, and NAS>4. (NCT04880031)
Methods: Patients (N=84) were randomized to once-monthly efimosfermin-300mg or placebo for 24-weeks. The primary endpoint was safety and tolerability. Exploratory efficacy endpoints were proportion of patients achieving fibrosis-improvement >1-stage without worsening of MASH, MASH-resolution without worsening of fibrosis, and a composite endpoint of fibrosis-improvement >1-stage and MASH-resolution analyzed in the biopsy analysis set (BAS, N=65).
Results: Patients (52.4% female; mean-age 54-yrs; mean-BMI 37.3 kg/m2; mean-HFF 20.4%; 43% F3 fibrosis; 57% type-2 diabetes) were administered efimosfermin-300mg (N=43), or placebo (N=41). In the BAS, a significantly higher proportion of patients treated with efimosfermin-300mg (N=34) achieved fibrosis-improvement without worsening of MASH (45.2% v 20.6%, p=0.038), and MASH-resolution without worsening of fibrosis (67.7% v 29.4%, p=0.002) versus placebo (N=31). The proportion of patients who achieved the composite endpoint of >1-stage fibrosis-improvement and MASH-resolution was 38.7% for efimosfermin-300mg versus 17.6% for placebo (p=0.066). In both groups, the most frequent treatment-related AEs were mild-to-moderate gastrointestinal events of nausea, diarrhea and vomiting. Overall, discontinuations were balanced with two efimosfermin patients who discontinued due to low-grade AEs. There was one treatment-related grade-3 serious AE.
Conclusions: Once-monthly efimosfermin significantly improved MASH-resolution and fibrosis-improvement at 24-weeks in patients with F2/F3-fibrosis due to MASH. In this study, efimosfermin was generally well-tolerated with a low rate of discontinuation due to AEs.

Poster Session 1
PF1-5 10244

Therapeutic Evaluation of Resmetirom and Semaglutide in the STAM Mouse Model: Bridging Surrogate and Clinical Outcomes

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Background: Resmetirom and semaglutide were recently approved for MASH based on histological surrogate endpoints such as NAFLD Activity Score (NAS) and fibrosis. However, validation of clinical outcomes including hepatocellular carcinoma (HCC), liver failure events, transplantation, and survival remains a major challenge. The STAM mouse model reproduces the full spectrum of disease progression from MASH to fibrosis, HCC, and death within 16 to 20 weeks, allowing evaluation of both surrogate and clinical outcomes. In this study, we first investigated whether resmetirom and semaglutide improve surrogate endpoints in STAM mice before proceeding to clinical outcome assessment.
Methods: Treatment with resmetirom or semaglutide was initiated at week 9 in STAM mice during the fibrotic phase. Animals were sacrificed at week 12, and liver tissues were subjected to HE and Sirius Red staining. NAS and fibrosis were evaluated as primary endpoints.
Results: Both agents significantly improved NAS and attenuated fibrosis in STAM mice. Resmetirom reduced fibrosis stage and improved metabolic markers, while semaglutide ameliorated steatosis, inflammation, and collagen deposition. These effects were consistent with clinical efficacy profiles observed in human studies.
Conclusions: Resmetirom and semaglutide reproduced their histological efficacy in the STAM model, demonstrating improvement of surrogate endpoints. Given the ability of STAM to evaluate spontaneous HCC and survival within a short timeframe, future studies will focus on clinical outcomes. Such data are expected to provide supportive preclinical evidence to reinforce the therapeutic value of these agents beyond surrogate endpoints.

Poster Session 2

PF2-1 10154

The Impact of Branch-Chained Amino Acid plus Ringer's Acetate Infusion in the Management of Dengue-Related Hepatitis

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Background: Dengue fever (DF) can cause hepatitis. Current management focuses on supportive care with fluid resuscitation, often using crystalloids. However, Branch-Chained Amino Acid (BCAA) and Ringer's acetate infusions are often preferred for liver injury. This study will compare the impact of combination of BCAA plus Ringer's acetate infusion against crystalloid solution alone for treating dengue-related hepatitis.
Methods: This retrospective study analyzed medical records from January 2020 to December 2024 at one hospital. Adult (over 18) DF patients with hepatitis who received either combination of BCAA plus Ringer's acetate (BCAA-RA group) or a crystalloid (Ringer's acetate or normal saline only) intravenously during admission were included. Patients with cirrhosis, chronic kidney disease, viral hepatitis B/C, fatty liver, diabetes, or alcoholism were excluded. The BCAA-RA group received 500ml of B1-aminofluid infusion daily, followed by Ringer's acetate for maintenance. The impact of BCAA plus Ringer's acetate infusion versus crystalloid on hepatitis resolution was estimated using an odds ratio (OR).
Results: A total of 128 patients met the inclusion criteria (86 BCAA-RA vs 42 Crystalloids). Both groups received identical medications (curcumin, lactulose, ursodeoxycholic acid, proton pump inhibitors, COX-2 inhibitors; no acetaminophen; dextrose 40% for hypoglycemia as needed). The odds of hepatitis resolution were greater in the BCAA-RA group than in the Crystalloid group (56vs.4; OR 2.9; 95%CI 1.67-4.18) as were the odds of thrombocytopenia improvement without platelet transfusion (47vs.12; OR 2.31; 95%CI 1.04-5.14).
Conclusion: This study suggests that combination of BCAA plus Ringer's acetate infusion offers more benefit in dengue-related hepatitis management.

PF2-2 10194

Understanding of the Involvement of Cxcl1-associated Neutrophil Infiltration in APAP-Induced Liver Injury

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Drug induced liver injury (DILI) is a major public health concern, often leading to the withdrawal of approved drugs. Acetaminophen (APAP), a widely used analgesic, is a leading cause of acute liver injury when overdosed. Excess APAP saturates glucuronidation and sulfation pathways, generating toxic N-acetyl-p-benzoquinone imine (NAPQI). Recent studies implicate neutrophil infiltration and chemokine signaling in worsening APAP-induced liver damage. CXCL1, a key neutrophil chemoattractant, is upregulated in both APAP and acute liver injury-related gene sets identified using a large language model (LLM). In mice, APAP overdose increased hepatic Cxcl1 expression and neutrophil infiltration, correlating with liver damage. Notably, liver specific Cxcl1 knockout mice exhibited reduced neutrophil infiltration and improved liver injury outcomes, supporting a pathogenic role of CXCL1. Additionally, APAP induced hepatocyte injury elevated reactive oxygen species (ROS), leading to oxidative DNA damage. Damaged hepatocytes released oxidized DNA via extracellular vesicles (EVs), which acted as damage-associated molecular patterns (DAMPs) to further amplify neutrophil driven inflammation. These findings reveal a dual mechanism in APAP induced hepatotoxicity involving CXCL1 mediated neutrophil recruitment and oxidized DNA driven inflammatory responses. This study highlights the importance of chemokine signaling and oxidative stress in DILI pathogenesis and may inform future therapeutic strategies targeting inflammation in drug-induced liver injury.

Poster Session 2
PF2-3 10191

Escherichia Coli Expressing the kpsM Gene Exacerbates Drug-induced Liver Injury

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Background and Aims: Drug-induced liver injury (DILI) is a leading cause of acute liver failure. Patients with DILI have disorders of the gut microbiota, yet little is known about the influence of gut microbes on this disease. Herein, we investigated the alterations of gut microbiota in DILI patients, and evaluated the contributions of *Escherichia coli* (*E. coli*) in the development of this disease.
Methods: Full-length 16S sequencing was performed on fecal samples from DILI patients. Mice colonized with genetically manipulated *E. coli* strains were subjected to the acetaminophen-induced liver injury (AILI) model. Intestinal epithelial *Fut2* gene knockout mice ($Fut2^{\Delta IEC}$) were used to assess the pathogenic mechanisms of the $kpsM^{+}$ *E. coli*. Hepatic metabolomic analyses were conducted in mice to clarify the effect of intestinal Fut2 protein on the host metabolism. Plasma metabolome of DILI patients was further validated the discoveries in mice.
Results: The percentage of subjects carrying *kpsM* were 12.1%, 50.0%, 85.7% in healthy controls, patients with mild DILI, and patients with moderate-to-severe DILI, respectively. The $kpsM^{+}$ *E. coli* exacerbated AILI through impairing gut barrier function and enhancing the expression of Fut2. $Fut2^{\Delta IEC}$ mice alleviated the aggravation of AILI caused by *E. coli* via up-regulating the hepatic levels of taurine and tauroursodeoxycholic acid. In addition, the level of plasma taurine was lower in patients with moderate-to-severe DILI than in those with mild DILI.
Conclusions: The $kpsM^{+}$ *E. coli* was associated with the progression of AILI in preclinical models, which worsened outcomes of AILI through disrupting taurine metabolism.

PF2-4 10105

Elucidating the Role of Ferroptosis in Acute Liver Injury Models

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Background: Acute liver injury (ALI), caused by drugs, viruses, or toxins, can lead to severe outcomes, making its prevention and treatment essential. Ferroptosis, an iron-dependent cell death marked by iron buildup and lipid peroxidation, differs from other cell death forms. Our group has shown that apomorphine, a medicine for Parkinson's disease, inhibits ferroptosis by reducing reactive oxygen species and lipid peroxidation. The research aims to elucidate the association between ferroptosis and ALI models, in which apoptosis and/or necrosis are major types of cell death. We explored the effect of apomorphine in ALI models.
Methods: We established ALI models in 8-week-old wild-type and hepatocyte-specific PTEN knockout (PTEN KO) mice using D-GalN/LPS (apoptosis model) and CCl4 (necrosis model). Mice were pretreated with apomorphine or DMSO as a control, followed by intraperitoneal injection of D-GalN/LPS or CCl4. Liver injury was assessed by measuring serum GOT and GPT levels collected 6 hours (D-GalN/LPS) or 24 hours CCl4 after injection. We assessed hepatic transaminase and mouse survival rates.
Results: There was no significant difference in GOT and GPT levels in the D-GalN/LPS model. However, the number of dead female mice was less in the apomorphine group compared to the control group. In CCl4-induced ALI for both wild-type and PTEN KO mice, there were no significant differences in GOT and GPT levels or survival rates between the control and apomorphine groups.
Conclusions: Apomorphine prevents D-GalN/LPS-induced death in female WT mice.

Poster Session 2
PF2-5 10208

Plastic Diets and Liver Dilemmas: Uncovering the Hepatotoxic Divide between Synthetic and Bioplastics

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The environmental persistence and limited degradability of synthetic plastics have raised substantial health concerns, particularly regarding their hepatotoxic potential. This study investigates the hepatic effects of dietary exposure to synthetic plastics compared to cassava starch-based bioplastics, modified with glycerol, in Wistar rats. Following a two-week acclimatization, rats were fed diets containing 20% plastic (plastic-to-feed ratio 2:8) for 28 days. Histopathological analysis of liver tissues revealed pronounced differences between treatment groups. Control rats maintained intact hepatic architecture, whereas starch-based bioplastic exposure induced mild hepatic fibrosis and focal inflammatory infiltration, suggesting partial biocompatibility. In contrast, synthetic plastic ingestion resulted in severe hepatic fibrosis, cellular dysplasia, and widespread inflammation, indicating higher toxicity. Serological profiling supported these findings, with elevated hepatic enzyme levels (alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], and bilirubin) detected in both treated groups. However, the synthetic plastic group exhibited significantly higher biomarker elevations, reflecting aggravated hepatic stress. Hematological assessment further revealed immunological perturbations, with reductions in white blood cell count and lymphocytes, and an increase in granulocytes, indicative of systemic inflammation and liver-associated immune compromise. Overall, the study highlights the hepatotoxic distinction between synthetic and starch-based bioplastics, positioning biodegradable alternatives as comparatively safer in terms of liver health. These findings underscore the need for molecular investigations, including transcriptomic and proteomic analyses, to elucidate pathways of plastic-induced liver injury and to validate the long-term safety of bioplastics.

Poster Session 3

PF3-1 10064

Enhanced Expression of the FTO Gene in the Liver Correlates with the Progression of Metabolic Dysfunction Associated Steatotic Liver Disease

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a metabolic disease that is strongly associated with obesity, hyperlipidemia, and type 2 diabetes mellitus. Overexpression of the fat mass and obesity-associated (FTO) gene is associated with obesity. Our study aimed to investigate FTO expression in the mouse model with MASLD.
Methods: A MASLD model was developed using a high-fat and high-carbohydrate diet for 24 weeks. ALT, AST, lipid profile, histological changes, and expression of FTO were monitored in plasma (ELISA) and liver tissue (RT-qPCR, IHC, WB) at 8, 19, and 24 weeks of diet intake.
Results: Body and liver weights significantly increased (p&It;0.05). In addition, the MAS score progressively increased (p&It;0.0001) with increased steatosis, ballooning, and lobular inflammation in the MASLD group compared to the control group. Pericellular fibrosis was observed at weeks 19 and 24. Biochemical parameters, including alanine transaminase, aspartate transaminase, triglyceride, and total cholesterol, were significantly increased (p&It;0.01). The plasma FTO level increased substantially in the MASLD group compared to the control group. Immunohistochemical (IHC) examination confirmed the nuclear expression of FTO at 8 and 19 weeks, but both cytoplasmic and nuclear expressions were observed at 24 weeks. A progressive increase in FTO expression was observed in the liver of HFHC mice (p&It;0.0001).
Conclusion: A MASLD model was developed and validated, and the NAS score was directly correlated with disease progression. An increase in FTO expression was observed in the HFHC model, indicating its positive correlation with metabolic dysfunction and could be a vital predictor of MASLD progression.

PF3-2 10116

Using Non-nutritive Sweeteners in a Fasting Period did not Disturb the Metabolic Benefits and might Improve Gut Microbiota in Obese Mice Practicing Intermittent Fasting

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Background: Intermittent fasting (IF) is a weight reduction strategy with metabolic benefits. This study aimed to clarify whether using non-nutritive sweeteners (NNS) would negatively affect the metabolic benefit of the IF.
Methods: Thirty-two C57BL/6NJcl male mice were divided into a healthy and an obese cohort, where obesity was induced by high-fat-high-fructose diets. Each cohort was subdivided into 4 subgroups: (1) non-IF, (2) alternate-day fasting (ADF) with water, (3) ADF with acesulfame K, and (4) ADF with stevia. After an 18-week intervention, fasting blood glucose (FBG), insulin resistance, lipid profiles, uric acid levels, liver histology, and gut microbiota were analyzed.
Results: ADF significantly reduced weight in both healthy and obese mice ($p<0.05$). Moreover, ADF significantly reduced serum cholesterol ($p<0.05$), prevented the increased FBG, and improved the histopathology of fatty livers. Moreover, the obese mice showed a decreased gut microbiota biodiversity while they had higher abundance of bacteria in the Lachnospiraceae family, a group of short-chain fatty acid fermenting bacteria highly associated with increased risk of metabolic disorders. Conversely, healthy and obese mice with ADF had increased the probiotic bacteria, *Lactobacillus spp*., whereas using NNS during fasting in obese mice decreased *Lachnoclostridium sp*., a member of Lachnospiraceae.
Conclusion: Using NNS did not interfere with the efficiency of weight reduction, metabolic outcomes, and liver histology improvement by the ADF and might have benefited in promoting a healthy gut microbiota in intermittently fasted obese mice. These suggested that NNS did not alter the IF's benefit in a short-term follow-up period in a mouse model.

Poster Session 3

PF3-3 10103

Non Alcoholic Fatty Liver Disease NAFLD The Estrogen Gut Liver Axis and the Emerging Role of Endometriosis

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Background: Nonalcoholic fatty liver disease (NAFLD) is an escalating global health concern with growing recognition of sex specific differences in its prevalence and pathophysiology. Although NAFLD is traditionally linked to metabolic dysfunction and postmenopausal women, emerging evidence suggests that reproductive age women are not immune, especially those with hormonal and inflammatory disorders like endometriosis. Estrogen plays a dual role in metabolic protection and disease modulation via interactions with adipose tissue, liver metabolism, and the estrobolome. Inflammation, gut dysbiosis, and immune dysregulation may further exacerbate NAFLD risk in women.
Methods: The literature search was conducted by systematically searching peer-reviewed articles from databases including PubMed, Scopus, and Web of Science. Relevant studies published between 2000 and 2024 were identified using keywords such as NAFLD, MAFLD, endometriosis, estrogen, gut microbiota and inflammation. We synthesised evidence from clinical, translational, and experimental studies on sex hormones, liver adipose crosstalk, gut microbiota, and inflammation in NAFLD and endometriosis.
Results: The review identifies shared pathophysiological pathways in NAFLD and endometriosis, including estrogen-driven signalling, oxidative stress, immune cell activation, and gut microbiota alterations. Limited but growing evidence points to an increased prevalence of NAFLD in women with endometriosis, suggesting that the chronic inflammatory and hormonal environment characteristic of endometriosis may predispose the liver to metabolic dysfunction.
Conclusions: Endometriosis may predispose women to NAFLD through estrogen dysregulation, inflammation, and gut liver reproductive axis disruption. Recognising these links is vital to improving metabolic liver disease management in women. Future interdisciplinary research should clarify these pathways to guide targeted therapies.

PF3-4 10233

Metabolic Dysfunction-associated Steatohepatitis Exacerbates LPS-induced Liver Injury and Mortality in Obese KK-Ay Mice

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common hepatic manifestation of metabolic syndrome and is associated with increased vulnerability to systemic inflammation and organ failure. However, the mechanisms underlying MASLD-related susceptibility to inflammatory liver injury remain poorly understood. This study aimed to investigate how MASLD exacerbates lipopolysaccharide (LPS)-induced liver injury and mortality, using obese KK-A^y mice fed a high-fat diet (HFD).
Methods: Male KK-A^y and C57BL/6J (Bl6) mice were fed either an HFD or a control diet for four weeks. All mice then received a single intraperitoneal injection of LPS (5 mg/kg), and survival was monitored for 24 hours. Liver injury was assessed by histology, TUNEL staining, and serum transaminase levels. Hepatic mRNA expression of inflammatory cytokines, pattern recognition receptors (PRRs), and LPS-binding protein (LBP) was measured by RT-PCR. Hepatic macrophage infiltration was analyzed using F4/80 immunostaining.
Results: Among HFD-fed KK-A^y mice, 76.9% died after LPS challenge, which was significantly higher than the 7.6% mortality observed in control diet-fed KK-A^y mice. Serum AST and ALT levels in HFD-fed KK-A^y mice were also significantly elevated compared to both Bl6 mice and control diet-fed KK-A^y mice. Histology revealed aggravated steatohepatitis and widespread hepatocyte apoptosis. Hepatic expression of TNF-α, IL-1β, TLR4, CD14, and LBP was markedly upregulated. Notably, IL-6 and LBP levels were elevated even prior to LPS exposure, suggesting a preactivated hepatic immune state.
Conclusion: MASLD enhances LPS-induced liver injury and mortality through amplified hepatic inflammation and innate immune activation in obese KK-A^y mice.

Poster Session 3
PF3-5 10145

Oral Ethanol Administration Induces Hepatitis in Mice with Combining Maternal Id-like Molecule and Melanocortin-4 Receptor Gene Deletions

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Background: Because of the worldwide reduction of viral hepatitis, basic and clinical research for steatohepatitis including alcohol-related will become more important in the future, but no stable and convenient mouse model of alcoholic hepatitis has been reported. We focused on that point and have studied to create alcoholic hepatitis model using transgenic mice.
Methods: We used female mice with the dysfunction of maternal Id-like molecule (Maid) and melanocortin-4 receptor gene (Mc4r). That Maid-KO; Mc4r-KO mice were administrated with normal (no ethanol containing) water (NW group) or 20% ethanol-containing water (ET group) *ad libitum* at 8 weeks of age. Mice were sacrificed at 12 weeks old, and the blood sample, liver and adipose tissue were collected.
Results: In 12 weeks old, the body weight gain was significantly reduced by alcohol administration (4.3 ± 3.5 g in the NW group, 0.2 ± 1.9 g in the ET group, $p < 0.01$). In addition, the liver fat deposition and inflammatory cell infiltration were also significantly increased by alcohol administration (the mean area of liver fat deposition was $8.4 \pm 2.6\%$ in the NW group, $15.4 \pm 2.1\%$ in the ET group, $p < 0.01$, and the mean CD45 positive area was $1.8 \pm 0.5\%$ in the NW group, $3.3 \pm 0.4\%$ in the ET group). Therefore, ethanol administration *ad libitum* in Maid-KO; Mc4r-KO mice induced hepatitis.
Conclusions: The Maid-KO; Mc4r-KO mice have a potential of alcohol-related hepatitis model with a simple method of *ad libitum* alcohol administration.

Poster Session 4

PF4-1 10232

Impact of Dapagliflozin on Liver Function and Body Composition in MASLD with T2DM: A Randomized Controlled Trial

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Background: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) have weight-reducing effects and are recommended in clinical guidelines for patients with metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes mellitus (T2DM), particularly those with obesity. However, their clinical benefits and potential risks in this population have not been fully evaluated. Therefore, the aim of this study was to investigate the efficacy and safety of dapagliflozin in patients with MASLD and T2DM, in comparison with vitamin E.
Methods: In this 24-week randomized controlled trial, 24 patients with MASLD and T2DM were assigned to receive either dapagliflozin (5 mg/day) or vitamin E (150 mg/day). Primary outcomes included serum AST, ALT, γ GT, type IV collagen, and the FIB-4 index. Secondary outcomes included BMI, HbA1c, lipid profile, ferritin, FibroScan parameters, and body composition.
Results: Intergroup comparisons showed no significant differences in efficacy between the two treatment groups. However, within-group analysis revealed significant reductions in AST and ALT levels in both groups. In the dapagliflozin group, AST decreased by 10.58 U/L and ALT by 24.67 U/L on average. Significant improvements were also observed in BMI (-0.90 kg/m^2), HbA1c, ferritin, and body fat. Additionally, a statistically significant reduction in skeletal muscle index (-0.133 kg/m^2) was detected in this group.
Conclusion: Dapagliflozin provided metabolic and hepatic benefits in patients with MASLD and T2DM, accompanied by a significant decrease in SMI. Careful monitoring of body composition is essential during SGLT2i treatment to mitigate the risk of sarcopenia.

PF4-2 10001

Validation of CASLI, Fibroscan-AST (FAST), and Agile3+ in a Russian Cohort of Patients with Metabolic Dysfunction-associated Steatotic Liver Disease

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Introduction: The heterogeneous course of metabolic dysfunction-associated steatotic liver disease (MASLD) across different populations necessitates the assessment of new indices and their validation at the local level.
Methods: We analyzed data from 43 patients who underwent transient elastography and had histologically confirmed MASLD to validate the newly developed index for detecting compensated advanced chronic liver disease – Compensated Advanced Steatotic Liver diseases Index (CASLI), as well as the Fibroscan-AST (FAST) and Agile3+ scores.
The CASLI index was calculated using the following formula:
$CASLI = 1 / (1 + e^{-z}) \times 100\%$
$z = -9{,}14 + 1{,}13 \times X_{T2DM} + 1{,}77 \times X_D + 0{,}05 \times X_{WC}$
where: X_{T2DM} – presence of type 2 diabetes mellitus (0 – absent, 1 – present), X_D – presence of dyslipidemia (0 – absent, 1 – present), X_{WC} – waist circumference (cm).
The discriminatory ability of the models was assessed using the area under the receiver operating characteristic curve (AUROC). Statistical significance was set at $p<0.05$.
Results: The AUROC for CASLI was 0.87±0.06 (95% CI: 0.75–0.99, p = 0.004); for the FAST score (detecting NASH + NAS≥4 + F≥2), 0.83±0.06 (95% CI: 0.7–0.95, p<0.0001); and for Agile3+ (detecting advanced fibrosis, F≥3), 0.82±0.08 (95% CI: 0.67–0.98, p = 0.003). To improve diagnostic accuracy in the studied cohort, recalibrated threshold values were determined: CASLI ≥0.2, FAST ≥0.52, Agile3+ ≥0.6.
Conclusions: The evaluated predictive models demonstrated their diagnostic effectiveness in identifying progressive MASLD. CASLI showed the highest performance; however, threshold values require adjustment to enhance diagnostic accuracy.

Poster Session 4

PF4-3 10005

Identification of Biomarkers for Progression from NAFL to NASH by Bioinformatics and Mendelian Randomization

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Background: Non-alcoholic fatty liver (NAFL) tends to progress to nonalcoholic steatohepatitis (NASH). This study focused on the biomarkers and molecular mechanisms of NAFL progression to NASH for the early detection and treatment.
Methods: The differentially expressed genes (DEGs) between NAFL and control groups and between NASH and NAFL groups were acquired by differential expression analysis, respectively. Intersection genes with up-regulated genes and intersection genes with down-regulated genes were collected and combined to obtain candidate genes. To obtain candidate genes with a causal relationship with NASH, Mendelian randomization (MR) was performed. Receiver operating characteristic (ROC) analysis and expression level verification were further implemented to gain biomarkers. Nomogram model, Gene Set Enrichment Analysis (GSEA), subcellular localization, molecular regulatory network, drug prediction, and molecular docking were employed to assess molecular modalities of biomarkers throughout the development of NAFL to NASH.
Results: 3 biomarkers (HELLS, CENPK, CDKN1A) were identified. The biomarkers displayed an excellent diagnostic capability for the progression of NAFL to NASH by nomogram model. The pathways in which biomarkers were enriched indicated that biomarkers might be related to some metabolic pathways such as tryptophan metabolism. The 4 miRNAs and 11 transcription factors (TFs) were regulated by multiple biomarkers. The 9 drugs, such as COPPER, were predicted by 3 biomarkers. The drug associated with all biomarkers, NAFL, and NASH was estradiol. Among them, molecular docking indicated that CDKN1A had the strongest binding to estradiol.
Conclusion: This study identified 3 biomarkers that were causally associated with NASH, providing new insights for potential therapeutic strategies.

PF4-4 10018

Impact of SGLT2 Inhibitors on Liver Imaging Screening and Fibrosis in Diabetes Patients with MASLD

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Background: Clinicians often underestimate the prevalence of steatotic liver disease (SLD) in diabetes patients, resulting in insufficient screening and referral. This study evaluated liver disease surveillance among Japanese diabetes patients treated with SGLT2 inhibitors (SGLT2I) and assessed treatment effects along with risk factors for persistent liver fibrosis.
Methods: In Study 1, 916 diabetes patients who received SGLT2I therapy for at least 6 months (2014-2022) were examined for the rate of liver imaging (abdominal ultrasound, CT, and MRI) performed before and after treatment. In Study 2, 263 diabetes patients with SLD treated with SGLT2I for over 1 year were evaluated for liver enzymes, liver function, platelet count, and fibrosis markers at baseline and after 1 year. Statistical analyses included chi-square tests, Mann-Whitney U tests, repeated measures ANOVA, and binary logistic regression.
Results: In Study 1, the liver imaging screening rate was 69.4%, with MASLD detected in 57.7% of cases. In Study 2, SGLT2I treatment led to significant reductions in ALT (40.3 to 30.7 U/L, $p < 0.01$), ALP (234.1 to 188.5 U/L, $p < 0.01$), gammaGT (65.2 to 55.3 U/L, $p < 0.01$), and ALBI score (-2.87 to -2.94, $p < 0.01$). Multivariate analysis revealed that a higher pre-treatment FIB-4 index (OR 5.113, $p < 0.01$) and greater alcohol consumption (OR 1.004, $p = 0.014$) were independently associated with a high FIB-4 index (>2.67) after 1 year.
Conclusion: Regular liver disease screening is warranted in diabetes patients. Those with preexisting liver fibrosis or significant alcohol intake may not experience improvement in fibrosis with SGLT2I therapy.

Poster Session 4
PF4-5　10024

Efficacy of Imeglimin Hydrochloride in Diabetic Steatotic Liver Disease: A Retrospective Analysis

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Background: Imeglimin hydrochloride is a novel agent that improves mitochondrial function and exerts dual glucose-lowering effects by stimulating pancreatic insulin secretion and enhancing hepatic and skeletal muscle metabolism. Although approved only in Japan, its efficacy in diabetic steatotic liver disease remains unestablished.
Methods: Two retrospective analyses were performed. In study 1, the rate of liver imaging was determined in 129 patients prescribed Imeglimin between 2021 and 2024. In study 2, 32 diabetic patients with fatty liver disease treated with Imeglimin for at least three months were assessed. Statistical analyses were performed using repeated measures ANOVA and the Wilcoxon signed-rank test.
Results: In study 1, more than one month-treatment was continued in 60 of 129 cases. Liver imaging was performed in 54 of these 60 cases (90%), with metabolic dysfunction-associated steatotic liver disease (MASLD) diagnosed in 33 (61.1%). In study 2, significant reductions were observed at three months in γglutamyl transferase (γGT, $p = 0.023$), lactate dehydrogenase (LDH, $p = 0.025$), and FIB-4 index ($p < 0.001$). At six months, decreases in γGT ($p = 0.005$), LDH ($p = 0.033$), and total cholesterol ($p = 0.036$) were noted, with further reductions in FIB-4 index ($p = 0.041$) at twelve months.
Conclusions: Imeglimin treatment in diabetic patients with steatotic liver disease was associated with frequent liver imaging and a high MASLD prevalence. Improvements in hepatic enzymes and lipid profiles suggest its potential to ameliorate hepatic dysfunction, dyslipidemia, and fibrosis.

Poster Session 5

PF5-1 10047

Efficacy and Safety of Nalmefene in Alcohol-Related Liver Disease

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Background: While complete abstinence remains the cornerstone of Alcohol-related liver disease (ALD) management, many patients struggle to maintain it. As such, harm reduction strategies, including pharmacotherapy aimed at reducing alcohol intake, have gained attention. Nalmefene, an opioid receptor modulator, has been shown to reduce alcohol consumption in patients with alcohol dependence, but real-world data on its hepatic benefits in ALD remain limited. Aim: To evaluate the efficacy and safety of nalmefene in patients with ALD, with a focus on its impact on alcohol consumption, liver function, and hepatic reserve capacity.
Methods: We conducted a retrospective observational study of 21 patients with clinically diagnosed ALD who received nalmefene at our institution between September 2019 and December 2023. Data on alcohol intake, liver function tests, and hepatic reserve capacity, AUDIT score were collected at baseline and at six months. Adverse events were also documented.
Results: Both heavy drinking days (HDD) and total alcohol consumption (TAC) showed a significant reduction one month after initiating nalmefene. Liver dysfunction also significantly improved along with HHD and TAC. No significant changes were observed in terms of hepatic function reserve. Most adverse events were up to grade to, and no serious adverse events were reported.
Conclusion: In this study, nalmefene effectively reduced alcohol intake in patients with ALD and was associated with measurable improvements in liver function and hepatic reserve. These findings support the potential role of nalmefene as part of a harm reduction strategy in patients unable to achieve full abstinence.

PF5-2 10164

A Retrospective Study on the Prognosis of Patients with Alcoholic Liver Cirrhosis

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Background: In Okinawa, alcoholic liver disease (ALD) is the most common cause of cirrhosis, with mortality exceeding the national average. Although abstinence is crucial in ALD management, behavioral change is often difficult.
Methods: We retrospectively analyzed 220 patients (180 males, 40 females) diagnosed with alcoholic liver cirrhosis (ALD–LC) at our institution and affiliated centers. Prognosis was evaluated in relation to abstinence, age, liver cancer, and clinical status at the time of abstinence.
Results: Among males, mortality was significantly lower in the abstinent group (27/82, 32.9%) than in the non-abstinent group (57/98, 58.1%; $P<0.01$), with better survival by Kaplan–Meier analysis. In females, mortality did not differ between the abstinent (8/17, 47.0%) and non–abstinent groups (10/23, 43.5%; $P=0.91$). Liver cancer–related deaths occurred only in males (20/64 deaths, 23.8%), and the mean age at death was older in liver cancer cases (59.6±9.0 years) than in non–liver cancer cases (52.0±9.3 years). Among patients who died despite abstinence, high MELD scores and the presence of encephalopathy or ascites were associated with poor prognosis. Even in non-abstinent males, reduced drinking was linked to better survival ($P=0.001$).
Conclusion: In male ALD–LC patients, abstinence was associated with better prognosis, while no such effect was seen in females. This may reflect advanced or irreversible disease at the time of abstinence. Early alcohol control is essential, ideally before progression to cirrhosis.

Poster Session 5
PF5-3 10173

Outcomes of Alcoholic Liver Disease in Liver Transplantation: A Systematic Review and Meta-analysis

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Background: Alcoholic Liver Disease (ALD) remains one of the leading causes of chronic liver disease worldwide, with Liver Transplantation (LT) being the only curative treatment for patients with end-stage disease. As such, understanding differences in transplant outcomes between ALD and non-ALD etiologies becomes essential in clinical decision-making. This SRMA aims to synthesise available evidence on survival and post-transplant outcomes in recipients with ALD compared to those with non-ALD, specifically non-alcoholic steatohepatitis (NASH).
Methods: We conducted a systematic search to identify relevant studies with ALD and NASH transplant outcomes. Odds ratios (ORs) for the outcomes were derived from pooled binary values using a random-effects model. For survival outcomes, we conducted an individual participant data meta-analysis (IPDMA) to estimate hazard ratios (HRs).
Results: We screened 3369 articles and eventually included 15 articles that contained post-LT outcomes in ALD and NASH groups. We obtained ORs for eight distinct post-transplant outcomes, including rejection, infections and renal complications. Compared to NASH recipients, patients with ALD had higher odds of de novo malignancies (OR = 2.545, 95% CI: 1.462-4.429, I2 = 77.87%). There were no significant differences in overall patient (HR = 1.227, 95% CI: 0.8145-1.8485) and graft (HR = 1.1955, 95% CI: 0.7645-1.8693) survival.
Conclusion: This study revealed significant differences in select post-transplant outcomes, with ALD patients exhibiting a higher risk of de novo malignancies post-LT but having comparable overall patient and graft survival to NASH recipients.

PF5-4 10097

How Sex and Age Modify the Influence of BMI, CMRFs, and Alcohol on SLD Diagnosis

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Background: Following the redefinition of MASLD, attention has increased regarding the role of cardiometabolic risk factors (CMRFs) and alcohol intake in SLD pathogenesis. However, detailed analyses of how BMI, CMRFs, and alcohol consumption contribute to SLD diagnosis across sex and age groups are lacking.
Methods: This multicenter, retrospective observational study analyzed data from 108,446 individuals who underwent abdominal ultrasound during routine health check-ups. Participants were categorized by age group (under 40, 40s, 50s, 60s, 70 or older) and BMI category (less than 18.5, 18.5 to 25, 25 to 27, 27 to 30, 30 to 35, over 35 kg/m^2). We assessed the prevalence of steatotic liver disease (SLD) according to BMI, number of CMRFs, and daily alcohol intake (g/day), stratified by sex and age group.
Results: SLD prevalence increased with BMI across all age and sex groups. In men, over 50% had SLD from a BMI of 25-27 kg/m^2; in women, this threshold was 27-30 kg/m^2. Peak prevalence appeared earlier in men (30s-50s) than in women (50s-70s). The proportion with four or more CMRFs was twice as high in men (32%) as in women (16%), with minor generational variation. Alcohol intake was generally higher in the non-SLD group, but in those aged 70 or older, SLD patients consumed more alcohol.
Conclusion: SLD prevalence rises with increasing BMI. Women appear less susceptible to SLD than men at similar BMI levels. High CMRF burden is more common in men, and age-specific patterns in alcohol-related SLD warrant further investigation.

Poster Session 5
PF5-5 10245

Drinking Patterns and the Risk of Alcoholic Liver Disease

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Background: Alcoholic liver disease poses a serious threat to human health, however, the link between alcohol consumption patterns and the risk of ALD is not fully understood.
Methods: 20 adult participants without ALD and other serious underlying diseases were selected from Liaoning Province, China, and their baseline information was collected. Through standardized questionnaires, participants' drinking frequency (daily, weekly, monthly, etc.), single drinking volume (converted into grams of pure alcohol), drinking types (Baijiu, beer, wine, etc.), and drinking duration were recorded in detail. The results showed that drinking frequency was closely related to the risk of ALD. Compared with those who drink alcohol once or twice a week, the risk of disease of daily drinkers is significantly higher. Those who drink Baijiu and other spirits for a long time alone have a 21% higher risk of disease than those who drink wine or beer for more than five years. The risk of disease of those who drink alcohol for more than five years increases with the increase of drinking years, and the risk of disease increases by 22% every five years.
Conclusion: Alcohol consumption patterns are a key influencing factor in the onset of ALD. Frequent and heavy alcohol consumption, preference for strong liquor, and long-term alcohol consumption can be used to develop precise health education and intervention strategies for different drinking patterns based on the results of this study, in order to reduce the incidence of ALD

Poster Session 6

PF6-1 10020

Novel Serum Marker Proteins for Alcohol Abuse Identified through Proteomic Analysis

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Introduction: Although the primary strategy for detecting heavy drinking relies on self-reporting, heavy drinkers tend to underestimate their alcohol consumption. Two serum samples-one on admission and one after 8 weeks of abstinence-were obtained from 20 patients with alcohol dependency. Using tandem mass tag labelling and LC-MS/MS, we performed comparative analyses of serum proteins to identify serum biomarkers for alcohol abuse. A comparative analysis of TMT-labeled glycoproteins revealed that three types of proteins increased more than three-fold eight weeks after abstinence, compared to the time of hospitalization. Notably, Protein X exhibited a 3.6-fold increase.
Methods: The study included 20 alcohol-dependent patients and 160 healthy subjects. The healthy subjects were divided into five groups based on their alcohol consumption: 32 non-drinkers (Level 0), 32 subjects 12 g of alcohol (Level 1), 32 subjects 24 g of alcohol (Level 2), 32 subjects 24-48 g of alcohol (Level 3), and 32 subjects 48 g or more of alcohol (Level 4).A lectin ELISA for glycated Protein X was developed, and serum samples from both alcohol-dependent patients and healthy subjects were measured.
Results: Glycoprotein X levels in healthy subjects were 0.05 ±0.10 AU/mL (Level 0), 0.06 ±0.01 AU/mL (Level 1), 0.05 ±0.01 AU/mL (Level 2), 0.03 ±0.00 AU/mL (Level 3), and 0.03 ± 0.01 AU/mL (Level 4). A significant difference ($p<0.001$) was observed between the Level 0-2 group and the Level 3-4 group.
Conclusions: Glycoprotein X was demonstrated to be a useful marker for assessing alcohol consumption.

PF6-2 10150

Comparative Liver Fibrosis Severity in Alcohol-Related Liver Disease and Chronic Viral Hepatitis Using Transient Elastography

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Background: Chronic liver fibrosis is a key determinant of prognosis in chronic liver disease, leading to cirrhosis and hepatocellular carcinoma. Although alcohol-related liver disease (ALD) and chronic viral hepatitis (HBV, HCV) are major global causes, their comparative fibrogenic potential in clinical populations remains underexplored.
Aims: To compare fibrosis severity between ALD and chronic viral hepatitis using transient elastography and characterize etiology-specific fibrogenic patterns.
Methods: This cross-sectional study included 64 patients with chronic liver disease (32 ALD, 32 HBV/HCV) from February 2023 to February 2025. Liver stiffness was assessed using FibroScan, and fibrosis was staged according to the METAVIR system (F0 - F4).
Results: Advanced fibrosis (F3 - F4) was significantly more prevalent in the ALD group. Cirrhosis (F4) occurred in 43.7% of ALD patients versus 18.7% in the viral group (p below 0.05). Mean fibrosis score was higher in ALD (F3.16 +/- 5.1) than in viral hepatitis (F2.44 +/- 3.2; p below 0.05). Early-stage fibrosis (F0 - F2) predominated in viral hepatitis. These findings suggest a more aggressive fibrogenic course in ALD, potentially due to persistent hepatocellular injury and pro-inflammatory mechanisms unique to alcohol exposure.
Conclusion: ALD is associated with more advanced fibrosis than viral hepatitis. Transient elastography effectively differentiates fibrotic severity across etiologies, supporting its role in guiding risk stratification and etiology-specific management strategies in chronic liver disease.

Poster Session 6

PF6-3 10200

Skeletal Muscle Loss and Elevated Phase Angle are Linked to Metabolic Dysfunction-associated Steatotic Liver Disease in Japanese Males

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the leading cause of chronic liver disease worldwide and is closely linked to metabolic syndrome. Skeletal muscle is essential for metabolism, however the evidence on the association between body composition and MASLD remains limited. This study investigated the impact of body composition, particularly muscle mass and phase angle (PhA), on MASLD in the general Japanese population.
Methods: We recruited 624 university staff and faculty members who underwent annual health checkups. MASLD was diagnosed using health checkup data and liver ultrasonography. Skeletal muscle mass index (SMI), fat mass index (FMI), and PhA were measured using bioelectrical impedance analysis. Sex-stratified multivariable logistic regression identified independent factors associated with MASLD. A restricted cubic spline (RCS) model demonstrated the influence of body composition on MASLD.
Results: Among 624 participants (median age, 46 years; 320 males), the prevalence of MASLD was 28% in total, 38% in males, and 17% in females. In males, lower SMI (odds ratio [OR], 0.33; 95% confidence interval [CI], 0.13–0.82; $p = 0.018$) and higher PhA (OR, 5.11; 95% CI, 2.14–12.77; $p < 0.001$) were independently associated with MASLD. These relationships were not observed in females. RCS models showed an inverse linear association between SMI and MASLD and a positive association between PhA and MASLD in males.
Conclusions: Skeletal muscle loss and elevated PhA are associated with MASLD in Japanese males. Further studies are needed to clarify sex-specific effects of body composition.

PF6-4 10214

A 50% Relative Decline in MRI-PDFF Predicts Fibrosis Improvement in Metabolic Dysfunction-associated Steatohepatitis

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Background: MRI–proton–density–fat fraction (MRI–PDFF) response, defined as ≥30% relative decline in liver fat, is associated with resolution of metabolic dysfunction–associated steatohepatitis (MASH), but its ability to predict fibrosis improvement is unclear. The association between MRI–PDFF super-response (≥50% fat reduction) and histologic outcomes has not been systematically evaluated.
Methods: We conducted a secondary analysis of a multi–center, randomized, placebo–controlled trial (Loomba et al., NEJM 2024) involving 163 adults (64% female) with biopsy–confirmed MASH and stage 2–3 fibrosis. Participants received pegozafermin or placebo for 24 weeks. Paired liver biopsies and MRI–PDFF were performed at baseline and study end. Primary outcomes were fibrosis improvement without MASH worsening and MASH resolution without fibrosis worsening. Logistic regression was used to evaluate associations, adjusting for age, sex, BMI, race/ethnicity, and type 2 diabetes.
Results: Median age and BMI were 56.0 (IQR 48.0–62.0) years and 36.5 (32.2–40.2) kg/m². MRI–PDFF super-response occurred more frequently in pegozafermin-treated patients than placebo (57.8% vs 11.1%, p<0.0001). Super–response independently predicted fibrosis improvement (adjusted OR 3.08, 95% CI 1.32–7.19, p=0.009), while standard response did not (adjusted OR 2.10, 95% CI 0.85–5.16, p=0.11). Both MRI–PDFF response and super–response predicted MASH resolution (adjusted OR 5.22 and 7.29, respectively; both p<0.01).
Conclusion: MRI–PDFF super-response is a strong independent predictor of fibrosis improvement and MASH resolution. These findings support its use as a surrogate endpoint in MASH trials and inform dose selection strategies for Phase 3 development.

Poster Session 6
PF6-5 10217

Role of Coffee Consumption among Patients with Steatotic Liver Diseases in Armenia

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Background: According to some studies regular coffee consumption has potential hepatoprotective effect, include patients with steatotic liver diseases (SLD). Historically, Armenia recognized as a country with high coffee consumption. Armenian coffee preparing with small coffee cups fresh water, add a teaspoon of finely-ground coffee into the jazzve (hourglass-shaped metal pot), and heat until it just starts to boil.
Methods 72 patients with steatotic liver diseases diagnosed rely on ultrasound and and new criterias for metabolic-dysfunction-associated (MAFLD) involved in the observational study. Mean age 51.0±12.3 (23-76 years old), 62.5%male, BMI 31.7±5.0kg/m2. 41% had diabetes, 70% with BMI>30kg/m2, FERR elevated in 47%, F4 had 14% of patients. We evaluated following also biochemical and lipids profile parameters: AST, ALT, GGT, GLUC, TG, cholesterol (CHOL), low density lipoprotein (LDL), ferritin (FERR). According to Armenians behevior of coffee consumptions we devided patients on two categories: low is 1 times per day and high - 2 and more times armenian version finely-ground coffee into the jazzve per day.
Results: Vast majority of Armenian patients with MAFLD (82 %) mentioned 0 to 1 cup Armenian coffee per day, only 18 % consume two or more times per day. Range and means±SD/SE of patients biochemical paratamiteres: FERR 24-1947ng/mL (396.7±61.4); TG 0.8-57 (3.3±0.8), CHOL 2.8-19.5 (5.9±2.3), HDL 0.4-1.8 (1.0±0.3), LDL 0.6-9.1 mmol/L (3.8±1.5), GGT 18-960U/L (83.4±14.8), ALT 8-339 (62.9±6.1), AST 12-192 (41.3±3.9), GLUC 4.4-24.6 mmol/L (6.8±2.9).
Conclusions: Armenian patients with steatotic liver diseases has demonstrated lower coffee consumption, more than half were obese and one fourth with T2DM.

Poster Session 7

PF7-1 10218

Risk of Liver-Related Events in MASLD: Impact of Cardiometabolic Risk Factor Count and Its Longitudinal Changes

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Liver-related events (LREs) can occur in patients with MASLD. We investigated the risk of LREs in patients with MASLD based on the cardiometabolic risk factor (CMRF) count and its changes over time. Data from patients with MASLD who underwent VCTE at 16 tertiary referral centers between February 2004 and January 2023 were analyzed. Patients who underwent follow-up examinations at 2 years were categorized based on changes in their CMRF count from baseline. LRE risk was evaluated using a multivariable-adjusted Cox proportional hazards model. Among 16,603 patients (mean [SD] age, 52.5 [13.7] years; 9600 [57.8%] were male), 316 (1.9%) patients developed LREs during a median follow-up of 51.7 months (IQR, 25.2-85.2). The risk of LREs increased gradually with a higher baseline CMRF count (1: reference; 2: HR=1.25 [95% CI: 0.78-1.98]; 3: HR=1.79 [95% CI: 1.17-2.76]; 4: HR=1.85 [95% CI: 1.19-2.86]; 5: HR=2.69 [95% CI: 1.59-4.54]; per 1-higher: HR=1.29 [95% CI: 1.15-2.90]). Among those with follow-up data, an increase in CMRF count was associated with a higher risk of LREs (per +1 change; HR=1.21 [95% CI: 1.18-1.27]), with a greater risk observed in those who consistently had high CMRF counts compared to those who newly developed high CMRF counts (per 1 baseline count; HR=1.23). Conversely, a reduction in CMRF count was associated with a lower risk of LREs (per -1 change; HR=0.86). Both baseline CMRF count and its longitudinal changes were significantly associated with LRE risks in MASLD patients. Accurate identification of these markers may facilitate personalized management of MASLD-related LRE risk.

PF7-2 10224

The Interplay of Hepatic Steatosis and Fibrosis in MASLD: Insights from a Clinical Scoring Approach

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Background: Non-invasive scores for steatosis and liver fibrosis in metabolic associated steatotic liver disease (MASLD) are essential for providing early diagnosis and cost-effective follow up, comparing their costly gold standard examination. This study aimed to evaluate the association between hepatic steatosis and liver fibrosis in MASLD using simple scoring and identify risk factors contributing to steato-fibrosis progression.
Methods: A prospective observational study of 244 adult MASLD was conducted from January to December 2024 at a tertiary hospital center in Makassar, Indonesia. Hepatic steatosis and liver fibrosis were assessed using Hepatic Steatosis Index (HSI), Fatty Liver Index (FLI), Fibrosis-4 Index (FIB-4) and NAFLD Fibrosis Score (NFS) confirmed by FibroScan liver stiffness. Associations between steatosis and fibrosis scores were analyzed using linear regression models with adjustments for risk factors such as age, BMI and platelets count.
Results: A significant positive association was observed between the NFS and FLI ($p=0.0017$) with NFS cutoff > -1.455 had sensitivity of 50% and specificity of 53.1%. No significant association was found between FIB-4/FLI, FIB-4/HSI or NFS/HSI ($p>0.005$). BMI was associated with increase steato-fibrosis risk factor (OR 1.28, 95%CI: 1.01-1.63, $p=0.042$) while age and platelets do not show significant risk.
Conclusion: This study showed hepatic steatosis and fibrosis may progress in parallel in MASLD using simple score combination NFS and FLI. These findings underscore the complementary utility of non-invasive scores in assessing disease severity. Longitudinal studies are needed to confirm and improve risk stratification.

Poster Session 7

PF7-3 10212

Halalopathy in Metabolic Dysfunction-Related Steatotic Liver Disease/MASLD Management: A Holistic Approach to Enhancing Quality of Life for Muslim Patients

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a global epidemic affecting approximately 24% of the world's population. Although lifestyle interventions and advanced pharmacological therapies demonstrate efficacy, treatment adherence remains suboptimal, particularly among Muslim patients whose religious values influence health decisions. The study aims to explore the role of halal-based therapy and religious alignment in improving clinical outcomes and health-related quality of life in Muslim patients with MASLD.
Methods: A systematic narrative review was conducted using databases such as PubMed, Scopus, and the WHO Halal Regulation Portal. Inclusion criteria focused on studies exploring halal hepatoprotective compounds, religious adherence, and patient behavior in Muslim populations.
Results: Three primary compounds are curcumin, silymarin, and Nigella sativa, have demonstrated significant efficacy in lowering ALT (mean 15-30 U/L) and improving steatosis in RCT studies. Halal nanoemulsion formulations of silymarin increased bioavailability by up to 2.7-fold. A survey of Muslim patients in Southeast Asia revealed that 74% would refuse therapy if its halal status was unclear, and 65% stated they would be more compliant if the therapy aligned with religious values. However, only 28% of the hepatoprotective herbal products available on the market have internationally recognized halal certification.
Conclusion: Hallalopathy can significantly improve treatment adherence and patient satisfaction in the management of MASLD in Muslim communities. The clinical efficacy of natural compounds such as curcumin, silymarin, and Nigella sativa is supported by randomized controlled trial (RCT) data, while religious alignment has been shown to positively influence health behaviors.

PF7-4 10066

Liver-related Event Risk in Steatotic Liver Disease According to Smoking Transitions and Subsequent Use of Nicotine Alternatives

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Background: This study aimed to evaluate the risk of liver-related events (LREs) in adults with steatotic liver disease (SLD) according to changes in combustible cigarette (CC) smoking status and subsequent use of nicotine and novel tobacco products (NNTPs), including electronic cigarettes and heated tobacco products. While the harmful effects of CC smoking are well established, the impact of NNTP use on liver health remains unclear.
Methods: 645,637 individuals with SLD was classified by CC smoking status (never smokers, quitters, initiators, and continuous smokers) and NNTP use. LREs incidence rates were calculated per 1,000 person-years. Subdistribution hazard ratios (SHRs) and 95% confidence intervals (CIs) were estimated using the Fine and Gray competing risk regression model.
Results: CC initiators had a higher LREs risk than never smokers (aSHR: 1.63; 95% CI: 1.44 to 1.84), as did continuous smokers (aSHR: 1.19; 95% CI: 1.01 to 1.40). Among recent initiators, NNTP use was associated with lower LREs risk (aSHR: 0.71; 95% CI: 0.53 to 0.95) in the propensity score matching. However, Inverse probability of treatment weighting analysis showed modestly increased risks in NNTP users among both quitters and initiators.
Conclusion: While NNTP use appears to reduce LREs risk among recent CC initiators, its overall effect varies by smoking status and warrants further investigation.

Poster Session 7
PF7-5 10067

Elevated M2BPGi is Associated with Increased White Matter Hyperintensities, Cognitive Impairment, and Slower Gait Speed in Older Adults with MASLD

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Mac-2 binding protein glycan isomer (M2BPGi), a liver fibrosis biomarker, has systemic implications. Cerebral white matter hypointensities (WMHs), indicative of ischemic changes, are associated with cognitive decline and gait disturbances. We investigated the association between M2BPGi, WMHs, cognitive function, and gait speed in community-dwelling older adults with metabolic dysfunction-associated steatotic liver disease (MASLD). This cross-sectional study included 607 adults aged 65 and older in Arao City, Japan (2016-2017). Key measurements included serum M2BPGi, MASLD (defined by Fatty Liver Index of 30 or higher and by its metabolic criteria), WMH volume (quantified from MRI), Mini-Mental State Examination (MMSE) scores (a test for global cognitive function), and 5-meter walk test. Associations were analyzed focusing on MASLD participants stratified by an M2BPGi cut-off of 0.9, adjusted for confounders. Among 253 MASLD participants, those with M2BPGi of 0.9 or higher (n=157) were more prevalent than those with M2BPGi less than 0.9 (n=96; p=0.03). Within the MASLD group, an M2BPGi level of 0.9 or higher was significantly associated with increased WMH volume (p=0.017). Furthermore, the M2BPGi 0.9 or higher group had significantly lower MMSE scores (mean 26.81 vs. 27.57, p=0.0376) and slower maximum gait speed (mean 3.43s vs. 3.09s, p=0.0484) compared to the M2BPGi less than 0.9 group.In older adults with MASLD, an M2BPGi level of 0.9 or higher is associated with greater WMH burden, poorer cognitive performance, and slower maximum gait speed. M2BPGi may serve as a non-invasive marker to identify MASLD individuals at higher risk for cerebrovascular changes and related functional impairments.

Poster Session 8

PF8-1 10015

Elafibranor Ameliorates Liver Fibrosis Development and Repairs Gut Barrier Function in a Mouse Alcohol-associated Liver Disease Model

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Background: Alcohol-associated liver disease (ALD) is a leading cause to liver-related morbidity and mortality, although there is no therapeutic modality to prevent ALD-related liver fibrosis. This study aims to evaluate the effects of elafibranor (EFN), PPARα and δ agonist, on liver fibrosis and gut intestinal barrier dysfunction in a mouse ALD model.
Methods: ALD-related liver fibrosis was induced in female C57BL/6J mice by feeding an ethanol-containing Lieber-DeCarli liquid diet and intraperitoneally injecting carbon tetrachloride (CCl4) for 8 weeks. EFN were orally administered during experimental period. Cell-based assays evaluated the effects of EFN on HepG2 lipotoxicity and Caco-2 barrier function.
Results: The ethanol plus CCl4-treated ALD mice showed hepatic steatosis, hepatocyte apoptosis and fibrosis which were significantly attenuated by treatment with EFN. EFN promoted lipolysis and β-oxidation as well as enhanced the autophagic and antioxidant capacity. We found that EFN exerted these effects in the ethanol-stimulated HepG2 cells primarily through PPARα activation. EFN also inhibited the Kupffer cells-mediated inflammatory response with blunted hepatic exposure of lipopolysaccharide and the TLR4/NF-kB signaling. EFN improved the intestinal hyperpermeability by restoring tight junction proteins and autophagy as well as by inhibiting apoptosis and proinflammatory response in ALD mice. The protective effect on intestinal barrier function was observed in the ethanol-stimulated Caco-2 cells, and this was predominantly mediated via PPARδ activation.
Conclusion: EFN ameliorates ALD-related fibrosis by inhibiting lipid accumulation and apoptosis by enhancing autophagic and antioxidant capacity in hepatocytes and by suppressing LPS/TLR4/NF-kB-mediated inflammatory responses by restoring intestinal barrier function.

PF8-2 10060

Hepatoprotective Potential of Phloretin in Alcohol-Induced Liver Disease (ALD) Rat Model: Biochemical and Molecular Evidence

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Background: Alcohol-induced liver disease (ALD) is a major global health burden, driven by oxidative stress and inflammation. This study evaluates the hepatoprotective effects of Phloretin (PHL) against ethanol-induced liver injury in rats.
Methods: Adult Wistar rats received 50% ethanol (8 to 12 mL/kg b.w., orally) for six weeks to induce ALD. PHL was administered orally one hour before ethanol at doses of 25, 50, and 100 mg/kg for the same duration. Silymarin (50 mg/kg) served as a positive control.
Results: PHL significantly modulated serum lipid profiles and liver enzymes, reducing levels of total cholesterol, triglycerides, LDL, bilirubin, GOT, and GPT, while improving HDL. It enhanced antioxidant defense by increasing superoxide dismutase (SOD) and reducing malondialdehyde and glutathione levels. PHL also regulated alcohol-metabolizing enzymes (CYP2E1, ADH, ALDH) and activated p-AMPK, suppressing lipogenesis. Furthermore, PHL attenuated inflammatory responses via inhibition of the TLR-4/NF-kappa B signaling pathway and exhibited anti-apoptotic effects by modulating BCl-2, BAX, and caspase-3 expression. It also alleviated fibrosis by downregulating the TGF-beta1/Smad pathway and alpha-SMA expression. Histopathological findings confirmed the protective effect of PHL.
Conclusion: PHL offers significant hepatoprotection in ALD by enhancing antioxidant defense, reducing inflammation, and preventing apoptosis and fibrosis. These findings highlight its potential as a natural therapeutic agent against alcohol-induced liver damage.
Keywords: Phloretin, ALD, hepatoprotection, oxidative stress, inflammation.

Poster Session 8

PF8-3 10179

Association between Metabolic Dysfunction-associated Steatotic Liver Disease and Young-onset Thyroid Cancer Risk in Men and Women: A Nationwide Cohort Study of Adults Aged 20-39 Years

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Background: The association between metabolic dysfunction-associated steatotic liver disease (MASLD) and the risk of thyroid cancer, particularly among young adults and across sexes, remains unclear. We aimed to investigate the sex-specific relationship between MASLD and thyroid cancer risk in young adults.
Methods: We conducted a nationwide cohort study of 5,327,649 individuals aged 20-39 who underwent health screenings through Korea's National Health Insurance Service (2009-2012), with follow-up until December 2018. MASLD was defined using the fatty liver index. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models.
Results: Over 39.2 million person-years, 32,845 individuals (10,180 men, 22,665 women) developed young-onset thyroid cancer. MASLD was associated with increased thyroid cancer risk in men (aHR: 1.282; 95% CI: 1.230-1.335), showing a dose-response by severity (moderate: 1.213 [1.157-1.271]; severe: 1.396 [1.324-1.471]; P-trend less than 0.01). Conversely, MASLD in women was linked to decreased risk (aHR: 0.931; 95% CI: 0.875-0.991), with an inverse dose-dependent trend (moderate: 0.963 [0.902-1.029]; severe: 0.832 [0.750-0.923]; P-trend less than 0.01).
Conclusions: MASLD is associated with increased young-onset thyroid cancer risk in men but reduced risk in women, suggesting significant sex-specific differences. These findings highlight the importance of tailored cancer risk assessments and monitoring for young adults with MASLD. Further studies are needed to elucidate the biological mechanisms behind these observed sex-based disparities.

PF8-4 10190

Serum Zinc Deficiency Reflects Nutritional Impairment rather than Fibrosis Severity in MASLD: A Biopsy-Based Study of 193 Cases

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Background: Zinc plays a key role in protein metabolism and immune function, and its deficiency is common in chronic liver disease. However, its clinical relevance in MASLD (metabolic dysfunction associated steatotic liver disease) remains unclear. We evaluated the relationship between serum zinc levels, histological fibrosis, and nutritional indicators in biopsy-proven MASLD.
Methods: We retrospectively analyzed 193 MASLD patients who underwent liver biopsy and had serum zinc measured at diagnosis without prior zinc supplementation. Fibrosis stage was assessed using Brunt classification (stage 3,4 as advanced). Clinical parameters including FIB-4 index, M2BPGi, albumin, and platelet count were compared. Correlation and multivariate analyses were performed.
Results: Serum zinc levels showed no significant correlation with Brunt stage or FIB-4 index. ROC analysis demonstrated poor performance of zinc in predicting advanced fibrosis (AUC = 0.45). Multivariate regression identified age, male sex, higher BMI, and lower platelet count as independent predictors, but not zinc. However, zinc levels were significantly correlated with M2BPGi ($r = -0.25$, $p = 0.0017$), and zinc-deficient patients (<60 μg/dL) had significantly lower albumin levels than the normal-zinc group ($p = 0.006$).
Conclusions: While serum zinc was not an independent predictor of advanced fibrosis in MASLD, it was significantly associated with markers of nutritional decline and hepatic synthetic dysfunction. These findings suggest that serum zinc may reflect metabolic and nutritional stress rather than fibrosis. Routine zinc assessment may help support metabolic management, especially in patients with hypoalbuminemia. Further studies investigating zinc and amino acid metabolism (e.g., BTR) in MASLD are warranted.

Poster Session 8
PF8-5 10140

Unraveling the Role of Hepatocyte-Specific DDIT4 in Alcohol-Induced Hepatic Injury

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Background: Nutritional imbalance combined with high alcohol consumption causes MetALD. DDIT4 is a highly conserved cellular stress-responsive protein induced by stress signals such as hypoxia, DNA damage, and ER stress. DDIT4 has been reported to exhibit various regulatory functions in different mammalian cells. However, the role of DDIT4 during alcohol-related hepatic injury remains undefined. In this study, we aimed to investigate the function of DDIT4 in hepatocyte during the development of MetALD.
Methods: To explore the function of DDIT4 in the progression of MetALD, we generated mice with hepatocyte-specific deletion of DDIT4 (DDIT4 LKO) and subjected them to 3-months High-fat diet plus multiple binge ethanol model to mimic MetALD condition. In MetALD conditions, we measured serum levels of ALT and AST to assess the extent of liver injury and performed total RNA sequencing to identifying associated signaling pathways between WT and DDIT4 LKO group.
Results: In MetALD model, DDIT4 LKO mice exhibited a significant reduction of MetALD-induced hepatic damages compared to WT mice, as evidenced by reduced serum ALT and AST levels. Total RNA sequencing revealed that the genes associated with RAS/MAPK, apoptosis and angiogenic signaling pathways were significantly downregulated in the liver of DDIT4 LKO mice to compare with WT mice in MetALD condition. These results were confirmed with in vitro study using primary hepatocytes and vascular endothelial cells.
Conclusion: This study demonstrates that downregulation of DDIT4 is crucial for reducing MetALD-induced liver injury and supports the potential of DDIT4 as a therapeutic target for MetALD.

Poster Session 9

PF9-1 10210

Culture Vs Health: How Traditional Drink Tuak be a Risk Factor Enhance Liver Disease?

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Tuak drink is one of the traditional drinks that are often found in various regions in Indonesia. This drink is generally served at various celebrations such as traditional events and communal activities as a symbol of togetherness and strengthening relationships in society. Tuak drink is made from fermented natural ingredients of palm sap obtained from sugar palm, coconut, or palm trees. The purpose of the research namely to identify the chemical content in Tuak drink, the mechanism of Tuak drink affecting stomach acid production and its relationship to liver disease. The research method used in this study is a qualitative method with the following stages: descriptive qualitative study, interviews and observations. Data analysis used in this study is descriptive analysis by describing the results of document literature analysis, interviews and observations. Based on the data analysis, two important findings were obtained, namely: First, Some chemical compound contained in Tuak drink are: saponins, phenols, triterpenoids, alkaloids, flavonoids and ethanol. Second, the chemical compound of ethanol from sucrose fermentation from palm sap causes an increase in alcohol content if the storage is longer (stored for 5 days) which reaches 10% with an acidity level (pH) reaching 4 so that if consumed in the long term and excessively it can trigger gastric epithelial infection. Based on these findings, it is concluded that consuming Tuak can trigger liver disease because it can trigger gastric epithelial infection due to two factors, namely endogenous destructive factors (high acid levels) and exogenous (high alcohol levels).

PF9-2 10023

Involvement of the ADAMTS13/von Willebrand Factor Axis in Acute Kidney Injury in Mice with Advanced Fibrotic Liver

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Background: Hepatorenal syndrome-induced acute kidney injury (HRS-AKI), characterized by the coexistence of acute kidney injury (AKI) and liver cirrhosis (LC), is a significant risk factor for poor outcomes in LC patients. Decreased a disintegrin-like metalloproteinase with thrombospondin type 1 motif 13 (ADAMTS13) activity and increased von Willebrand factor (vWF) antigen levels are associated with LC progression and portal hypertension. We investigated the role of the ADAMTS13/vWF axis in AKI using a mouse model with advanced fibrotic liver.
Methods: Wild-type (WT), ADAMTS13-deficient (Adamts13-/-) mice and vWF-deficient (vWF-/-) mice comprised the negative control and AKI groups. AKI was induced by intraperitoneal carbon tetrachloride (CCl4), and lipopolysaccharide administration to emulate systemic inflammation on a fibrotic background. Effects of ADAMTS13/vWF alterations on liver and kidney injury in the fibrotic mouse model were evaluated.
Results: AKI groups of WT mice exhibited increased serum AST/ALT and BUN/creatinine levels, as well as reduced blood flow in both liver and kidney. AKI groups also demonstrated inflammatory changes, renal injury markers and oxidative stress markers in the kidney. Significantly greater changes in AKI group of Adamts13-/- mice were observed. Conversely, vWF-/- mice were protected from liver and kidney damage and exhibited the improvement of tissue blood flow, inflammation, and oxidative stress responses.
Conclusion: An imbalanced ADAMTS13/vWF axis may play a critical role in AKI progression with LC. These results suggest that regulating vWF via recombinant ADAMTS13 may offer a novel therapeutic approach for managing AKI in patients with LC.

Poster Session 9

PF9-3 10092

A Case of Esophago-Tracheal Fistula during Atezolizumab plus Bevacizumab after Endoscopic Submucosal Dissection of the Esophagus

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Case Report: A man in his early 60s with type 2 diabetes mellitus and alcohol addiction had been treated for esophageal squamous cell carcinomas via endoscopic submucosal dissection (ESD) at 0 month, 30 months, and 36 months. He received two courses of 5-fluorouracil plus 60 Gy of radiation after the initial ESD and underwent endoscopic balloon dilatations at 3 and 6 months after the initial and last ESD, respectively. Computed tomography (CT) prior to the last ESD showed suspected multiple hepatocellular carcinomas in the cirrhotic liver. At 40 months, transarterial chemoembolization was performed for the tumors in the segment 8, followed by chemotherapy with Atezolizumab plus Bevacizumab for the tumors in the left lobe at 43 months. At 47 months, he was diagnosed with aspiration pneumonia and a large esophago-tracheal fistula on the CT scan, which was considered unsuitable for stent insertion, and therefore required palliative surgical management. Considering the high perioperative mortality risk in Child-Pugh B liver cirrhosis, he underwent esophageal bypass surgery and recovered well. Although prolonged surgical wound healing was suspected at the sites of the esophageal stump, gastric tube anastomosis, and abdominal incision, he was in a stable condition until fatal bleeding from the tracheo-arterial fistula on postoperative day 44. Conclusions: This case highlights the challenges of treating patients with end-stage alcoholic liver cirrhosis, who have severe tissue fragility and impaired wound healing, especially when further combined by the mechanical, pharmaceutical, and surgical stressors of consecutive therapies for esophageal and hepatocellular carcinomas.

PF9-4 10109

Dynamic Status of Metabolic Syndrome and Hepatocellular Carcinogenesis: A Big Data Analysis from Japan

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Background/Aim: Metabolic syndrome (MetS) is a known risk factor for hepatocellular carcinoma (HCC), but the specific roles of each MetS component and the effects of changes in MetS status over time remain unclear. This study aimed to assess these factors using a large-scale Japanese health dataset.
Methods: We analyzed medical data from 2.71 million Japanese individuals collected between 2005 and 2020. The study evaluated the incidence of HCC in relation to MetS, preMetS (an early stage of MetS), and five MetS components: triglycerides >150 mg/dL, HDL-C <40 mg/dL, fasting blood glucose >110 mg/dL, blood pressure >130/85 mmHg, and BMI >25 kg/m^2. Participants were categorized based on MetS status at the beginning and end of the observation period into four groups: MetS-free, MetS-developed, MetS-persistent, and MetS-recovered.
Results: Among the 2.71 million individuals, 63,435 developed HCC. Compared with the non-MetS group, both the MetS group (HR 1.42, 95% CI 1.39-1.45) and the preMetS group (HR 1.26, 95% CI 1.22-1.29) had significantly increased HCC risk. A higher number of MetS components was associated with progressively increased HCC incidence. Individuals who developed or maintained MetS over time had a higher risk of HCC than MetS-free individuals, whereas those who recovered from MetS had a reduced risk.
Conclusion: MetS and even preMetS are significant risk factors for HCC. Importantly, improvement in MetS status may help prevent HCC. These findings suggest that early identification and management of MetS could play a key role in liver cancer prevention.

Poster Session 9
PF9-5 10072

Predictive Utility of Polygenic Risk Scores for Metabolic Dysfunction-Associated Fatty Liver Disease

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Background: The polygenic risk scores (PRSs), which aggregate genetic susceptibility from multiple single nucleotide polymorphisms (SNPs) have been proposed as one of the useful tools for identifying patients with chronic diseases. Currently, fewer studies regarding PRS for predicting metabolic dysfunction-associated fatty liver disease (MAFLD) have been performed in an Asian population. This study aimed to evaluate the predictive utility of PRS for MAFLD in the Korean population.
Methods: We analyzed 13,457 samples (4,061 cases and 9,396 controls) from a comprehensive health promotion center who underwent abdominal ultrasonography, biochemical testing, and genetic studies. Hepatic steatosis was assessed using abdominal ultrasonography and MAFLD was diagnosed according to APASL guideline. MAFLD cases were categorized into two groups: obese (≥25 kg/m^2, n=3,453) and non-obese (<25 kg/m^2, n=608). The PRS were calculated using 10 significant SNPs for MAFLD, weighted by effect sizes using PLINK software.
Results: An area under the receiver operator characteristic curve (AUC) of PRS for the MAFLD was 0.569 (95% CI: 0.558 to 0.579): 0.564 (95% CI: 0.553 to 0.575) for obese MAFLD and 0.597 (95% CI: 0.574 to 0.621) for non-obese MAFLD. When considering the age and sex into PRS model, the AUC of the PRS for obese MAFLD and non-obese MAFLD were 0.703 and 0.713, respectively.
Conclusions: This study demonstrated that clinical variables including age and sex could improve the risk prediction of PRS based on the SNPs. The current study suggests that the optimized PRS model could be an effective tool for screening population at risk of developing MAFLD.

Poster Session 10

PF10-1 10038

Effects of Probiotics on Gut Microbiota in Patients with Type 2 Diabetes

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Objective: To evaluate the effects of probiotic supplementation on gut microbiota composition and glucose metabolism in patients with type 2 diabetes (T2DM).
Methods: Sixty T2DM patients were randomly assigned to a probiotic group (n=30) and a control group (n=30). The probiotic group received a daily oral probiotic supplement along with standard therapy, while the control group received standard therapy alone for 12 weeks. Fasting plasma glucose (FPG), HbA1c, HOMA-IR, and fecal gut microbiota composition were measured before and after the intervention.
Results: After 12 weeks, the probiotic group showed significant reductions in FPG, HbA1c, and HOMA-IR ($P<0.05$), along with increased levels of beneficial bacteria such as Bifidobacterium and Lactobacillus, and decreased levels of potentially harmful bacteria such as Bacteroides. No significant changes were observed in the control group. Improved microbiota diversity was positively correlated with insulin sensitivity.
Conclusion: Probiotic supplementation can effectively improve gut microbiota composition and glycemic control in T2DM patients, suggesting potential as an adjunctive treatment strategy.

PF10-2 10046

Misclassification of Alcohol Use Disorder in MASLD and MetALD: Prevalence, Clinical Characteristics, and Outcomes

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Background and Aims: Within MetALD, there exists a continuum where the condition can conceptually shift between being MASLD or ALD. This study aimed to investigate the prevalence and clinical characteristics of misclassified alcohol use disorder (AUD) among patients with MASLD and MetALD.
Methods: The study included a total of 3,362,552 participants from the National Health Screening Program. Steatotic liver disease was defined as a Hepatic Steatosis Index 36 or higher. Significant alcohol intake was calculated based on a self reported questionnaire. AUD was defined as having received medical care for an alcohol-related condition at least once during the study period. The average follow-up period for participants was 9.8 years. The misclassified AUD as MASLD and MetALD groups demonstrated significantly higher cumulative incidence rates for both HCC and liver related complications compared to the pure MASLD and MetALD.
Results: MASLD and MetALD prevalence were 23.8% and 1.9%, respectively. AUD was identified in 1.1% (8,481 individuals) of MASLD and 4.7% (2,989 individuals) of MetALD cases. Misclassified AUD was associated with significantly higher all cause and liver-related mortality. Adjusted hazard ratios for liver related mortality were 6.53 for AUD misclassified as MASLD and 6.98 for AUD misclassified as MetALD. Extrahepatic cancer mortality risk was also elevated (adjusted hazard ratio: 1.33 in MASLD; 1.44 in MetALD).
Conclusions: A significant number of AUD cases were misclassified as MASLD and MetALD in crosssectional assessment of alcohol consumption. The AUD misclassified as MASLD or MetALD had higher liver-related mortality than the pure MASLD and MetALD groups.

Poster Session 10
PF10-3 10093

Features of the Course of Metabolically Associated Fatty Liver Disease in Lean Elderly Residents of Mid-altitude Areas

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Background: Patients with MAFLD are prone to insulin resistance, glucose metabolism abnormalities, and non-communicable diseases. Mitochondrial dysfunction and oxidative stress contribute to progression toward MASH, especially in elderly individuals. MAFLD and T2DM often coexist and mutually aggravate each other, particularly in high-altitude environments.
Methods: A cross-sectional comparative study was conducted in 733 ethnic Kyrgyz individuals from low-altitude (750 – 800 m; n=319) and mid-altitude (2046 – 2300 m; n=414) regions of Central Asia. Subgroups included control, MAFLD, and MAFLD with T2DM. Parameters assessed included anthropometry, body composition (bioimpedance), biochemical markers of carbohydrate and lipid metabolism, liver enzymes, cytokine levels, and fibrosis risk (FIB4 and elastography). Statistical analysis was performed using SPSS 16.0.
Results: Progression from MAFLD to T2DM was associated with significant increases in waist circumference and body fat, especially in men. Lean elderly men with MAFLD and T2DM demonstrated reduced muscle mass, consistent with sarcopenia. MAFLD was associated with hypertension and coronary artery disease regardless of BMI, with highlanders showing increased rates of hypertension even in non-obese individuals (38.9%). Midaltitude residents with MAFLD (± T2DM) showed significantly lower glucose, ALT, HbA1c, and triglyceride levels. Inflammatory cytokines increased with fibrosis stage and positively correlated with waist circumference, ALT, TNFα, and cytokine index.
Conclusion: MAFLD in lean elderly individuals at mid-altitudes is characterized by visceral adiposity, sarcopenia, and inflammation. These findings highlight the need for personalized approaches to MAFLD management, incorporating geographic, metabolic, and age-related factors.

PF10-4 10114

Screening for Metabolic-associated Fatty Liver Disease in Type 2 Diabetes Patients Using Non-invasive Scores and Ultrasound: A Cross-sectional Study in Egypt

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is common among patients with type 2 diabetes mellitus (T2DM) and contributes significantly to hepatic and systemic complications. This study aimed to evaluate the reliability of non-invasive scoring systems and abdominal ultrasonography in diagnosing and screening MAFLD among Egyptian T2DM patients.
Methods: A cross-sectional study was conducted on 300 T2DM patients attending an outpatient clinic. Liver enzymes, non-invasive fibrosis indices (FIB-4 and NAFLD Fibrosis Score [NFS]), and steatosis indices (Hepatic Steatosis Index [HSI] and Fatty Liver Index [FLI]) were assessed alongside abdominal ultrasound. Patients were stratified based on MAFLD diagnosis, and logistic regression was used to identify predictors of disease presence and severity.
Results: The prevalence of MAFLD was 46.33%. FIB-4 (AUC 0.826; 95% CI: 0.778-0.875) and NFS (AUC 0.964; 95% CI: 0.942-0.986) showed high diagnostic accuracy for fibrosis. HSI (AUC 0.847; 95% CI: 0.803-0.890) and FLI (AUC 0.835; 95% CI: 0.789-0.881) effectively identified hepatic steatosis. Mean HSI was 38.31, and mean FLI was 68.78, indicating a high probability of liver steatosis. Mean FIB-4 was 1.94, and NFS was 0.56, reflecting moderate fibrosis risk. Ultrasound confirmed steatosis in 80.58% of patients. Predictors of MAFLD included higher BMI, increased waist circumference, elevated ALT, AST, GGT, albumin, dyslipidemia, and poor glycemic control (HbA1c).
Conclusion: Non-invasive indices, combined with ultrasound, are reliable tools for early detection of MAFLD in T2DM patients, supporting timely intervention and prevention of disease progression.

Poster Session 10
PF10-5 10229

Noninvasive NASH-FibroTest in Armenian Patients with Steatotic Liver

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Background: It is well-known that ultrasonography can detect hepatic steatosis only when exceeding 15-20%, with a sensitivity ranging between 60-94% and specificity between 88-95%. The limitations of biopsy and the developing of reliable noninvasive blood tests no longer considered liver biopsy as mandatory screening of liver in steatotic liver disease. Noninvasive NASH-FibroTest (BioPredictive) is designed to provide a comprehensive assessment of fibrosis, steatosis, and necroinflammatory activity.
Methods: 25 patients with MAFLD were involved in the study (60% male), 31-69 years old (47.2±12.5), 44% overweight and 56% with obesity, 24% with T2DM. Besides 10 parameters of NASH-FibroTest (alpha2-macroglobulin, haptoglobin, apolipoprotein A1, ALT, AST GGT, total bilirubin, serum fasting glucose, triglycerides (TG), cholesterol (CHOL) plus age and gender) we adjusted high density lipoprotein (HDL), low density lipoprotein (LDL) and ferritin (FERR) reference value for female 4.63-204.00 for male 21.81-274.66 ng/mL.
Results: Results of Fibrotest F4 had 12%, F3 8%, F2 4%, F1-2 36%; SteatoTest results S3 severe steatosis (>32%) - 16%, S2-3 and S2 significant steatosis (6-32%) 28% and 8%, S1-2 20%; NashTest N3 4.2%, N2 41.7%. N1 37.5%; ActiTest A3 4.2%, A2 41.7%, A1 37.5%. Range and mean±SD/SE: FERR 26.2-1056.4 (254.4±60.5) ng/mL; GLUC 4.35-13.3 (6.13±1.99); TG 0.69-5.4 (2.19±1.06), HDL 0.64-1.27 (0.97±0.17), LDL 1.55-5.48 (3.38±0.98), CHOL 2.96-6.77 (4.87±0.89) mmol/L, GGT 15-163 (52.3±33.7), ALT 19-168 (51.8±32.7), AST 14-62 (29.9±12.7) U/L.
Conclusion: Noninvasive NASH-FibroTest show advanced fibrosis and cirrhosis in 20%, severe and significant steatosis in 44% and severe and moderate steatohepatitis due to metabolic disorders is 46% of patients with steatotic liver disease.

Poster Session 11

PF11-1 10026

Aging Increased the Susceptibility of Liver Fibrosis through Enhancing NAT10-mediated ac4C Modification of TGFβ1 mRNA

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Background: The epidemiological observational studies unveiled that aging is one of the risk factors for liver fibrosis, and the hepatic tissues in the elderly harbor more fibrotic lesions when compared to those in young people. Previous investigations found that TGFβ1 was elevated with aging and promoted liver fibrosis. However, the underlying mechanisms of aging and liver fibrosis remain largely unknown.
Methods: CCl_4- and DDC-induced liver fibrosis animal models were used in this study. The distribution of ac4C RNA modification was monitored by the acRIP-seq. The RNA-protein interaction was examined by the RNA Immunoprecipitation.
Results: We found that the middle-aged mice were more susceptible to the CCl_4-induced liver fibrosis when compared to the young mice. Clearance of *in vivo* senescent cells by senolytics drug ABT263 significantly suppressed liver fibrosis. The RNA ac4C-modifying enzyme NAT10 was transcriptionally activated by TGFβ1/SMAD2/3 axis and highly expressed in the aging liver as well as liver fibrosis mouse model. Suppression of NAT10 by its inhibitor Remodelin or specific shRNA attenuated senescence and activation of hepatic stellate cells. Subsequent studies found that NAT10 directly triggered the ac4C RNA modification of TGFβ1 mRNA by physically interacting with the RNA binding protein PTBP1, enhancing the stabilization of TGFβ1 mRNA and subsequent activation of TGFβ/SMAD signaling pathway. Animal studies demonstrated that inhibition of NAT10 by Remodelin significantly alleviated liver fibrosis and cellular senescence.
Conclusions: Our study identified a previously unknown mechanism of how TGFβ1 drives cellular senescence and liver fibrosis through NAT10-mediated ac4C mRNA modification.

PF11-2 10082

Dietary Fermented Rice Bran Inhibit Liver Fibrosis and Hepatic Stellate Cells Activation in Mice

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Background: Rice bran, the main by-product of rice milling, contains various nutrients which possess hepatoprotective activities. After fermentation, rice bran can increase its nutritional value and the content of bioactive substances, thereby increasing its economic value. This study investigate the effects of fermented rice bran on the carbon tetrachloride (CCl4)-induced liver fibrosis in Mice.
Methods: Mice were fed a 10% fermented rice bran-containing diet or a normal diet with or without the injection of 20% CCl4 twice a week for 7 weeks to induce a liver fibrosis model.
Results: Administration of a fermented rice bran-containing diet did not affect the body weight, food and water intake in hepatotoxic CCl4-treated mice. The histopathological H&E staining images showed that CCl4 induced significantly irregular infiltration of borders, perinuclear vacuoles, and regional inflammation in the liver, whereas mice administered a fermented rice bran-containing diet expressed less abnormal hepatic morphology. In the control diet-fed group, CCl4 injection resulted in higher gene expression of α-SMA, COL1A1, and TGF-β and collagen deposition in liver tissues, whereas these fibrogenesis-related genes were down-regulated in fermented rice bran-fed mice. We also found that the amount of proline is increased after fermentation process. At the molecular regulatory manner, proline pre-treatment inhibited the activation of hepatic stellate cells through decreasing Smad2/3 phosphorylation. In conclusion, the administration of a fermented rice bran-containing diet may have beneficial effects on liver fibrogenesis via alleviate hepatic stellate cells activation.

Poster Session 11

PF11-3 10183

A Bioinformatics Dissection of TGF-β Signaling in Human Hepatic Stellate Cells: Uncovering Novel Fibrogenic Genes

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Background: Liver fibrosis and portal hypertension, affecting 3.3% of the global population, are driven by hepatic stellate cell (HSC) activation and transdifferentiation. Transforming growth factor beta (TGFβ) is a key mediator, with GIPC (synectin) as an important downstream adaptor. However, gene networks regulated by TGFβ and GIPC in human HSCs remain unclear. This study aims to clarify TGFβinduced transcriptomic changes, elucidate GIPC's role, and identify novel fibrosis-related targets using integrative bioinformatics analysis.
Methods: Gene expression data (GSE151251) were obtained from the Gene Expression Omnibus (GEO). Differentially expressed genes (DEGs) from TGFβstimulated HSCs, with and without GIPC knockdown, were identified using GEO2R. Enrichment analyses (GO and KEGG) were conducted via Enrichr. Protein protein interaction (PPI) networks were constructed using Cytoscape with STRING (confidence cutoff>0.9). Top hub genes were identified using maximal clique centrality (MCC) via CytoHubba and MCODE.
Results: We identified 1,989 DEGs (849 upregulated, 1,140 downregulated) in TGFβstimulated HSCs. Upregulated genes were enriched in pathways such as hypertrophic and dilated cardiomyopathy and products including endoplasmic reticulum lumen and collagen-containing extracellular matrix. Downregulated genes were related to autolysosome, basolateral plasma membrane, TNF signaling, and cytokine-cytokine receptor interactions. The PPI network included 615 DEGs (615 nodes, 1,038 edges). Key hub genes identified by MCC were IFI44, IFIT3, STAT1, MX1, IFIT1, OAS3, IFIH1, IFIT2, IFI6, and ITGB1.
Conclusion: This study reveals key transcriptomic changes in TGFβstimulated HSCs and identifies hub genes as potential regulators of liver fibrosis, providing a foundation for future therapeutic research.

PF11-4 10196

Characterization of Hepatocyte Plasma Membrane Proteins that Regulate Hepatic Stellate Cell Activation

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Background: Liver cirrhosis is a fatal disease primarily driven by sustained activation of hepatic stellate cells (HSCs). In a healthy liver, HSCs remain quiescent by adhering to hepatocytes (Heps) via spine-like structures. Upon liver injury, this adhesion is disrupted, triggering HSC activation. This study aimed to elucidate the molecular mechanisms by which attachment to hepatocyte plasma membranes (Hep PM) restrict HSC activation, using a unique in vitro culture system.
Methods: We established an in vitro culture system using Hep PM fractionated from mouse Heps to quantitatively evaluate their effects on HSC activation. Using this system, we analyzed HSC morphology and gene expression. Mouse derived-Heps, Hepa1-6-derived PM was used as a comparative control. Comprehensive proteomic analysis of the Hep PM fractions was performed to identify candidate proteins. RNA-seq of HSCs cultured with Hep PM and a compound screening assay were also performed.
Results: In the presence of Hep PM, HSCs maintained a quiescent morphology with dendritic extensions. Expression of HSC-activation markers such as αSMA and COL1A1 was significantly downregulated, while the quiescence marker MMP1 was upregulated. These effects were specific to primary Hep PM and were not observed with Hepa1-6 PM. Based on these results and integrative analysis, candidate molecules were selected. Functional validation of these candidates is currently in progress.
Conclusion: Physical adhesion to Hep PM plays a critical role in suppressing HSC activation. This study provides new insights into Hep-HSC interactions and highlights potential targets for antifibrotic therapy.

Poster Session 11
PF11-5 10235

Fibroblast Growth Factor (FGF) 18 Promotes Proliferation and Migration of Murine Hepatic Stellate Cells

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Background: Fibroblast growth factor (FGF) 18 has been shown to facilitate hepatic fibrogenesis; however, the precise mechanisms have not been elucidated. Here we investigate the direct effect of FGF18 on isolated hepatic stellate cells (HSCs).
Methods: HSCs were isolated from mouse livers and cultured for 7 days. Day 2-cultured cells were treated with FGF18 (10 ng/mL) and/or PDGF-BB (10 ng/mL) for 5 days. Day 7-HSCs were treated with gliotoxin (1.5μM) to induce apoptotic cell death. Cell counts and DNA synthesis were assessed using WST-1 assay and BrdU incorporation, respectively. Cellular migration was measured by time-lapse microscopy. Expression levels of COL1A1, αSMA, TGFβ1-3, and PPARγ mRNA were measured by real-time RT-PCR.
Results: Incubation with FGF18 significantly increased cell counts of cultured HSCs about 4.5-fold on Day 7, as similar to PDGF. Co-incubation with FGF18 and PDGF further increased cell counts, significantly higher than PDGF alone. Indeed, BrdU incorporation was 1.8- and 1.5-fold higher in cells treated with FGF18 and PDGF, respectively, whereas co-incubation with FGF18 and PDGF enhanced BrdU incorporation 2.3-fold. FGF18, however, did not prevent gliotoxin-induced cell death in Day 7 HSCs. On the other hand, FGF18 also enhanced migration of HSCs significantly on Day 5. FGF18 did not affect mRNA expression of COL1A1, αSMA, TGFβ1-3, and PPARγ in primary-cultured HSCs.
Conclusion: FGF18 promotes proliferation and migration, but does not prevent apoptosis of HSCs. FGF18 is less likely to affect collagen synthesis nor transactivation process in HSCs directly. In conclusion, FGF18 appears to be a simple mitogen in HSCs.

Poster Session 12

PF12-1 10028

Optimal Hemoglobin A1c (HbA1c) Target for Preventing Liver-related Complications in Individuals with Type 2 Diabetes Mellitus (T2DM) with and without Cirrhosis: A Territory-Wide Retrospective Cohort Study from 2000 to 2023

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Background: Glycemic control in T2DM and cirrhosis individuals is challenging due to restricted options of anti-diabetic agents and risk of hypoglycemia. This study aims to determine optimal target HbA_{1c} for preventing liver-related events in individuals with T2DM, with and without cirrhosis.
Methods: This retrospective study included adult individuals with T2DM, with or without cirrhosis after excluding individuals with missing demographic data, human immunodeficiency virus infection, type 1 diabetes, and liver-related complications before T2DM diagnosis or within 2 years. The primary outcome was liver-related events and non-liver-related death was competing events. Restricted cubic spline analysis was used to assess relationship between HbA_{1c} and the liver-related events and to identify optimal HbA_{1c} level associated with the lowest risk.
Results: Of 1,130,282 individuals with T2DM, 42,622 (3.8%) had cirrhosis (mean age 70.9 years, 58.2% men). After adjustment for covariates, a non-linear relationship existed between HbA_{1c} level and risk of liver-related events in cirrhotic group (p for linearity = 0.01, p for cause-specific hazard ratio [CSHR] = 0.004). Individuals with HbA_{1c} 6.5-7.7% had a lower risk of developing liver-related complications. In contrast, a linear relationship was observed in individuals without cirrhosis (p for CSHR = 0.003), with increased risk from 6.7% or above (Figure 1).
Conclusion: Compared to <6.7% in noncirrhotic group, a higher target HbA_{1c} <7.7% for cirrhotic group can reduce the risk of liver-related complications. Given the potential impact of extrahepatic complications and medication, caution is needed when HbA_{1c} is excessively low in cirrhotic patients.

PF12-2 10099

Liver Stiffness Measurement, Doppler Ultrasound, and Serum Non-Invasive Markers as Predictors of Varices and Variceal Bleeding in Cirrhotic Patients

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Background: Variceal bleeding is a life-threatening complication of cirrhosis, necessitating reliable non-invasive predictors to reduce reliance on invasive endoscopic screening. This study evaluated the diagnostic accuracy of liver stiffness measurement (LSM), Doppler ultrasound, and serum biomarkers (FIB-4, APRI, PC/SD ratio) in predicting gastroesophageal varices and variceal bleeding in cirrhotic patients.
Methods: A cross-sectional study of 144 cirrhotic patients stratified into three groups: no varices (n = 37), non-bleeding varices (n = 41), and variceal bleeding (n = 66). All participants underwent LSM, Doppler ultrasound (portal vein hemodynamics), laboratory non-invasive tests (FIB-4, APRI, PC/SD), and esophagogastroduodenoscopy (EGD). Diagnostic performance was assessed using ROC curves, AUC, sensitivity, specificity, and multivariate logistic regression.
Results: LSM more than 30 kPa predicted variceal bleeding with 90% sensitivity (AUC 0.91), outperforming Doppler parameters (AUC 0.41-0.55). For varices detection, LSM more than 20 kPa and PC/SD ratio less than 900 showed high accuracy (AUC 0.90 and 0.84, respectively). FIB-4 (cutoff 3.0) and APRI (cutoff 1.0) also demonstrated strong predictive value (AUC 0.80-0.81). Multivariate analysis identified LSM (OR 1.12, p<0.001), FIB-4 (OR 1.84, p=0.001), and platelet count (OR 0.95, p<0.001) as independent predictors.
Conclusion: LSM and serum biomarkers (FIB-4, PC/SD) are highly accurate non-invasive tools for predicting variceal bleeding and presence of varices, enabling risk stratification and reducing unnecessary EGDs. Doppler ultrasound showed limited clinical utility. These findings support integrating LSM and serum biomarkers into cirrhosis management protocols.

Poster Session 12

PF12-3 10209

Hemobilia Due to Spontaneous Arterioportal Fistula in a Liver Abscess : A Rare Case Report

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Background: Hemobilia, the presence of blood within the biliary tree, is an uncommon yet potentially life-threatening cause of gastrointestinal bleeding. While trauma and iatrogenic interventions are common etiologies, spontaneous arterioportal fistula (APF) secondary to liver abscess is extremely rare. We present a unique case of hemobilia due to spontaneous APF complicating a liver abscess.
Methods: A 59-year-old male presented with fever, right upper quadrant pain, and subsequently developed melena and obstructive jaundice. After initial imaging suggested a liver abscess, percutaneous drainage was performed. Persistent gastrointestinal bleeding and cholestasis prompted further evaluation using Endoscopic Retrograde Cholangiopancreatography (ERCP) and Computed Tomography (CT) angiography.
Results: ERCP confirmed hemobilia by demonstrating active bleeding from the biliary orifice. CT angiography identified an arterioportal fistula in segment VIII of the liver. The patient was managed with biliary stenting followed by selective transarterial embolization using coils and glue. The intervention resulted in cessation of bleeding and resolution of jaundice. Follow-up imaging showed complete obliteration of the fistula and resolution of the abscess.
Conclusion: Spontaneous arterioportal fistula is an exceedingly rare cause of hemobilia, particularly in the setting of a liver abscess. High clinical suspicion, timely endoscopic and radiologic evaluation, and prompt embolization are critical for favorable outcomes. This case underscores the need to consider vascular complications in patients with liver abscess and gastrointestinal bleeding.

PF12-4 10034

Analysis of Lesions of Liver in Postmortem Cases in Indian population

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Introduction: Lesions of the liver cause significant morbidity and mortality even without causing significant signs and symptoms. A liver biopsy may not give the exact picture. An autopsy study may be a better choice.
Method: A retrospective analysis of the histopathological findings of autopsy cases was done during the years 2020-23. Only those cases were selected that showed positive histopathological findings in the heart, lung, liver, spleen, kidney, and brain. A total of 70 cases were taken. The age group was between 4 and 77 years old. Males and females were 52 and 18, respectively. Of the 70 individuals, 41 had liver lesions that were clinically significant; these are the cases that are being discussed here.
Result: The most common lesion was a moderate to severe degree of hepatic steatosis, which showed foci of cirrhosis in 14/70 (20%). Grossly, most of the cases were mixed types of cirrhosis: macronodular and micronodular. The next prominent group of diseases was cirrhosis (9/70), 12.8%. Other common diseases were chronic hepatitis and granuloma, 4/70 (5.7%) each. Cardiac cirrhosis was seen in 2/70 cases. Nonalcoholic hepatic steatosis was seen in the case of an 11-month-old male baby who presented with umbilical granuloma on gross examination, and his lung also showed pneumonic features. Other conditions, like hydatid cyst, metastasis from cancer, and acute inflammatory cell infiltration in chronic hepatitis, were seen in 1/70 cases.
Conclusion: Histopathology of autopsy specimens is conducted at limited centers. This diminishes the opportunity for medical professionals to learn about liver pathology.

Poster Session 12
PF12-5 10211

Traditional Use of Gabus Fish by the Mandar People: Relevance to Liver Health and Post Surgical Healing

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Liver disease often leads to reduced albumin levels in the body, impairing tissue regeneration and fluid balance. Albumin supplementation has been shown to support recovery in patients with hepatic disorders. This study explores the traditional use of Gabus fish (Channa striata), a freshwater species rich in albumin, by the Mandar people of West Sulawesi, Indonesia, particularly for accelerating wound healing after surgery. Using a meta analysis approach, data were collected through interviews and field observations in the Lena area, Campalagian district, and supported by a review of scientific literature on the fish's chemical composition. Results revealed that Channa striata contains essential nutrients including omega 3, iron, phosphorus, calcium, vitamins A and B1, and notably, high levels of albumin. The presence of albumin is particularly significant in supporting tissue repair, reducing inflammation, and restoring plasma protein levels functions highly relevant for patients with liver dysfunction. These findings suggest that Gabus fish, traditionally used for surgical recovery, may also offer therapeutic potential in the dietary management of liver disease by aiding protein replenishment and promoting hepatic cell regeneration. Further clinical studies are recommended to evaluate its efficacy in liver-related treatments.

Poster Session 13

PF13-1 10166

Predicting Spontaneous Clinical Recompensation in Liver Transplant Candidates: A Competing Risks Analysis of the UNOS Registry

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Background: Liver transplantation remains the definitive therapy for end-stage liver disease. However, recompensation is poorly understood and its predictors remain unclear.
Methods: We conducted a retrospective cohort study using the United Network for Organ Sharing registry from 2000 to 2025, identifying adult liver transplant candidates (>18 years) listed for their first transplant. Patients with malignancy, acute hepatic necrosis, prior transplant, or missing key data were excluded. The primary outcome was delisting due to clinical improvement. Death and transplantation were treated as competing risks. Random survival forest (RSF) model was applied to identify predictors of recompensation, using variable importance and minimal depth as selection metrics.
Results: Of 127,978 candidates, 8,493 (6.6%) were delisted due to improvement. Compared to others, these individuals had significantly lower MELD scores (median 13 vs. 18), lower INR and creatinine, and higher albumin (all $p < 0.001$). Recompensated patients were also more likely to be female and less likely to have MASLD, diabetes, or obesity. The RSF model demonstrated robust performance (C-index = 0.80 at 1 year, AUC = 0.80, Brier reduction = 0.341 at 10 years). The most important predictors were baseline diagnosis, age, and albumin level. Diagnosis of alcohol-associated liver disease strongly predicted recompensation, while MASLD and HCV were negatively associated.
Conclusion: Recompensation is a distinct clinical outcome occurring in a minority of liver transplant candidates. Machine learning using RSF models enables accurate prediction and identifies key contributors such as underlying etiology and nutritional status. These findings may refine transplant eligibility and resource allocation decisions.

PF13-2 10202

Impact of Deep Breathing, Laughter Yoga, and Clapping Exercises on Hypoglycemia and Quality of Life in Post-Liver Transplantation Patients in Central Delhi

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Background: Severe hypoglycemia marked by neuroglycopenic symptoms is a recently recognized but uncommon complication following liver transplantation. Post-operative recovery is often complicated by metabolic disturbances, anxiety, and impaired sleep quality. This study explores the effectiveness of non pharmacological interventions deep breathing exercises, laughter yoga, and clapping therapy in improving glycemic control and overall well-being in post-liver transplantation patients. To evaluate the impact of integrated mind-body therapies on hypoglycemia episodes, mental health parameters, and sleep quality in post liver transplant recipients.
Methods: A cross-sectional study was conducted in the central Delhi metro population, involving 328 liver transplant recipients aged 40 to 60 years. Baseline data included age, family history of hypoglycemia, BMI, anxiety and stress levels, sleep quality, and biochemical markers (fasting glucose, insulin, HbA1c, and OGTT). Participants underwent a structured 30-minute educational session followed by a 30-minute guided regimen of laughter yoga and clapping exercises daily for one month.
Results: Post-intervention analysis revealed significant improvements in sleep quality ($p<0.001$), and a marked reduction in hypoglycemic episodes, anxiety, and depressive symptoms. These findings were more pronounced in individuals who adhered consistently to the prescribed regimen and lifestyle modifications.
Conclusion: The study underscores the importance of incorporating holistic, non pharmacological therapies such as laughter yoga and breathing exercises in post-liver transplant care. These approaches enhance mental and metabolic health, potentially improving long-term outcomes. Future strategies should focus on structured educational programs and integrating lifestyle interventions into routine post-operative protocols.

Poster Session 13

PF13-3 10068

Regional Differences in HCC Etiology: Interim Report from the A-HOC Consortium

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Background: The APASL Hepatology/Oncology Consortium (A-HOC) is a multi-institutional effort to understand the clinical characteristics and outcomes of hepatocellular carcinoma (HCC) across the Asia-Pacific region. As the etiology of HCC is changing, especially with an increasing number of non-B, non-C (NBNC) cases, this study aims to clarify regional differences and identify emerging trends, with particular attention to steatotic liver disease.
Methods: Since April 2023, anonymized data on HCC patients diagnosed from 2013 onward have been collected via a secure, IRB-approved REDCap system. Participating centers across Asia provided structured data on demographics, liver disease etiology, tumor status, treatment, and survival outcomes. Comparative analyses were conducted between Japanese and non-Japanese cohorts.
Results: A total of 6,257 cases were registered by March 2025. In Japan, the proportion of HCV-related HCC has declined, while NBNC-HCC, including alcohol- and MASLD-related cases, has steadily increased. In contrast, HBV remains the dominant etiology in other Asian countries, with little rise in NBNC or MASLD-related HCC. Notably, overall survival stratified by BCLC stage was similar between regions, despite differing backgrounds.
Conclusion: This interim analysis reveals a growing burden of NBNC-HCC in Japan, driven by metabolic and lifestyle-related liver disease. In contrast, viral hepatitis continues to predominate elsewhere in Asia. A-HOC provides valuable real-world insights that support region-specific strategies for HCC prevention and management in the era of steatotic liver disease.

PF13-4 10077

Temporal Relationship between Hepatocarcinogenesis after Sustained Virologic Response and Insulin Resistance in Patients with Chronic Hepatitis C

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Background: Preneoplastic nodules showing hypointensity in the hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI (EOB-MRI) are a known risk factor for hepatocellular carcinoma (HCC) after sustained virologic response (SVR). However, de novo hepatocarcinogenesis also occurs and its pathogenesis remains unclear. Insulin resistance (IR) is associated with hepatitis C virus and may contribute to hepatocarcinogenesis. This study investigated the association between hepatocarcinogenesis after SVR and changes in IR before and after SVR.
Methods: We retrospectively analyzed 112 patients with chronic hepatitis C who achieved SVR and underwent multiple follow-up EOB-MRI, identifying 66 hypervascular HCCs. We examined characteristics of hepatocarcinogenesis after SVR. Changes in IR were assessed using the homeostasis model assessment of insulin resistance (HOMA-IR).
Results: 66 newly developed HCCs were observed in 39 patients. The multistep group, defined by preneoplastic nodules preceding hypervascularization, included 26 nodules in 21 patients. The de novo group, where hypervascular lesions developed without preceding nodules, comprised 40 nodules in 17 patients. Compared to the multistep group, the de novo group had significantly lower FIB-4 index, higher total bilirubin, higher levels of protein induced by vitamin K absence-II, larger tumor size, and more frequent increases in HbA1c after SVR. Notably, in the de novo group, HOMA-IR was significantly decreased at the time of hypervascular HCC appearance compared with levels before SVR.
Conclusions: Hepatocarcinogenesis after SVR occurs via multistep progression from preneoplastic nodules and de novo pathways. De novo HCC development is associated with metabolic alterations, including changes in IR, underscoring the need for metabolic monitoring even after SVR.

Poster Session 14

PF14-1 10180

Lenvatinib Plus TACE for HCC: A Comparison of the Protocols and the Clinical Utility of Lenvatinib Continuation

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Background: Lenvatinib plus TACE (LEN+TACE) is a growing strategy for intermediate-stage HCC, but evidence beyond the TACTICS-L trial is limited. Key unresolved clinical questions remain regarding the optimal TACE protocol (scheduled vs. on-demand) and the significance and duration of post-TACE lenvatinib continuation. We retrospectively examined the prognostic impact of these factors.
Methods: We analyzed 63 HCC patients (scheduled: n=40, on-demand: n=23) who underwent initial LEN+TACE. Response was evaluated at 4 weeks post-TACE (4wOR: mRECIST).
Results: No significant differences were observed between the scheduled and on-demand groups in PFS (6.5M vs. 10.2M, p=n.s.), OS (44.8M vs. 25.8M, p=n.s.), or 4wOR (67% vs. 70%, p=n.s.). However, patients with post-TACE lenvatinib continuation had significantly longer PFS (8.2M vs. 6.2M, p=0.03) and OS (35.6M vs. 19.0M, p=0.007). A significant positive correlation was noted between the duration of post-TACE lenvatinib continuation and PFS (r=0.35, p=0.02) and OS (r=0.37, p=0.01). The on-demand group in the Up-to-7 OUT cohort had a significantly longer duration of post-TACE lenvatinib continuation (184 days vs. 46 days, p=0.02) compared to the scheduled group.
Conclusion: Although there were no significant differences in outcomes between the two TACE protocols, a longer duration of post-TACE lenvatinib continuation was associated with improved prognosis. Optimizing the duration of post-TACE lenvatinib continuation is a crucial area for future research.

PF14-2 10185

Therapeutic Sequences of Systemic Therapy after Atezolizumab Puls Bevasizumab Based on BR-HCC Expert Consensus 2023

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Background: Atezolizumab plus Bevacizumab (Atezo+Bev) is widely used as a first-line treatment for advanced hepatocellular carcinoma (aHCC). The BR-HCC Expert Consensus 2023 recently played a role in identifying candidates for conversion surgery.
Aim: This study aimed to evaluate current treatment strategies after Atezo+Bev therapy, including conversion or combination therapy, based on BR-HCC Expert Consensus 2023.
Methods: We retrospectively analyzed 54 patients (46 males; median age 73 years) with aHCC who received Atezo+Bev as first-line therapy between October 2020 and August 2024 and had evaluable initial treatment response (based on RECIST 1.1 and mRECIST).
Results: The cumulative overall survival (OS) rates at 6, 12, and 24 months were 93.8%, 80.8%, and 68.1%, respectively. The progression-free survival (PFS) rates at 6, 12, and 24 months were 70.3%, 59.8%, and 16.4%. The objective response rate (ORR) and disease control rate (DCR) were 18.5% and 72.2% by RECIST 1.1, and 29.6% and 74.1% by mRECIST. Although the difference was not statistically significant, OS and PFS tended to be shorter in BCLC-C than in BCLC-A/B and in R than in BR1/2. Patients who underwent conversion or combination therapy showed a better OS. Resection was achieved in 2 of 12 R cases (16.7%), 3 of 18 BR1 cases (16.7%), and 2 of 24 BR2 cases (8.3%).
Conclusion: The BR-HCC Expert Consensus 2023 provides valuable guidance on the conversion strategies after Atezo+Bev. The advancement of conversion and combination therapies is anticipated to enhance the potential for achieving CR in systemic treatment of aHCC.

Poster Session 14

PF14-3 10188

Mass-forming Eosinophilic Hepatitis Mimicking Recurrent Hepatocellular Carcinoma after Surgical Resection: A Case Report

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Background: Mass-forming eosinophilic hepatitis is extremely rare and may radiologically mimic malignant liver tumors, especially recurrent hepatocellular carcinoma (HCC). Histologic confirmation is essential for diagnosis.
Case Presentation: A man in his 50s with a history of partial hepatectomy and cholecystectomy for moderately differentiated HCC (S5,6, pT2) presented during routine follow-up with multiple new hepatic nodules seen on CT and EOB-MRI. These lesions showed ring enhancement and hepatobiliary phase hypointensity, initially suggesting tumor recurrence. However, tumor markers were normal. Laboratory tests revealed marked eosinophilia and elevated serum IgE. Parasitic serologies and gastrointestinal endoscopy found no clear secondary cause. Ultrasound-guided liver biopsy of the S4 lesion revealed no tumor cells but showed focal hepatocyte dropout and dense lobular eosinophilic infiltration, consistent with eosinophilic hepatitis. Subsequent imaging, CT and EOB-MRI, showed spontaneous regression of some nodules and emergence of new ones in different liver segments. This supported a diagnosis of inflammatory rather than neoplastic lesions. The patient remained asymptomatic and was managed without corticosteroids.
Discussion: This case demonstrates mass-forming eosinophilic hepatitis mimicking HCC recurrence. Its dynamic nature, with lesion regression and new formation, reflects transient inflammation rather than malignancy. Histological evaluation was critical for avoiding misdiagnosis and unnecessary treatment. Peripheral eosinophilia and atopic background supported the diagnosis.
Future Direction: Serially stored serum and liver tissue samples will be used to explore the immunopathogenic mechanisms underlying hepatic eosinophilic infiltration.

PF14-4 10118

Impact of PNPLA3 Genetic Variant on NBNC-HCC Recurrence

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Background: PNPLA3 genetic variant has been reported to correlate with liver steatosis, liver cirrhosis and liver carcinogenesis, whereas no report has been shown regarding its correlation with prognosis after curative resection for HCC.
Patients and Methods: One hundred and sixteen patients who underwent hepatectomy for NBNC HCCs were enrolled from July 2009 to December 2018. PNPLA3 (rs738409) was genotyped. They were divided into two group major homozygout (CC group) and minor allele carriers (CG/GG group). The clinical background and long term outcome were compared. In addition, the factors correlated with HCC recurrence were compared among CG/GG group.
Results: Among 116 patients, 96 (82.7%) were G allele carriers. There was no difference in clinicopathological background, tumor factors or operative factors between two groups. 5-year recurrence free survival was 66.7% in CC group and 31.5% in CG/GG group (p=0.02). But there was no difference for the first 2 post-operation year. Twenty two patients in CG/GG group who showed recurrence within a year were excluded and divided into two groups A group (no recurrence for more than 5 years, n=39) and B group (recurrence within 5 year, n=35). A group showed lower BMI (22.9 vs 25.3, p=0.01) and higher incidence of diuretics intake (17.5% vs 2.8%, p=0.01) (there was no difference in the incidence of hyper tension). There was no difference regarding other medication history or smoking history.
Conclusions: PNPLA3 genetic variants correlated with HCC recurrence. Body weight loss may play a key to prevent from HCC recurrence among PNPLA3 minor carriers.

Poster Session 14
PF14-5 10158

Evaluation of the Diagnostic Performance of the GAAD Score with a 2.57 Cutoff for Hepatocellular Carcinoma in Vietnamese Patients

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Background: Early detection of hepatocellular carcinoma (HCC) in patients with chronic liver disease remains challenging, as most cases are diagnosed at late stages. GAAD Score, a composite biomarker, was developed to optimize HCC diagnosis. This study evaluates the diagnostic performance of a GAAD Score cutoff of 2.57 compared with individual biomarkers in a Vietnamese cohort.
Methods: In a retrospective analysis, 2,606 patients presenting to the Hepatology Department of Medic Center from September 2023 to January 2025 were included. Demographic, laboratory, imaging, and final diagnostic data were collected. HCC was confirmed by imaging and/or histopathology. Cutoffs applied were GAAD Score >=2.57, AFP >=20 ng/mL, and PIVKAII >= 28.6 (males) / 27.8 (females) ng/mL. Diagnostic performance was assessed by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating characteristic curve (AUC).
Results: Among 2,606 patients, 128 (4.9%) were diagnosed with HCC. At the GAAD Score cutoff, AUC was 0.986 (95% CI: 0.978 - 0.991), sensitivity 86.7%, specificity 98.4%, PPV 74.0%, and NPV 99.3%. PIVKA-II yielded AUC 0.896, sensitivity 75.8%, specificity 95.9%, while AFP achieved AUC 0.875, sensitivity 67.2%, specificity 93.5%. Evaluation of 41 GAAD cutoffs (1.0 - 4.9) confirmed 2.57 as optimal.
Conclusions: GAAD Score at 2.57 outperforms AFP and PIVKA-II alone for HCC screening in low-prevalence populations. Its high NPV and low false-positive rate support its use as an effective clinical screening tool.

Poster Session 15

PF15-1 10055

Metastatic Liver Tumors: A Retrospective Spectrum of Differential Diagnoses from a North Indian Tertiary Health Center

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Space-occupying liver lesions can be broadly categorized as benign or malignant, with the latter further divided into primary and metastatic types. This study aimed to evaluate the histomorphological and immunohistochemical profiles of metastatic liver lesions and to develop a diagnostic approach for identifying the primary site, particularly in round-cell and spindle cell tumors. A retrospective cross-sectional analysis was conducted from July 2021 to March 2023 at the Department of Paediatrics, National Institute of TB and Respiratory Diseases, New Delhi. All patients diagnosed with metastatic liver lesions during this period were included. Histomorphological and immunohistochemical findings were reviewed, and data were analyzed using Stata 14.0. A total of 367 cases were included. The mean age was 56.8 years (range: 11 months to 87 years; median: 58 years; interquartile range: 46 to 65 years), with a female predominance (54.8%). Adenocarcinomas were the most common histological type (67.7%), followed by neuroendocrine tumors (13.9%) and melanomas (1.4%). The most frequent primary sites were pancreaticobiliary (53.1%), lung (15.8%), breast (8.9%), and colorectal (5.1%). Rare entities included spindle cell tumors, lymphomas, melanomas, and germ cell tumors. The liver is a common site for metastases, with adenocarcinoma being the most prevalent histological subtype. Pancreaticobiliary cancers were the predominant primary source. A stepwise diagnostic approach using immunohistochemistry and clinicoradiological correlation is vital for accurate identification and appropriate clinical management.

PF15-2 10096

Imaging-Pathology Discordance in a Rare Case of Mucinous Intrahepatic Cholangiocarcinoma Presenting as a Cystic Liver Lesion

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Background: Mucinous intrahepatic cholangiocarcinoma (iCCA) is a rare subtype of bile duct cancer that may present with atypical imaging features. In some cases, it closely resembles benign cystic hepatic lesions, such as mucinous cystic neoplasms, making diagnosis particularly challenging. We report a case of mucinous iCCA with benign-appearing radiologic findings, ultimately diagnosed as malignant on histopathology, highlighting a rare instance of imaging-pathology discordance.
Methods: A 63-year-old male presented with right upper quadrant pain, jaundice, and tea-colored urine. ERCP revealed biliary ectasia without obstruction. MRI with primovist showed a 4.3 cm lobulated, septated, T2 hyperintense cystic mass in the left periportal region, causing mild dilation of the left intrahepatic and proximal common bile ducts. The lesion lacked bile duct communication and showed no contrast enhancement on all imaging phases. Tumor markers were within normal limits. CT-guided core biopsy and subsequent histopathologic analysis were performed.
Results: The lesion's cystic morphology, minimal vascularity, and absence of ductal involvement suggested a benign cystic neoplasm. However, histopathologic evaluation revealed mucinous adenocarcinoma. PET-CT showed no extrahepatic disease, confirming the diagnosis of primary mucinous intrahepatic cholangiocarcinoma.
Conclusion: This case underscores the diagnostic challenge posed by mucinous iCCA presenting as a benign-appearing cystic liver lesion. The benign imaging features and lack of biliary communication lowered suspicion for cholangiocarcinoma. Histopathology was essential for diagnosis. This rare presentation contributes to the limited literature and highlights the importance of considering iCCA in atypical cystic liver lesions.

Poster Session 15
PF15-3 10054

Clinicopathological Insights into Pediatric Liver Tumors: A North Indian Tertiary Hospital Setting

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Pediatric primary liver tumors represent the third most common group of solid abdominal neoplasms in children, which accounts for approximately 0.5% to 2% of all paediatric neoplasms. This study aimed to determine the incidence of pediatric liver tumors over a five-year period and to assess their clinical behavior, correlate alpha-fetoprotein (AFP) levels, and examine their histopathological features. Patient records for paediatric liver tumors treated over the past five years were retrospectively retrieved from the tumor board and medical records. Gross examination and review of all slides were conducted to confirm the pathological diagnosis, followed by clinicopathological correlation. A total of 57 paediatric liver tumors were identified over the five-year period, with 87% being malignant and 31% benign. Hepatoblastoma was the most common tumor, accounting for 76.8%, of which 85.4% of the pure epithelial type. The second most common primary tumor was epithelioid hemangioendothelioma, with 15.4% predominantly in females, followed by 9% each of hepatocellular carcinoma and undifferentiated embryonal sarcoma, and 4% hepatocellular adenoma. Serum AFP levels were elevated in hepatoblastoma and hepatocellular carcinoma, remained normal in hepatocellular adenoma and embryonal sarcoma, and were increased in some cases of epithelioid hemangioendothelioma. The spectrum of liver tumors in children is distinct from that in adults. Hepatoblastoma is the most common pediatric liver tumor, followed by epithelioid hemangioendothelioma. With advancements in pathological diagnosis, refined surgical staging, improved radiological techniques, and standardized multimodal therapies, a substantial number of children diagnosed with these highly malignant tumors can anticipate improved survival outcomes.

PF15-4 10131

XRCC1 Gene Polymorphism and the Risk of Hepatocellular Carcinoma in Egypt

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Background: Several major risk factors for hepatocellular carcinoma (HCC) have been identified, including chronic infection of hepatitis B virus (HBV) and hepatitis C virus (HCV). Nevertheless, only a fraction of infected patients develops HCC during their lifetime suggesting that genetic factors might modulate HCC development. X-ray repair cross complementing group1 (XRCC1) participates in the repair pathways of DNA.
Aim: To investigate the association between XRCC1 gene polymorphism and HCC in Egyptian chronic hepatitis C patients.
Methods: This study was assessed on 40 patients with HCC secondary to chronic HCV infection who were compared to 20 cirrhotic HCV patients and 40- age and gender- matched healthy control group. After collection of relevant clinical data and basic laboratory tests, c.1517G C SNP of XRCC1 gene polymorphism was performed by (PCR-RFLP) technique.
Results: A statistically higher frequency of XRCC1 (CC, GC) genotypes and increased (C) allele frequency in patients with HCC was found in comparison to cirrhotic HCV patients as well as control group. In addition, patients with the XRCC1 (CC, GC) genotypes had significantly higher number and larger size of tumor foci and significantly higher Child Pugh grades. Multivariate analysis showed that the presence of c.1517G C SNP of XRCC1 gene is an independent risk for the development of HCC in chronic HCV patients with 3.7 fold increased risk of HCC development.
In conclusion: XRCC1 gene polymorphism could be associated with increased risk of HCC development in chronic HCV Egyptian patients.

Poster Session 15
PF15-5 10089

Hepatocyte Nuclear Factor 1 Alpha Variants as a Risk Factor for Hepatocellular Carcinoma Development with/without Diabetes Mellitus

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Background: HNF1A gene variants have been reported to be involved in developing mature onset diabetes mellitus (DM). Many studies reported the role of DM as a risk factor for hepatocellular carcinoma (HCC) development. We evaluated the HNF1A (the hepatocyte nuclear factor 1 homeobox A) genetic variants as a cofactor with DM for HCC development in hepatitis C virus (HCV)-infected patients.
Methods: We enrolled 140 subjects; 30 (HCC without DM), 30 (HCC with DM), 40 patients (DM with no HCV, 80 as a control group. Liver function tests, hepatitis viral markers, alpha-fetoprotein (AFP), fasting sugar and HBA1c and HNF1A (rs2464196 and rs1169310) using real-time polymerase chain reaction (PCR) were done for all participants.
Results: The frequency of HNF1A rs2464196 (AA) genotype in patient groups (DM, HCC, HCC+DM) was significantly higher compared to the control group (P=0.006, P=0.018, P 0.001 respectively). The combined dominant model (AA + GA) of rs2464196 was significantly higher than the (GG) genotype in patient groups (DM, HCC, HCC+DM) than the control group. In addition, the frequency of the AA genotype is more prevalent in HCC+DM (73%) compared to the group of DM or HCC patients. In contrast, the HNF1A rs 1169310 (TT, TC or CC genotypes) showed no significant difference among the four studied groups and their T or C allele distributions.
Conclusion: This finding suggested that the HNF1A rs2464196 (AA) genotype could be associated with DM and may raise the possibility of HCC development among HCV-infected patients who harbor this genotype more than (GG).

Poster Session 16

PF16-1 10004

Prognostic Significance of Skeletal Muscle Mass in Patients with Alcoholic Cirrhosis

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Background: This study aimed to assess the prognostic significance of hand grip strength (HGS) and skeletal muscle mass index (SMI) in patients with liver cirrhosis (LC).
Methods: Out of 941 patients with LC, 619 were assessed for HGS and computed tomography-based skeletal muscle mass index (CT-SMI). They were then categorized into two groups: alcoholic cirrhosis (AC; n = 226) and nonalcoholic cirrhosis (NAC; n = 393).
Results: The overall prevalence of sarcopenia was 16.4% and 21.1% in the AC and NAC groups, respectively. Three factors, including SMI below 42 cm ^{2}/m^2 in males and 38 cm^2/m^2 in female, ALB&It; 3.7 g/dL, sodium levels below 138 mEq/L, and five factors, including HGS below 28 kg in males and below 18 kg in females, incidence of ascites, ALB &It;3.5 g/dL, cholinesterase levels below 200 U/L, and sodium levels below 138 mEq/L, were identified as prognostic factors for mortality in the AC and NAC groups, respectively. In the AC group, overall survival (OS) was significantly lower in patients with normal HGS + low SMI (pre-sarcopenia) than in those with normal SMI and HGS. OS was also significantly lower in patients with low SMI + low HGS (sarcopenia) than in those with dynapenia. In the NAC group, OS was significantly lower in patients with normal SMI + low HGS (dynapenia) than in those with normal SMI and HGS. OS was also significantly lower in sarcopenia than in pre-sarcopenia.
Conclusions: In the AC group, SMI could serve as a more powerful predictor of survival than HGS.

PF16-2 10215

The Role of Non-Invasive Methods and Serological Biomarkers in the Diagnosis and Morphological Characterization of Autoimmune Hepatitis with Correlation to Liver Biopsy Findings

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Background: The study aimed to evaluate the correlation between non-invasive methods including transient elastography (TE), Aminotransferase to platelet ratio index (APRI), and the Fib-4 index with liver biopsy results in autoimmune hepatitis (AIH). Additionally, immunological and morphological differences between seronegative and seropositive forms were analyzed.
Methods: Fifty-five patients diagnosed with AIH based on the International Autoimmune Hepatitis Group (IAIHG) criteria were included. All patients underwent laboratory testing including ALT, AST, and platelet count, as well as ANA and AMA detection using indirect immunofluorescence. Liver stiffness and steatosis were measured by TE (FibroScan, M probe), along with APRI and Fib-4 index. Liver biopsies were performed by a single specialist. Histological evaluation was conducted by a pathologist blinded to clinical and imaging data, using the METAVIR scoring system. Patients with more than 3 months between tests were excluded. Sensitivity, specificity, and the Youden index were calculated.
Results: Results: Transient elastography demonstrated high sensitivity for detecting fibrosis stages F>=2 (97.56%), F>=3 (96.97%), and F>=4 (100%), with high specificity for F>=2 (92.86%) and F>=3 (90.91%). Sensitivity for steatosis stages S>=2 and S>=3 exceeded 97%, though specificity was moderate. No significant clinical or morphological differences were observed between the seronegative and seropositive groups.
Conclusion: Transient elastography is a reliable non-invasive method for staging fibrosis and steatosis in AIH, outperforming APRI and Fib-4 in diagnostic accuracy. In seronegative cases, liver biopsy remains necessary to confirm the diagnosis and initiate therapy.

Poster Session 16
PF16-3 10030

Drug- induced Autoimmune Hepatitis

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Background: Drug-induced autoimmune hepatitis (DIAIH) is a rare but important clinical entity that mimics idiopathic autoimmune hepatitis (AIH) both clinically and histologically. It is triggered by certain medications in genetically predisposed individuals and poses diagnostic and therapeutic challenges due to its overlapping features with classical AIH and drug-induced liver injury (DILI). At present, there are still few reports on this condition both globally and in Vietnam.
Introduction: DIAIH represents a subset of liver injury that shares features with idiopathic AIH but is precipitated by drug exposure. The exact mechanisms underlying DIAIH remain unclear. It is hypothesized that certain drugs act as haptens or modify self-antigens, triggering a loss of immune tolerance in susceptible individuals.
Clinical and Histological Features: Patients with DIAIH often present with non-specific symptoms. Histologically, DIAIH is indistinguishable from idiopathic AIH, showing interface hepatitis, plasma cell infiltration, and sometimes rosetting of hepatocytes.
Diagnosis: The diagnosis of DIAIH is based on a combination of clinical history, laboratory findings, and liver biopsy. Key elements include the temporal relationship between drug exposure and onset of hepatitis, presence of autoantibodies (ANA, ASMA), elevated IgG, and histological findings.
Management: Initial management involves prompt discontinuation of the offending drug. Corticosteroid therapy may be required in more severe cases or when there is no improvement after drug withdrawal. The long-term need for immunosuppressive therapy is less common than in idiopathic AIH.
Keywords: hepatitis, liver disease

PF16-4 10184

The Liver That Looked Malignant: Autoimmune Hepatitis Masquerading as Malignancy-A case for Clinical Judgment in Hepatology

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Background: Autoimmune Hepatitis (AIH) is a rare, immune-mediated liver disease without a pathognomonic marker. Diagnosis relies on serology, absence of virology markers and histopathology. Treatment can be delayed while awaiting biopsy, leading to clinical deterioration. In severe cases, extensive necrosis and ductular reaction may obscure hallmark histologic features such as interface hepatitis and plasma cell infiltration, complicating diagnosis even after biopsy.
Methods: Case Report Results/Case-Presentation: A 68-year-old woman presented with jaundice, ascites, severe vomiting, giddiness and leg swelling. Investigations showed hepatocellular liver injury, coagulopathy, hyponatremia and elevated CA19-9(700U/mL). Autoimmune serology supported AIH(ANA>640, LC-1 positive, IgG23.98); viral hepatitis screens were negative. Initial CT suggested cirrhosis without obvious signs of malignancy. However subsequent MRCP revealed extensive ill-defined T2-weighted hyperintensity, delayed enhancement in multiple hepatic lobes with encasement of hepatic veins and intrahepatic IVC(See Fig1.), suggesting infiltrative malignancy; even though autoimmune serology suggested otherwise. Liver biopsy showed confluent necrosis with florid ductular reaction-without malignant features or hallmarks features of AIH. Despite histological ambiguity, corticosteroids were initiated after integrating the temporal sequence of her clinical presentation, imaging and histology findings. She was subsequently placed on a tapering regime of corticosteroids with azathioprine later added the patient improved clinically with resolution of ascites, giddiness and vomiting. Liver enzymes, CA19-9, and coagulation parameters normalized, and follow-up imaging remained stable without evidence of malignancy.
Conclusion: Untreated AIH can progress to necrosis and ductular reaction, mimicking intrahepatic malignancy. While early biopsy is crucial, clinical judgment is also important in guiding management as histology can be inconclusive.

Poster Session 16
PF16-5 10120

Inhibitory Effects of Haskap Fruit Extract on Animal Models of Primary Biliary Cholangitis and Primary Sclerosing Cholangitis

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Background: The effects of haskap fruit on primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) have not been elucidated. In this study, we examined the effects of haskap fruit extract on animal models of PBC and PSC.
Methods: 1. PBC: Eight-week-old female Cyp2c70/Cyp2a12 double knockout mice were intraperitoneally injected with 2OA-BSA to induce PBC. The mice were divided into the control (normal diet), low-, medium-, and high-dose groups (normal diet supplemented with 0.15%, 0.75%, and 1.5% haskap fruit extract, respectively). After 8 weeks, the mice were sacrificed, and serum biochemical and histopathological analyses were performed.2. PSC: Four-week-old male Abcb4-/- mice were divided into the control, low-, and high-dose groups (the diets were the same as above). After 10 weeks, the mice were sacrificed, and similar analyses were performed.
Results: 1. PBC: Serum AST, ALT, and ALP levels tended to be lower in the medium- and high-dose groups than in the control group. Histopathologically, cholangitis activity, fibrosis score, and PBC stage tended to be lower in the medium-dose group than in the control group.2. PSC: Serum ALT levels were significantly lower in the low-dose group than in the control group and ALP levels were significantly lower in the high-dose group than in the control group. On image analysis of the hepatic tissues, the number of CD3-, CD4-, and CD8-positive cells was significantly smaller in the low- and/or high-dose groups than in the control group.
Conclusions: Haskap fruit extract showed promising effects on animal models of PBC and PSC.

Poster Session 17

PF17-1 10056

Prevalence and Genotypes Distribution of Virus Hepatitis B and Hepatitis Delta Virus in Chronic Liver Diseases in Kazakhstan

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NSCS named after A. N. Syzganov. Kazakhstan. Almaty

Background: The geographical distribution of HBV and HDV genotypes is uneven and has its own clinical and organizational implications for health systems. Despite the introduction of vaccination and successful antiviral therapy the prevalence of chronic hepatitis B (with or without delta agent) increased over the past 5 years. This study aimed for the first time to investigate the molecular epidemiology of HBV and HDV in Kazakhstan.
Methods: Total 834 chronic hepatitis B (with or without delta agent) patients were included to the study from 2020 to 2024. The material was collected from the regional 13 hepatological clinics of Kazakhstan. Genotyping of HBV/HDV isolates was carried out using phylogenetic analysis of null-binary sequences of Kazakhstani isolates, in comparison with the reference sequences. Nucleotide sequence alignment was performed using the ClustalW algorithm, the neighbor-joining method was used for the construction of phylogenetic trees and subsequent analysis.
Results: Overall 341 samples were PCR-positive and genotyped for HBV. Comparison and phylogenetic analysis of nucleotide sequences of HBV isolates showed that they were represented by genotypes HBV-D (95.9%), HBV-A (3.5%) and HBV-C (0.6%). The identity of the nucleotide sequences of Kazakhstani isolates were: HBV-D (95-100%); HBV-A (97.2-100%) and HBV-C (99%). 256 samples were PCR positive and genotyped for HDV, all of them belonged to genotype 1.
Conclusion: This study describes for the first time the molecular epidemiology of hepatites in Kazakhstan. The data obtained expand knowledge of global viral epidemiology; have potential implications for public health policy and further clinical research on chronic hepatitis in Kazakhstan.

PF17-2 10069

Fat Accumulation as a Risk Factor for HCC and Extrahepatic Cancers After SVR: A Prospective Study Based on Fibro Scan derived Stratification

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Background and Aims: In Japan, the etiology of hepatocellular carcinoma (HCC) has shifted from hepatitis C virus (HCV) infection to steatohepatitis. We aimed to evaluate the impact of hepatic steatosis and fibrosis on cancer development after achieving sustained virologic response (SVR) in a prospective cohort.
Methods: We prospectively followed 651 SVR patients treated between July 2013 and December 2021. Patients were classified into four groups using pre-treatment FibroScan values (VCTE cutoff: 15.4 kPa; CAP cutoff: 229 dB/m): Group A (low fibrosis/low fat), B (high fibrosis/low fat), C (low fibrosis/high fat), D (high fibrosis/high fat). The incidence of malignancy was calculated using person-years.
Results: During a median follow-up of 5.44 years, 107 malignancies occurred in 99 patients. The overall cancer incidence was 3.68 per 100 person-years. HCC incidence per 100 person-years was 1.01 (A), 4.88 (B), 1.37 (C), and 6.10 (D). High fibrosis increased HCC risk fivefold, and high fat increased it 1.3-fold. Extrahepatic cancer incidence was 1.48 (A), 0.96 (B), 2.61 (C), and 2.91 (D) per 100 person-years. While fibrosis had little effect on extrahepatic cancer, high steatosis doubled the risk.
Conclusions: Post-SVR fat accumulation is associated with a 1.3-fold increased risk of HCC and a >2-fold increased risk of extrahepatic cancers. These findings highlight the need for longitudinal surveillance that addresses not only liver fibrosis but also hepatic steatosis.

Poster Session 17
PF17-3 10070

Post-SVR Dynamics of Hepatic Steatosis: Divergent Patterns by Fibrosis Stage and Implications for HCC Risk

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Background: While direct-acting antivirals (DAAs) achieve sustained virologic response (SVR) in hepatitis C virus (HCV) infection, post-SVR changes in hepatic steatosis remain underexplored, particularly in relation to fibrosis stage and hepatocarcinogenesis.
Methods: We analyzed serial FibroScan data from 519 patients with SVR after DAA therapy. Controlled attenuation parameter (CAP, dB/m) changes were classified as improved (more than 10 dB/m decrease), worsened (more than 10 dB/m increase), or stable. Patients were stratified by baseline fibrosis stage (Groups 1 to 4). Associations with hepatocellular carcinoma (HCC) and extrahepatic malignancies were examined.
Results: CAP improved in 220 patients (42%), worsened in 177 (34%), and remained stable in 28 (5%). In Group 1 (mild fibrosis), CAP tended to worsen (11 worsening vs. 5 improving), whereas in Group 4 (advanced fibrosis), CAP tended to improve (75 improving vs. 43 worsening) ($p = 0.027$). HCC incidence was significantly higher in the CAP improvement group than in the worsening group (29/220 vs. 12/177, $p = 0.046$).
Conclusions: Post SVR steatosis changes differ by fibrosis stage. CAP improvement was common in advanced fibrosis, possibly reflecting fibrosis regression. However, fat reduction alone did not indicate lower cancer risk. These findings highlight the need for careful long term monitoring after virologic cure.

PF17-4 10138

Evaluation of Shortened DAA Regimens (Sofosbuvir + Velpatasvir, Sofosbuvir + Daclatasvir) in Chronic Hepatitis C Patients Based on Early Virological Response

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Background: Chronic hepatitis C virus (HCV) infection remains a significant global health burden. Direct-acting antivirals (DAAs) have revolutionized treatment outcomes; yet optimizing treatment duration to reduce cost and improve access remains crucial - especially in resource-limited and underserved healthcare settings.
Aims: This study aimed to assess the efficacy and safety of individualized shortened DAA regimens in chronic HCV patients, guided by HCV RNA levels on treatment day 7.
Method: A prospective, multi-center study recruited treatment-naive chronic HCV patients who received either Sofosbuvir/Velpatasvir (SOF/VEL) or Sofosbuvir/Daclatasvir (SOF/DAC). Patients were allocated to 4, 8, or 12 week treatment arms based on viral load at day 7. The primary outcome was sustained virological response at 12 weeks post-treatment (SVR12). Secondary measures included liver biochemistry (ALT, AST, bilirubin), FIB-4 scores, and safety assessment.
Results: In patients with HCV RNA below the lower limit of quantification (LLOQ) at day 7, SVR12 rates were 92.3 percent (8 week group) and 97.8 percent (12 week group), with no statistically significant difference. The 4 week group showed higher relapse rates. SOF/DAC showed slightly better viral clearance in shorter regimens. Liver function (ALT, AST, bilirubin) and FIB-4 scores improved. No serious adverse events were reported.
Conclusion: Shortened DAA regimens tailored by early virologic response are effective and safe in selected patients. An 8 week course offers comparable efficacy to standard therapy, with potential for cost savings and improved adherence. This strategy aligns with the WHO's goal of eliminating HCV by 2030.

Poster Session 17
PF17-5 10204

Evaluation of HCVDuo as a Primary Tool for Hepatitis C Screening in Japan

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Under Japan's Health Promotion Act, hepatitis C virus (HCV) screening has been implemented in health checkups since 2002. In response to high HCV prevalence and the need to reduce reliance on costly PCR testing, the Viral Hepatitis Epidemiological Research Group of the Ministry of Health, Labour and Welfare (MHLW) proposed a protocol based on HCV antibody levels, which was adopted for community-based screenings. This study assessed the performance of the newly developed HCVDuo reagent as a primary screening tool using 966 health checkup panel sera and 21 positive seroconversion sera from dialysis patients. HCVDuo, which qualitatively detects both HCV antibodies and core antigens, successfully identified 78% of HCV-RNA positive cases when both markers were present. In rare cases where the core antigen was positive but the antibody was negative, a follow-up test after one month is recommended. While HCVDuo demonstrated 100% sensitivity for HCV-RNA, its core antigen sensitivity alone was 78.3%, highlighting the need for further improvement. Notably, HCVDuo showed reduced accuracy when tested with samples from dialysis patients, particularly in early infection stages. This suggests the current screening protocol requires further consideration for high-risk populations.

Poster Session 18

PF18-1 10189

PARPBP as a Prognostic Biomarker Linked to Tumor Differentiation and Immune Microenvironment in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) shows a high recurrence rate even after curative resection, necessitating reliable prognostic markers. We focused on PARPBP (PARP1 binding protein), identified using a murine orthotopic HCC model, and examined its clinical relevance in human HCC.

Methods: We analyzed 96 resected HCC specimens from Osaka Metropolitan University Hospital (2014-2020). PARPBP expression and CD8-positive tumor-infiltrating lymphocyte (CD8+ TIL) density were evaluated by immunohistochemistry. Functional analyses using Huh7 and HepG2 cells were conducted to assess the role of PARPBP in cell proliferation.

Results: PARPBP expression was significantly higher in moderately and poorly differentiated HCC than in well-differentiated tumors. High PARPBP expression was associated with shorter recurrence-free and overall survival (both P less than 0.001). Multivariate analysis identified high PARPBP expression, high CD8+ TIL density, and AFP greater than or equal to 10 ng/mL as independent predictors of prognosis. Notably, the combination of high PARPBP expression and low CD8+ TIL density was linked to the worst outcomes. Functionally, PARPBP knockdown suppressed Huh7 cell proliferation, while PARPBP overexpression conferred resistance to DNA synthesis inhibition in HepG2 cells.

Conclusion: PARPBP expression is associated with tumor differentiation and prognosis in HCC. Combined evaluation with CD8+ TIL density enhances prognostic prediction, suggesting PARPBP as a promising biomarker and potential therapeutic target in HCC.

PF18-2 10083

ANGPTL6 Regulates Epithelial Mesenchymal Transition in Liver Cancer

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Liver cancer accounts for 4-6% of global cancer deaths. Although sorafenib is an effective drug, only a small proportion of patients respond to it. Moreover, many patients develop resistance after 6 months of sorafenib treatment. Therefore, identifying new therapeutic targets is urgently needed. Angiopoietin like protein 6 (ANGPTL6) is a member of ANGPTL family, which shares structural similarity with angiopoietin. ANGPTL6 is mainly secreted by liver. Recent study found ANGPTL6 may participate in glucose and lipid metabolism and promote cancer cells growth and metastases. However, the role of ANGPTL6 in liver cancer remains unclear. In this study, we cultured hepatocellular carcinoma (HCC) cells and established ANGPTL6-knockdown HCC cell line to figure out the effects and underlying mechanisms of ANGPTL6. Based on TCGA database, the mRNA expression levels of ANGPTL6 decreased in HCC patients. Additionally, HCC patients with lower expression levels showed poorer survival. Among different HCC cell lines, Hep3B and HepG2 showed lower expression levels of ANGPTL6. Accordingly, we treated Hep3B and HepG2 with recombinant ANGPTL6 protein. We found that with rhANGPTL6 treatment, migration ability of HCC cells was inhibited. The mRNA expression levels of mesenchymal markers decreased; while the protein expression levels of epithelial markers increased in rhANGPTL6-treated HCC cells. HuH7 cells exhibited higher expression levels of ANGPTL6, hence we established shANGPTL6-HuH7 cell lines. Compared to control cells, shANGPTL6 cells displayed enhanced migration capacity. In conclusion, ANGPTL6 inhibited HCC cells migration through regulation epithelial-mesenchymal transition. ANGPTL6 might be a new therapeutic target of liver cancers.

Poster Session 18

PF18-3 10107

The Effectiveness of Hepatitis Medical Care Coordinator Certification among Dentists: Seven Years of Progress by the Aichi Dental Association

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Background: Since 2018, the Aichi Dental Association (ADA) has been conducting a hepatitis awareness project to promote better public awareness and professional understanding of hepatitis. Since 2021, ADA has held annual training and certification programs for hepatitis medical care coordinators (hepatitis-Co). This study evaluated the seven-year outcomes of ADA's initiative and the effectiveness of hepatitis-Co certification for dentists.
Methods: A survey was conducted in November 2024 among 3,939 ADA members, resulting in 678 responses (response rate: 17.2%). Respondents included 95 hepatitis-Co, 140 attendees of hepatitis-related lectures who were not certified as hepatitis-Co (attendees), and 443 non-attendees. The survey assessed changes in dentists' knowledge, professional development, and attitudes toward hepatitis patients.
Results: Hepatitis-Co demonstrated significantly higher engagement in continuous education and patient referrals to specialists compared to attendees and non-attendees (both $p < 1.0 \times 10^{-3}$). Additionally, 96.8% of hepatitis-Co (92/95) reported positive changes compared to 85.7% of attendees (120/140) and 69.5% of non-attendees (308/443) ($p < 1.0 \times 10^{-3}$, each). Knowledge about hepatitis was significantly deeper among hepatitis-Co compared to attendees and non-attendees (both $p < 1.0 \times 10^{-3}$). Furthermore, hepatitis-Co coordinators demonstrated substantial reductions in stigma and prejudice against hepatitis patients compared to both groups (both $p < 1.0 \times 10^{-3}$).
Conclusions: The hepatitis-Co certification for dentists effectively improves professional practices, reduces stigma, and facilitates patient referrals. Furthermore, ADA's hepatitis awareness programs demonstrate positive impacts even on dentists who have never attended hepatitis-related seminars, promoting broader hepatitis awareness. The success of this project in Aichi, with 21.4% of hepatitis-Co being dentists, highlights its potential for broader implementation and public health practices.

PF18-4 10168

Photocatalytic Degradation of Methylene Blue to Mitigate Liver Disease: A Step Toward Sustainable Wastewater Treatment

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Methylene blue (MB), widely used in various industries, poses significant health risks to human health. MB exposure induces oxidative stress and hepatotoxicity, contributing to liver injury and exacerbating liver diseases such as steatosis and fibrosis. The liver's central role in detoxification makes it particularly vulnerable to MB-induced reactive oxygen species (ROS) generation, which leads to cellular damage and impaired hepatic function. Therefore, the effective removal of MB from wastewater is critical to mitigate its adverse effects on liver health. This study investigates an advanced photocatalytic approach for the effective degradation of MB in aqueous systems using a novel photocatalyst. The photodegradation of MB was conducted under UV light exposure using the synthesised photocatalyst. Various operational parameters, including initial dye concentration, pH, UV light wattage and reaction time, were studied to enhance the photodegradation efficiency. The photocatalytic degradation of MB was measured using Ultraviolet-Visible (UV-Vis) spectroscopy. Under optimised conditions, the results demonstrated rapid and effective removal of MB from aqueous solutions. These results highlight the potential of advanced photocatalytic technologies as sustainable solutions for removing hepatotoxic contaminants from industrial effluents, thus reducing oxidative stress-related liver damage in exposed populations. Overall, the findings underscore the crucial importance of addressing MB pollution to mitigate its adverse effects on liver disease progression, providing a promising pathway for safeguarding both environmental and public health.

Poster Session 18
PF18-5 10123

Comparison of Machine Learning Algorithm in Predicting Living Status of Hepatitis Patients

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Background: Hepatitis is an inflammation of the liver caused by various infectious viruses and noninfectious agents, resulting in a range of health issues, some of which can be fatal. Predicting hepatitis allows for early identification of the infection, enabling timely intervention and treatment. Early detection can prevent the progression of the disease to more severe stages, reducing the risk of complications such as liver cirrhosis and cancer. In this study, we will use an artificial intelligence approach to classify patients based on the possibility of living or dying using several attributes.
Methods: This study will compare several algorithms such as artificial neural network (ANN), K nearest neighbor (knn), and support vector machine (SVM). The data obtained from Kaggle with a total of 142 data with 19 attributes, such as age, sex, steroid, antivirals, fatigue, malaise, anorexia, liver big, liver firm, spleen palable, spiders, ascites, varices, bilirubin, alk phosphate, sgot, albumin, protime, and histology.
Results: The model will be evaluated using three test metrics, namely accuracy, sensitivity and specificity. Based on the results obtained, it can be seen that the artificial neural network provides the most optimal results with the highest accuracy. The results obtained were influenced by an unbalanced amount of data.
Conclusions: Based on the results of the comparison carried out on the ANN, svm, and knn methods, the results showed that the most optimal algorithm was the ANN algorithm. For further development, the availability of large amounts of data will greatly influence the performance of the algorithm.

Poster Session 19

PF19-1 10198

Photothermally Modulated Liposome Enabling Efficient Release of Glucose Analogue Safely Displays Vigorous Antitumor Effect against Liver Cancer

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Background and Aim: A glucose derivative, 2-deoxy-D-glucose (2DG), exerts cytotoxic effects against several cancers through suppression of Warburg effect. However, the clinical application of 2DG is not recognized because of adverse events due to high dose administration. We developed a novel drug delivery system (DDS) which delivers and releases 2DG efficiently into cancer cells, using thermodynamic cell engineering. The aim of this study was to assess antitumor effect and safety of this DDS against liver cancer.
Methods: Liposomal nanoparticles (LNPs) encapsulated 2DG having a photothermal agent (a near-infrared [NIR] absorbing dye) embedded in the polymer membrane were engineered, with their surface modified with cancer-targeting cyclic peptide (iRGD) (called iRGD-2DG-NanoHT). The antitumor effect of iRGD-2DG-NanoHT was assessed in murine HCC models [diethylnitrosamine(DEN)-induced mice].
Results: NIR absorbing dye was more accumulated in liver tumors in mice treated with iRGD-2DG-NanoHT than those with 2DG-NanoHT (without iRGD). Mice treated with iRGD-2DG-NanoHT showed significantly reduced tumor volume with more necrotic tumor cells and increased mononuclear cell infiltration than those treated with 2DG alone or iRGD-NanoHT. Mechanistically, treatment with iRGD-2DG-NanoHT displayed cytotoxicity based on ferroptosis via reduction of GSH/GPX4 axis, and induced HMGB-1 (DAMPs)-mediated antitumor immunity. Treatment with ferroptosis inhibitor Ferrostatin-1(Ferr-1) abrogated the antitumor effects and antitumor immunity of the DEN-induced mice treated with iRGD-2DG-NanoHT.
Conclusions: iRGD-2DG-NanoHT has potential as a new therapeutic treatment for liver cancer based on its cancer-specific DDS.

PF19-2 10088

Inhibition of HAV Replication by Azathioprine in Vitro

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Background: With medical progress, immunosuppressants have been widely used. However, it is unknown whether immunosuppressants have an inhibitory effect on HAV replication or not. Thus, we examined the effect of several immunosuppressants affect HAV replication in vitro.
Methods: Effects of azathioprine, cyclosporin or mycophenolic acid on HAV replication were examined in Huh7 cells and its derived cells. HAV HM175/18f genotype IB competent replicon, or incompetent replicon and infectious HAV HA11-1299 genotype IIIA were used in HuhT7 and Huh7 cells, respectively. HAV replicon replication was evaluated by reporter assay. HAV RNA levels were measured by real-time RT-PCR. Cell viability was measured by MTS assay.
Results: 1) Without the cytotoxicity, 48 hr-treatment of 50 ng/mL and 250 ng/mL cyclosporin or 1 μg/mL and 10 μg/mL mycophenolic acid had no inhibitory effects on HAV HA11-1299 genotype IIIA replication (1.5-FC and 11.5-FC or 1.2-FC and 1.2-FC, respectively). 2) 48 hr-treatment of azathioprine had significantly inhibitory effects on HAV HA11-1299 genotype IIIA replication (0.6-FC ($p<0.05$) and 0.4-FC ($p<0.05$) at 0.5 μmol/mL and 1.0 μmol/mL, respectively) and cell viability was 106% and 93%, respectively, compared to the untreated control (100%). 3) Compared to the control (100%), 24 hr-treatment of 0.5 μmol/mL and 1.0 μmol/mL azathioprine, respectively, also had inhibitory effects on HAV competent replicon (68% ($p<0.05$) and 56% ($p<0.05$)) or incompetent replicon replication (91% (N.S.) and 82% ($p<0.05$)).
Conclusion: Azathioprine could inhibit HAV replication in human hepatocytes. Azathioprine may be one of the useful immunosuppressants for liver transplantation for HAV-infected acute liver failure/acute-on-chronic liver failure.

Poster Session 19

PF19-3 10101

Novel Multi-Epitope Subunit Vaccine for Hepatitis Viruses: An Immunoinformatic Approach

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Background: Hepatitis viruses (HAV, HBV, HCV, HDV, and HEV) are major global health concerns, causing both acute and chronic liver infections that can lead to liver cirrhosis and hepatocellular carcinoma. Despite the availability of some preventive vaccines, effective immunization strategies against all five major hepatitis viruses remain incomplete. A universal multi-epitope subunit vaccine, designed through immunoinformatics, could offer a broad-spectrum preventive solution by targeting conserved, immunodominant regions across various hepatitis virus types.
Method: To develop a novel preventive approach, advanced immunoinformatics tools were employed to design a multi-epitope subunit vaccine targeting hepatitis A, B, C, D, and E viruses. Full proteomes of these viruses were retrieved, and the most immunogenic proteins were identified. From these, highly antigenic and non-allergenic T-cell (CTL and HTL) and B-cell epitopes were predicted and screened. An adjuvant was incorporated at the N-terminal of the vaccine construct to enhance immunogenicity. Virtual screening was also used post-therapy to identify potential inhibitors of viral proteins for adjunctive therapeutic development.
Results: The final vaccine construct included top-ranked CTL and HTL epitopes along with B-cell and IFN-&gamma-inducing epitopes, ensuring the stimulation of both humoral and cell-mediated immune responses. The construct was predicted to be highly antigenic and non-allergenic, supporting its safety and potential efficacy.
Conclusion: This in silico-designed multi-epitope subunit vaccine offers a promising and innovative strategy for preventing infections caused by hepatitis viruses. By targeting multiple viral types, it holds the potential to reduce the global burden of liver disease and may complement current vaccination efforts and antiviral therapies.

PF19-4 10037

Influence of Gut Microbiota on the Gut-Brain Axis and Neurological Disorders

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Objective: To explore the role of gut microbiota in regulating the gut-brain axis and its impact on neurological disorders such as anxiety, depression, and Alzheimer's disease.
Methods: A comprehensive literature review was conducted to summarize recent findings on the interaction between gut microbiota and the central nervous system. Key mechanisms including neural signaling, immune modulation, and microbial metabolites were analyzed. Selected animal and clinical studies were reviewed to assess microbiota changes in neurological conditions.
Results: Gut microbiota diversity and stability were found to significantly influence brain function via the gut-brain axis. Microbial metabolites such as short-chain fatty acids, inflammatory mediators, and neurotransmitter precursors play important roles. Animal studies showed that dysbiosis leads to behavioral abnormalities, while probiotic supplementation improves anxiety and cognitive symptoms. Clinical evidence also indicates altered gut microbiota profiles in patients with depression and Alzheimer's disease.
Conclusion: The gut microbiota is a key regulator of the gut-brain axis and contributes to the pathogenesis of various neurological disorders. Targeting the gut microbiome may offer a novel therapeutic strategy for improving brain health and managing neuropsychiatric conditions.

Poster Session 19
PF19-5 10086

Rice Contamination and Liver Disease Risk: A Study on Pesticide Effects on Rice Nutritional Quality

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To meet global rice demand, farmers sometimes use high concentrations of insecticides, leading to pesticide-contaminated crops. Since people consume rice daily over long periods, understanding how these high pesticide levels affect the grain is crucial. Prior research indicates that consuming pesticide-affected foods can increase the risk of various liver conditions, including steatotic liver disease (SLD), hepatitis, and even liver cancer. Our study investigated the effects of elevated pesticide concentrations on *Oryza sativa* variety MR263. We grew rice in a controlled environment and exposed it to pesticide levels four and six times higher than normal. We then analyzed changes in total protein and antioxidant activity using Bradford and APX tests, respectively. Our findings showed significant alterations ($p<0.05$) in both total protein and ascorbate peroxidase (a key antioxidant enzyme), especially in rice exposed to a six-fold pesticide concentration. This suggests that high pesticide spraying leads to heavy metal accumulation and oxidative stress in rice. For consumers, this oxidative stress is a serious health concern, potentially contributing to the development and progression of steatotic liver disease, liver inflammation, and other severe liver-related illnesses. Therefore, accurate identification of antioxidant proteins in pesticide-exposed rice is essential. This information will be vital for developing biosensors to detect significant pesticide contamination, helping to safeguard public health from these diet-related liver disorders.

Poster Session 20

PF20-1 10002

Comparison of Effectiveness of Mycophenolate Mofetil Associated with Standard Dose or Low Dose Tacrolimus for Liver Transplantation Immunosuppression

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Background: Liver transplantation necessitates lifelong immunosuppressive therapy to prevent graft rejection. This systematic review evaluates the effectiveness of mycophenolate mofetil (MMF) in combination with standard-dose (SD) versus low-dose (LD) tacrolimus in liver transplant recipients.
Methods: A systematic search was conducted across databases including PubMed, Cochrane, and Embase for studies published from 2000 to 2024. Inclusion criteria focused on randomized controlled trials (RCTs) and observational studies involving human subjects aged >18. Primary outcomes included graft survival, acute rejection rates, and patient survival, while secondary outcomes encompassed renal function, infection rates, and adverse effects.
Results: Out of 85 initially identified studies, 81 were excluded based on predetermined criteria. Ultimately, four studies involving a total of 255 patients (standard-dose: n = 131; low-dose: n = 124) were included for analysis. The findings indicated that mycophenolate mofetil (MMF) combined with tacrolimus, whether standard-dose or low-dose, allowed for a significant reduction in tacrolimus dosage, effectively minimizing nephrotoxic effects. Graft and patient survival rates were comparable between the MMF-tacrolimus regimen using standard and low doses. Additionally, the MMF group exhibited lower rates of acute rejection and showed improvements in renal function.
Conclusion: The combination of MMF with either standard-dose or low-dose tacrolimus is an effective immunosuppressive strategy for liver transplant recipients. Both approaches facilitate a reduction in tacrolimus dosage while maintaining similar safety and efficacy. The MMF-tacrolimus regimen contributes to lower rates of acute rejection, with comparable graft and patient survival rates. Further research is warranted to optimize immunosuppressive protocols and enhance patient outcomes.

PF20-2 10234

Assessment Of Segment 5 and Segment 8 Congestion in Right Lobe Liver Graft

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Background: In liver transplant liver graft should be healthy and without any congestion after anastomosis of its corresponding vessels. In right lob graft segment 5 and segment 8 draining veins are divided. If those veins of segment 5 and segment 8 which are draining into middle hepatic veins are significant then they should be reconstructed. There are different ways which are used to assess these veins apart from the radiological assessment.
Method: In series of cases where there is graft to weight ratio is marginal then assessment of the segment 5 and segment 8 become more important. First parameter is that's during the donor surgery when these veins are ligated if there more congestion of segment 5 and segment 8 is noted then it means may be these will be reconstructed. Secondly, the size of segment 5 and segment 8 veins are more then 5 mm then it is better to reconstruct. Third stage is after perfusion of the cytoplegic fluid in these vessels is observed during bench surgery. If there is significant flow then it need to be reconstructed.
Result: No complications was observed by following this visual observation.
Conclusion: In recent advances in transplant surgery and at the advent of radiological assessment of blood vessels, it is easy to assess that which vein may need to reconstruct. But still there is still value of visual observation of flow of blood in segment 5 and segment 8 veins to reduce the congestion of the corresponding segments.

Poster Session 20

PF20-3 10061

Liver-Targeted Nanoparticle Delivery of Tacrolimus Enhances Immunosuppression and Minimizes Systemic Toxicity in a Rat Liver Transplant Model

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Background: Tacrolimus is a cornerstone immunosuppressant used in liver transplantation (LT), yet its therapeutic efficacy is constrained by systemic toxicity and a narrow therapeutic window. Nanotechnology-based drug delivery systems have the potential to enhance tissue specificity and pharmacokinetic profiles of immunosuppressive agents. To assess the efficacy and safety of a liver-targeted, nanoparticle-encapsulated tacrolimus formulation in a rat model of orthotopic liver transplantation.
Methods: LT was performed in Wistar rats. Postoperative groups were administered either conventional tacrolimus or a polymer-based nanoparticle formulation of tacrolimus intravenously. Drug biodistribution was tracked using fluorescent-tagged nanoparticles. Outcome measures included serum drug levels, liver enzyme profiles, histological rejection scores (Banff criteria), and renal toxicity markers.
Results: The nanoparticle formulation achieved selective hepatic accumulation with sustained systemic exposure. Compared to conventional tacrolimus, the nano-formulated group showed significantly reduced graft inflammation, lower transaminase levels, and minimal renal toxicity. Histopathological evaluation revealed attenuated rejection and preserved hepatic architecture.
Conclusion: Liver-targeted delivery of tacrolimus via nanoparticle carriers significantly improves immunosuppressive efficacy while reducing off-target toxicity. This approach offers a promising advancement in post-transplant pharmacotherapy with high translational potential.

PF20-4 10090

Role of Fibroscan in the Early Detection of hepatocellular carcinoma in 1000 Cirrhotic Egyptian Patients

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Background: Hepatocellular carcinoma (HCC) is common primary malignancy of the liver. We studied the role of ultrasound elastography (FibroScan) in early detection of HCC in cirrhotic patients as well as verifying whether it could be used as a tool for identifying cirrhotic patients who are at high risk of developing HCC.
Method: We enrolled 1000 patients with cirrhosis who were classified into: group I 500 with cirrhosis and HCC and group II 500 patients with no HCC. Tumour characteristics were assessed. Tumor staging was done. Transient elastography was done.
Results: Patients with HCC had a mean age of 57.3 years old, while cirrhotic non-HCC patients are younger with a mean age of 51.4 years old. Also HCC commonly presented in males (86%) more than females (14%). Liver stiffness was significantly higher in HCC patients compared to cirrhotic patients. The sensitivity and specificity in diagnosis of HCC were 76% and 87% respectively at cut-off of 30.5 kpa with 91.8% accuracy. Fibroscan has a positive significant correlation with tumour size (P 0.001), Child-Pugh (P 0.001), Okuda classification (P 0.001), CLIP staging (P 0.001) and Tokyo classification (P 0.001) among HCC patients. It was found that likelihood of HCC risk was correlated with increase of liver stiffness. At liver stiffness of 25-30 kpa the probability of HCC is 93%
Conclusion: Fibroscan has an important role in early detection of HCC in cirrhotic patients with cut off 30.5 Kpa. Cirrhotic patients with liver stiffness more than 30 kpa are most likely to have HCC.

Poster Session 20
PF20-5 10127

DNA Methyltransferases as Biomarkers for HCV Related Hepatocellular Carcinoma

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Background: The alteration in DNA methylation that was observed in HCC patients suggests a possible role of DNA methyltransferases (DNMTs) in the disease pathogenesis in addition to potential role as a disease biomarker. Aim: To study the change in DNMTs expression in chronic HCV infectedpatients as potential non-invasive biomarker for diagnosis of hepatocellular carcinoma.
Methods: 26patients with HCC, 45 patients with liver cirrhosis, 20 chronic HCV patients and 20 as a control group were enrolled. Real-Time Quantitative Reverse Transcription PCR was performed for all study participants.
Results: A significant difference in DNMTs expression was observed among the studied groups. ROC curve analysis revealed that with a cutoff value of 3.16 for DNMT3A expression, sensitivity and specificity were 80.8 and 95.6% respectively and area under curve (AUC) was 0.958, p 0.001for discriminating hepatocellular carcinoma among post hepatitis C cirrhotic patients.Besides DNMT3B relative expression cutoff value of 3.10 showed 84.6% sensitivity and 77.8% specificity and AUC was 0.888, p 0.001. On the other hand, cutoff value 0.65 for DNMT1 relative expression showed 92.3% sensitivity and 44.4% specificity and AUC was 0.72, p= 0.002. DNMT1, DNMT3A and DNMT3B have significant positive correlation with the level of AFP (p-value = 0.003, 0.004 and 0.008 respectively). The relative expression of DNMT3B was significantly correlated to focal lesion size (p-value = 0.015). High DNMTs expression was significantly associated with the presence of multiple focal lesions but not with the Child Pugh grade.
Conclusion: The mRNA levels of DNMTs could be a potential biomarker for early detection of HCC development.

Poster Session 21

PF21-1 10079

Establishment of a Reproducible Rat Model for Orthotopic Liver Transplantation to Study Post Transplant Immunomodulation and Regeneration

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Background: Liver transplantation (LT) is the definitive treatment for end-stage liver disease. However, the molecular mechanisms governing post-transplant immunoregulation, ischemia-reperfusion injury, and liver regeneration remain incompletely understood. Reliable preclinical models are essential for investigating these complex biological responses and for evaluating novel therapeutic strategies.
Objective: To develop and validate a robust orthotopic liver transplantation model in rats for the investigation of early immunological responses and regenerative mechanisms post-transplantation.
Methods: Male Lewis rats underwent LT using a modified Kamada two-cuff technique. Postoperative evaluation included survival analysis, liver function tests (ALT, AST, bilirubin), and histopathological scoring. Expression of inflammatory markers (TNF-alpha, IL-1beta) and regenerative genes (HGF, PCNA) was assessed via qPCR and immunohistochemistry. Experimental groups received targeted immunomodulators to evaluate their effects on ischemia-reperfusion injury and hepatocyte regeneration.
Results: The model achieved a 72-hour survival rate more than 85%, with consistent hepatic reperfusion and graft viability. Biochemical parameters indicated transient liver injury, corroborated by histological evidence of inflammatory infiltration and hepatocellular necrosis in untreated controls. Animals receiving immunomodulators showed reduced inflammation, enhanced hepatic architecture, and increased expression of regeneration-associated genes.
Conclusion: This validated rat LT model offers a reliable and translationally relevant platform for investigating post-transplant immune responses and regenerative therapies. It provides a valuable tool for testing novel immunosuppressive agents and liver-protective strategies in a controlled preclinical setting.

PF21-2 10062

Hepatic Neuro Axis Crosstalk After Liver Transplantation: Neuroinflammatory Consequences and Pharmacological Neuroprotection in a Rodent Model

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Background: Although liver transplantation (LT) is a life saving intervention for end stage liver disease, systemic inflammation and post-transplant neurocognitive deficits remain poorly understood. Increasing evidence implicates a bidirectional interaction between hepatic function, systemic immunity, and central nervous system (CNS) homeostasis referred to as the hepatic neuro axis. To elucidate the impact of LT on neuroinflammatory responses and cognitive function, and to assess the efficacy of CNS targeted pharmacological strategies in a rat LT model.
Methods: A syngeneic orthotopic liver transplant model was established in male Wistar rats. Post transplant assessments included systemic cytokine profiling, blood-brain barrier (BBB) integrity assays, microglial activation (Iba 1), and cognitive performance via the Morris water maze. Treatment groups received intranasal delivery of dimethyl fumarate (DMF) or Nrf2 pathway agonists. Brain tissues were analyzed for inflammatory and mitochondrial markers using qPCR, Western blotting, and immunohistochemistry.
Results: Liver transplantation induced marked neuroinflammation, characterized by elevated TNF alpha, IL 6, and NLRP3 expression, along with compromised BBB function and impaired spatial memory. Pharmacological interventions attenuated microglial activation, restored mitochondrial homeostasis, and significantly improved cognitive outcomes.
Conclusion: These findings highlight the clinical significance of hepatic neuro axis interactions in post-transplant pathology. Targeting neuroinflammation through intranasal Nrf2 activation may offer a promising therapeutic strategy to preserve cognitive function following LT.

Poster Session 21

PF21-3 10134

Paradoxical Association between Steatotic Liver Disease and Favorable Hepatic Outcomes in HCV Patients with SVRs

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Background: How genetic predispositions and steatotic liver disease (SLD) affect the outcomes of chronic hepatitis C (CHC) patients with sustained virological responses (SVRs) remains elusive.
Methods: A 15–year prospective study of CHC patients with SVRs was conducted.
Results: Among 965 CHC patients? the baseline and 24–week post–HCV therapy SLD rates were 64% and 54%? respectively; PNPLA3–rs738409 G allele was negatively correlated with MTHFR–rs1801133 T allele (Pearson ´s correlation: –0.078? p=0.025). At baseline? body mass index (BMI)? cirrhosis (OR: 0.34; 0.20–0.56) and PNPLA3 G allele (1.28; 1.03–1.60) were associated with SLD. At 24 weeks posttherapy? BMI? the fibrosis–4 index (0.86; 0.75–0.99)? cirrhosis (0.23; 0.14–0.40)? HOMA–IR? the ALT level and MTHFR T allele (0.66; 0.48–0.91) were associated with 24–week SLD in SVR patients. Longitudinally? higher BMIs and ALT levels? poorer metabolic profiles? and greater cumulative incidences of cardiovascular events (71% vs. 64%? p=0.026) but lower fibrosis–4 indices and cumulative incidences of cirrhosis (16% vs. 34%? p=0.001) and HCC (7% vs. 16%? p=0.001) were noted in patients with than in sex– and age–matched patients without 24–week SLD. A 24–week SLD was negatively associated with the cumulative incidences of cirrhosis (HR: 0.548; 95% CI HR: 0.281–0.894) and HCC (0.637; 0.32–0.99).
Conclusions: Poorer metabolic profiles and greater cardiovascular but lower hepatic event cumulative incidences were noted in patients with than those without 24–week SLD. The paradoxical association between SLD and hepatic events might stem from the negative correlation between PNPLA3 G allele and MTHFR T allele? which are HCV–specific SLD factors.

PF21-4 10029

A Pilot Study on Hepatitis B Core Related Antigen (HBcrAg) as a Novel Marker for Monitoring Antiviral Therapy in Chronic Hepatitis B Patients

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Background: Chronic Hepatitis B (CHB) affects over 400 million people globally, posing a significant health challenge. While HBV DNA quantification remains the gold standard for monitoring antiviral therapy, it is costly and not widely accessible. Hepatitis B core-related antigen (HBcrAg), encompassing HBeAg and HBcAg, has emerged as a promising, cost-effective alternative due to its correlation with viral replication and intrahepatic cccDNA.
Aim: This pilot study aimed to assess HBcrAg's utility in guiding therapy discontinuation and predicting relapse in CHB patients.
Methods: Sixty-three patients on nucleos(t)ide analogue therapy (entecavir, tenofovir, or tenofovir alafenamide) were included. Both retrospective and prospective data were evaluated using HBcrAg, HBV DNA, HBsAg, HBeAg, and liver function tests. Patients who achieved HBcrAg and HBV DNA negativity after more than12 months of therapy were followed for six months post-therapy cessation.
Results: All patients were initially HBV DNA negative, and all 63 also tested negative for HBcrAg. After six months of stopping therapy, five patients showed HBV DNA reactivation, each preceded by HBcrAg reappearance. The remaining 58 patients stayed negative for both markers, indicating no relapse.
Conclusion: HBcrAg negativity correlated strongly with sustained viral suppression, suggesting its potential as a reliable and non-invasive biomarker to guide safe antiviral therapy discontinuation. It offers a practical alternative to HBV DNA testing, especially in resource-limited settings. Further large-scale prospective studies are warranted to confirm its predictive value.

Poster Session 21
PF21-5 10049

Acute Viral Hepatitis in Hospitalized Children: Clinico-Biochemical, Ultrasonographic and Etiological Findings from North India

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Hepatitis is a serious public health issue worldwide, including in India, with various viral agents causing acute viral hepatitis (AVH). This paper aimed to investigate the etiology, clinical features, laboratory parameters, and sonological findings of AVH in children. A cross-sectional study was conducted at the Department of Paediatrics, National Institute of TV and Respiratory Diseases, New Delhi, Delhi, from August 2023 to November 2024. A total of 119 paediatric cases of AVH aged 1-16 years were included. Clinical evaluation, laboratory investigations, and ultrasound findings were recorded. A cross-sectional study was conducted at the Department of Paediatrics, National Institute of TV and Respiratory Diseases, New Delhi, Delhi, from August 2023 to November 2024. A total of 119 paediatric cases of AVH aged 1-16 years were included. Clinical evaluation, laboratory investigations, and ultrasound findings were recorded. The findings highlighted that AVH is primarily caused by HAV, which remains a serious health threat in India. Effective prevention strategies focusing on improved sanitation, clean water supply, and universal immunization against HAV and HBV are crucial to reduce morbidity and mortality.

Poster Session 22

PF22-1 10053

Dual Burden of Infections: Seroprevalence of Acute Viral Hepatitis among Dengue Patients in Northern India

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Dengue fever and acute viral hepatitis have emerged as significant global public health challenges, including India. Acute viral hepatitis is most commonly caused by the Hepatitis A virus (HAV) and the Hepatitis E virus (HEV), both of which are transmitted through faeco-oral route. This retrospective study aimed to assess the prevalence of acute viral hepatitis among clinically suspected dengue cases presented at the National Institute of TV and Respiratory Diseases in 2024. To identify the presence of acute viral hepatitis caused by HAV and HEV, 119 specimens were selected from dengue-suspected clinical samples in 2024, based on the presence of symptoms indicative of acute viral hepatitis. Later, serological diagnosis was performed on these samples using anti-HAV IgM and anti-HEV IgM ELISA kits. Based on seropositivity for IgM antibodies, 7 (6.5%) dengue virus (DENV) seropositive samples tested positive for both HAV and HEV. Among DENV seronegative cases, 18 (29.7%) samples were positive for HEV, and 5 (3.8%) samples were positive for HAV, indicating the potential for misdiagnosis due to overlapping symptoms. Co-infection with both HAV and HEV was observed in 3 samples. Thus, the presence of acute hepatitis infections among the dengue cases both monsoon and post-monsoon seasons. Overlapping of clinical manifestations of these diseases can lead to misdiagnosis incidences raising risk for underreporting of the true cases of acute viral hepatitis infection. Based on the findings, it is recommended that dengue-suspected patients with selected symptoms during both monsoon and post-monsoon seasons should also be screened for acute hepatitis infections.

PF22-2 10050

Clinicoepidemiology and HCV Core Antigen Assay Diagnosis of Hepatitis C: Findings from a Tertiary Care Hospital of North India

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Hepatitis C virus (HCV) is a leading cause of primary hepatocellular carcinoma and chronic hepatitis in India. Diagnostic approaches include serological and molecular assays, with the HCV core antigen (HCVcAg) assay gaining recognition as a cost effective alternative to HCV RT PCR testing. The present study included 159 suspected hepatitis cases at the National Institute of Tuberculosis and Respiratory Diseases, from June 2022 to July 2023. Seroprevalence was assessed using the Qualisa HCV ELISA. Genotyping was performed with the AmpliSens HCV genotype PCR kit. A total of 60 seronegative and 30 seropositive samples underwent testing for HCV core antigen and HCV RT PCR. The performance of the HCV core antigen assay was evaluated using HCV RT PCR as the gold standard. Among the 159 patients studied, 30% were seropositive for HCV, with the majority belonging to the 40 to 59 age group. Surgery and blood transfusion emerged as significant risk factors. Co infections included human immunodeficiency virus (HIV) in 4.3% of cases and hepatitis B virus (HBV) in 8.2%. Genotype 3a was identified as the most prevalent. The HCV core antigen assay demonstrated excellent diagnostic performance, with a sensitivity of 97.6%, specificity of 94.3%, positive predictive value of 86.1%, negative predictive value of 98.3%, and overall accuracy of 91.3%. The findings indicate that HCV core antigen serves as a reliable and cost effective alternative to HCV RT PCR for diagnosing HCV infection. Consequently, routine screening in high risk populations is crucial for early detection and prevention of HCV related complication.

Poster Session 22

PF22-3 10052

Clinical Profile and Outcomes of Hepatitis A Virus Associated with Severe Acute Liver Injury in Adults: A Case Study of Delhi, India

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This study aimed to assess the clinical profile of patients with Hepatitis A Virus (HAV)-related severe acute liver injury (sALI) and to identify potential predictors for its progression to acute liver failure (ALF). A single-centre retrospective analysis was conducted on adult patients admitted with sALI at the National Institute of Tuberculosis and Respiratory Diseases, New Delhi, from May 2023 to August 2024. Clinical, demographic, and laboratory parameters were compared between patients with sALI alone and those who progressed to ALF. A multivariate logistic regression model was used to identify predictors of progression. Among the 32 patients meeting the sALI criteria, 69.2% had sALI alone, while 30.8% progressed to ALF. Compared to those who developed ALF, patients with sALI alone had lower leukocyte counts, rates of acute kidney injury, MELD scores, and levels of arterial lactate, ammonia, procalcitonin, and ferritin. Three patients (9.1%) progressed to ALF, with one reported death (4%). Baseline ammonia and leukocyte counts showed trends toward predicting progression to ALF; however, neither reached statistical significance after adjustment. The unadjusted odds ratio (OR) for ammonia was 1.1 (95% CI: 0.03 to 1.6), and for leukocyte count was 1.3 (95% CI: 0.9 to 1.9). Ammonia levels had an area under the receiver operating characteristic curve of 0.9 (95% CI: 0.6 to 1.8; p = 0.005). Comorbidities did not significantly affect outcomes. In conclusion, HAV commonly presents as sALI in young adults, with approximately 10% progressing to ALF. Baseline ammonia levels may serve as a useful early predictor of progression.

PF22-4 10222

Hepatocellular Risk Outcomes of Long-term Treatment of Chronic HBV Infection: Network Meta-analysis

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Background: Chronic Hepatitis B virus (HBV) infection is one of the leading risk factors for hepatocellular carcinoma (HCC), accounting for approximately 33% of HCC cases. HCC has a poor prognosis with a 5-year survival rate and is the 5th most common cause of cancer worldwide. Entecavir is a first-line treatment that effectively suppresses HBV replication, but its impact on reversing liver damage and preventing HCC remains limited. This study aims to compare the long-term HCC risk associated with various antiviral therapies for chronic HBV.
Methods: A literature search through PubMed, Scopus, and ScienceDirect identified 8 studies comparing various treatments to Entecavir (ETV), including: 2 studies on ETV + biejia ruangan compound (RGT), 2 on Adefovir (ADV), 1 on ETV + thymosin-alpha1, 1 on Lamivudine, 1 on Tenofovir (TDF), and 1 with no treatment. A frequentist network meta-analysis was conducted using the netmeta package in R, applying a common-effects model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using ETV monotherapy as the reference.
Results: We found that TDF (OR 0.33) and ETV + RGT (OR 0.50) are significantly better than ETV alone, while Adefovir (OR 0.81), ETV + thymosin-alpha1 (OR 0.90), Lamivudine (OR 1.04), placebo (OR 1.11), and Adefovir (OR 1.90) do not yield significant results.
Conclusion: These findings suggest that TDF and ETV + RGT potentially offer better protection against HCC in chronic HBV patients, making them promising options for long-term therapy. However, more studies are needed to confirm their benefits and assess potential side effects.

Poster Session 22
PF22-5 10144

Co-occurrence Hepatic Steatosis and Hepatitis B Virus, Hepatic Steatosis and Hepatitis C Virus at a Tertiary Referral Hospital in Indonesia

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Background: The MASLD epidemic has increased in the general, chronic Hepatitis-B (CHB), and chronic Hepatitis-C (CHC) populations. This study aimed to determine the association between Hepatic steatosis (HS) and each Hepatitis-B Virus (HBV) or Hepatitis-C Virus (HCV), and analyzed the influence of HS on both HBV and HCV virology in patient with chronic hepatitis.
Methods: In this retrospective cross-sectional study, the subjects were patients with CHB or CHC, antiviral treatment-naïve, at Dr. Sardjito General Hospital, a tertiary hospital in Yogyakarta, Indonesia, from May 2022-April 2025. HS was assessed by transient elastography, defined as controlled attenuation parameter (CAP) ≥248dB/m.
Result: In 283 patients with CHB (median age: 42 years, 52.6% males, 20.5% cirrhosis, 33.6% elevated ALT), there were 76 patients with HS and 207 patients non-steatosis. Severe steatosis had lowest HBV DNA level compared with other groups (4.58-4.36-3.72 log10IU/mL in none, mild/moderate, and severe steatosis, P=0.03). Most patients were HBeAg negative (67.8%), steatosis status was not influenced by HBeAg status (CHB+HS vs CHB, 23.7% vs 35.3%, P=0.064). In 58 patients with CHC (median age of 47.5 years, 67.2% males, 41.4% cirrhosis, 53.4% elevated ALT), there were 15 patients with SH and 43 patients non-steatosis. The HCV RNA level was not influenced by the liver steatosis grade (5.81-6.2-6.5 log10IU/mL in none, mild/moderate, and severe steatosis, P=0.3).
Conclusion: Steatosis has a negative correlation with HBV virology, demonstrating decreased HBV DNA expression in CHB+MASLD, in contrast to CHC, not influenced by the liver steatosis grade. CHC patients had a higher of cirrhosis and elevated ALT.

Poster Session 23

PF23-1 10041

Creatinine-to-cystatin-C Ratios Predict Liver Fibrosis in Patients with Metabolism-associated Steatotic Liver Disease for Reducing Risk of Liver-related Death

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Background: In metabolic dysfunction-associated steatotic liver disease (MASLD), fibrosis stage ≥F2 has been reported to be associated with liver-related mortality, including hepatocellular carcinoma, as well as overall mortality. It is also known that the prevalence of sarcopenia increases with the progression of liver fibrosis in MASLD. Therefore, in this study, we investigated the utility of the serum creatinine/cystatin C ratio (Cr/CysC), a recently proposed surrogate marker of skeletal muscle mass, as a potential marker for liver fibrosis.
Methods: We analyzed the association between serum cystatin C levels and histological findings using stored serum samples from 104 MASLD patients who underwent liver biopsy at our institution.
Results: In the ≥F2 group (n=60), age, proportion of female patients, AST, γ-GTP, FIB-4 index, and ELF score were significantly higher compared to the <F2 group (n=44), whereas platelet count, albumin, and Cr/CysC were significantly lower. The Cr/CysC ratio decreased significantly with the progression of liver fibrosis. The cutoff value of Cr/CysC for predicting fibrosis stage ≥F2 was 0.664 (AUROC: 0.621). Liver fibrosis stage was negatively correlated with skeletal muscle mass index (SMI), and Cr/CysC showed a moderate positive correlation with SMI. Of the 104 patients with MASLD, 56 had both a FIB-4 index ≥1.3 and an ELF score ≥9.87, and 84% of them (47/56) were classified as having fibrosis stage ≥F2. Of these 56 patients, 34 had a Cr/CysC ratio <0.664, and 91% (31/34) of them had fibrosis stage ≥F2.
Conclusion: Cr/CysC may serve as a potential marker of liver fibrosis in MASLD.

PF23-2 10043

Allyl Nonanoate: A Bile Metabolite and Potential Biomarker for Hepatic Fibrosis in MASLD

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Background: MASLD is a complex metabolic disorder with a diverse spectrum. This study aimed to classify patients with MASLD into molecular subtypes based on the underlying pathophysiology.
Methods: We performed high-throughput RNA sequencing on 164 liver tissue samples from healthy controls and patients with MASLD. The clustering was based on individual genes or pathways that showed high variation across the samples. Second, the clustering was based on single-sample gene set enrichment analysis.
Results: Optimal homogeneity was achieved by dividing the samples into four clusters (one healthy control and three MASLD clusters I-III) based on the top genes or pathways with differences across the samples. No significant differences were observed in waist circumference, blood pressure, glucose, ALT, or AST levels between cluster I patients with MASLD and the healthy controls. Cluster I showed the clinical features of lean MASLD. Cluster III of MASLD demonstrated hypertension and a T2DM prevalence of 57.1% and 50.0%, respectively, with a significantly higher fibrosis burden than clusters I and II. Cluster III was associated with severe fibrosis and abnormal glucose homeostasis. In MASLD cluster I, the sphingolipid and GPCR pathways were upregulated, whereas the complement and phagocytosis pathways were downregulated. In MASLD cluster II, the cell cycle and NOTCH3 pathways increased, whereas the PI3K and insulin-related pathways decreased. In MASLD cluster III, increased activity occurred in the IL-2/4 and ECM pathways, coupled with decreased serotonin 2A/B pathways.
Conclusion: MASLD can be divided into three distinct molecular phenotypes, wherein each is characterized by a specific molecular pathway.

Poster Session 23

PF23-3 10073

Pathophysiological Mechanisms Linking MASLD and NCDs and Their Association with Mortality

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Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease and metabolic dysfunction-associated fatty liver disease, has emerged as a critical public health challenge due to its close association with metabolic dysfunction and the global burden of non-communicable diseases (NCDs). Its pathogenesis is intricately linked to insulin resistance, obesity, type 2 diabetes, dyslipidemia, and cardiovascular disease, which are collectively the leading causes of morbidity and mortality worldwide. This review explores the role of MASLD in NCDs, including type 2 diabetes, cardiovascular diseases, chronic respiratory diseases, and cancer, emphasizing the shared mechanisms, such as chronic inflammation, oxidative stress, and lipotoxicity. Additionally, mortality of the NCDs, as well as steatotic liver disease subtypes, including MASLD, MASLD with increased alcohol intake, and alcoholic liver disease, is reviewed. This review underscores the need for integrated, multidisciplinary approaches that prioritize early detection, lifestyle interventions, and novel pharmacological therapies to manage MASLD and its associated comorbidities effectively. Core tip: Metabolic dysfunction-associated steatotic liver disease drives the progression of cardiovascular disease, cancer, and type 2 diabetes through insulin resistance, chronic inflammation, and hepatic steatosis, contributing to increased mortality. Comprehensive management targeting metabolic dysfunction and liver health is essential to reduce long-term mortality and morbidity.

PF23-4 10087

Pediatric Nonalcoholic Steatohepatitis in a Patient with Heterozygous Familial Hypobetalipoproteinemia

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Background: Heterozygous familial hypobetalipoproteinemia (FHBL) is a semi-autosomal disorder caused mainly by mutations in the *APOB* gene. While heterozygous individuals are usually asymptomatic, they may develop nonalcoholic fatty liver disease (NAFLD), and progression to nonalcoholic steatohepatitis (NASH) is rarely reported in children.
Methods: A 12-year-old non-obese boy was referred for persistent elevation of liver enzymes and hypolipidemia detected during a school health checkup. Laboratory testing revealed low LDL-C (31 mg/dL) and apolipoprotein B (19 mg/dL). Abdominal ultrasound showed fatty liver. Liver biopsy revealed steatosis, hepatocellular ballooning, lobular inflammation, and perisinusoidal fibrosis. Genetic testing identified a heterozygous *APOB* pathogenic variant (c.7537C>T), confirming FHBL.
Results: Despite nutritional and exercise guidance, liver enzyme levels remained elevated. Oral vitamin E (1.5 mg/kg/day) was initiated one month after biopsy. AST and ALT levels gradually normalized within eight months, and hepatic echogenicity improved. At three years and six months follow-up, the patient remains asymptomatic with normal liver function and imaging. His father, who also had hypolipidemia and fatty liver, had not undergone genetic testing.
Conclusion: This case highlights that heterozygous FHBL can present with pediatric-onset NASH despite the absence of obesity. Early recognition through lipid profiles and histology, followed by antioxidant therapy, can achieve biochemical remission and may prevent long-term liver damage.

Poster Session 23
PF23-5 10231

Unveiling the True Burden of Steatotic Liver Disease: Mortality Risks by Subtype and Fibrosis Stage in a UK Nationwide Cohort

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Background: Steatotic liver disease (SLD) is the most prevalent chronic liver condition. We investigated the associations between SLD, fibrosis stage, and overall and cause specific mortality, with a focus on SLD subtypes.
Methods: We analysed 486,156 (54.2% female) UK Biobank participants. SLD cases were identified using fatty liver index. Causes of death were confirmed via death registries. Cox models estimated associations between SLD, SLD subtypes, FIB4 score, and mortality outcomes, including overall mortality, mortality from liver related diseases, cardiovascular disease (CVD) and extrahepatic cancers.
Results: SLD was identified in 178,336 participants: 73.5% with MASLD, 19.0% with MetALD, and 6.4% with ALD. Over a median follow-up of 13.8 years, 20,766 (11.6%) deaths occurred among people with SLD and 21,754 among those without (7.1%), suggesting a higher mortality rate in SLD than in non-SLD (8.78 vs. 5.25 /1000 personyears). All SLD subtypes were associated with higher overall mortality: MASLD (HR (95%CI):1.32 (1.29,1.35)), MetALD (1.16 (1.12,1.20)), and ALD (1.36 (1.29,1.44)). Excess mortality was primarily driven by extrahepatic cancer (42.5%) and CVD (24.2%), while liver related deaths were concentrated among those with ALD and fibrosis. A strong dose response relationship was observed between FIB4 stratification and mortality, particularly for liver related deaths (29.23 (24.86,34.37)). These associations were independent of cardiometabolic risk factors.
Conclusion: SLD is independently associated with increased overall and cause specific mortality, with substantial variation across subtypes and fibrosis severity. Extrahepatic cancer and CVD are the leading contributors to excess mortality. These findings underscore the need for integrated care strategies.

Poster Session 24

PF24-1 10125

Deep Learning-Based Inference of Liver-Primed Monocyte-Stromal Crosstalk Predicts Fibrosis-Linked Lower Urinary Tract Dysfunction in Males

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Background: Systemic fibrotic signaling originating from the liver may influence extrahepatic fibroinflammatory remodeling, although its impact on peripheral organs remains insufficiently characterized. We hypothesized that liver-conditioned immune-stromal interactions drive fibrotic dysfunction in distant tissues, such as the prostate. This study aimed to decode liver-immune-stromal crosstalk and develop a deep learning framework to predict stromal fibrosis-linked lower urinary tract dysfunction (LUTD) in males.
Methods: We integrated transcriptomic datasets from the Gene Expression Omnibus, including peripheral immune single-cell RNA sequencing (GSE267033), matched liver bulk transcriptomes (GSE267031), and hepatic stellate cell-derived fibrosis gene signatures (GSE256398). Ligand-receptor interactions were inferred using CellPhoneDB to identify liver-influenced monocyte-fibroblast signaling axes, such as CCL2-CCR2 and TNFSF10-TNFRSF10B, enriched in advanced hepatic fibrosis (NAS ≥5). These features were input into a graph attention network trained to classify LUTD patients into high- and low-fibrosis risk groups using transcriptomic proxies of prostate stromal remodeling.
Results: The model achieved an AUROC of 0.82 (95% CI: 0.79-0.85). High-risk cases demonstrated a 7.9-fold increase in monocyte-derived CCR2 signaling ($p = 3.1x10^{-5}$) and suppression of stromal R-spondin-Wnt targets. In a retrospective LUTD cohort (n = 142), 78.9% of high-risk predictions aligned with IPSS ≥19 and uroflowmetry < 10 mL/s. SHAP analysis identified CCR2 activation and Wnt suppression as key predictive features. These findings support a model where liver-primed immune signaling drives fibrotic remodeling in peripheral stromal tissues.
Conclusion: This study reveals a novel liver-to-prostate fibrotic axis, supporting the concept of hepatic-driven systemic fibrosis and enabling non-invasive prediction of extrahepatic fibrotic dysfunction through deep learning.

PF24-2 10022

Beneficial Effects of Milk-Derived Extracellular Vesicles on Liver Fibrosis Progression by Restoring Intestinal Barrier Integrity

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Background: Extracellular vehicles (EVs) are bilayer membrane vesicles released from various cells into the extracellular space, participating in multiple life processes. Recent studies have indicated that bovine milk-derived EVs (B-mEVs) suppress inflammation, have anti-tumor effects, and protect the intestinal barrier in an in vivo model. Whether EVs from bovine milk exert a beneficial effect against MASH is worth investigating. We explored the effect of B-mEVs on MASH-related liver fibrosis by modulating the gut barrier function.
Methods: MASH-related liver fibrosis was induced in female C57BL/6J mice by feeding them a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) for eight weeks. B-mEVs (1.2 mg/kg) were orally administered every two days for four weeks. Seven-week-old female C57BL/6J mice were randomly divided into four groups and treated for 12 weeks as follows, n=5 for each; a)normal chow with vehicle; b)normal chow with B-mEVs; c)CDAHFD diet with vehicle; d)CDAHFD diet with B-mEVs. The mice were then sacrificed for histological analyses to assess the effect of B-mEVs on steatohepatitis and fibrosis. Intestinal barrier integrity was also evaluated by the intestinal permeability using FITC-dextran and immunohistochemistry of tight junction proteins (TJPs).
Results: B-mEVs significantly suppressed macrophage expansion, proinflammatory responses, and liver fibrosis in CDAHFD-fed mice by blocking hepatic translocation of lipopolysaccharide (LPS) and activating toll-like receptor (TLR) 4 signaling. Moreover, B-mEVs improved intestinal permeability by restoring TJPs like ZO-1, Occludin, and Claudin-2.
Conclusions: B-mEVs reduced MASH-related fibrosis by inhibiting lipid accumulation and macrophage expansion and suppressing LPS/TLR4/NF-κB-mediated inflammatory responses by restoring intestinal barrier function.

Poster Session 24

PF24-3 10076

miR-4449 Modulates the Progression of MASH-induced Fibrosis by Regulating the Merlin-TAZ Pathways

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Background: While majority of patients with metabolic dysfunction associated fatty liver disease (MAFLD) exhibit benign clinical courses, those with metabolic dysfunction associated steatohepatitis (MASH) accompanied by hepatic fibrosis experience poor prognoses compared to individuals with metabolic dysfunction associated fatty liver (MAFL) or MASH without hepatic fibrosis. This study aimed to investigate the role of miR-4449 in the progression of MASH-induced fibrosis.
Method: Liver tissue and sera were obtained from MAFLD patients who underwent liver biopsies at Korea University Guro Hospital. MicroRNA sequencing was performed using sera, and mRNA sequencing was conducted using liver tissue from patients with biopsy-confirmed MAFLD. In vitro lipotoxicity was induced in mouse hepatocytes (HepG2 and Huh7 cells) by treating them with palmitic acids (PA).
Results: A total of 24 MAFLD patients were recruited, with 15 having MAFL or MASH without fibrosis, and nine presenting with MASH accompanied by fibrosis. MiRNA sequencing analysis revealed significant differences in the expression levels of 31 miRNA sequences between the two groups, with miR-4449 exhibiting the most prominent upregulation in MASH-fibrosis compared to the MAFL or MASH without fibrosis group. PA treatment increased the expression level of miR-4449 in both supernatant and hepatocytes. Conversely, the expression of merlin, a potential target of miR-4449, decreased in PA-treated hepatocytes compared with vehicle-treated hepatocytes. Additionally, merlin expression levels significantly decreased in MASH patients with fibrosis compared to those without fibrosis.
Conclusion: MiR-4449 was found to regulate merlin expression and TAZ phosphorylation in hepatocytes during lipotoxicity. miR-4449 may serve as a promising novel therapeutic target in MASH-fibrosis.

PF24-4 10157

Usefulness of the Stroop Test to Predict Decompensation Events in Patients with Cirrhosis: A Prospective Cohort Study

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Background: The Stroop test is a point-of-care test to identify covert hepatic encephalopathy (CHE). However, whether the Stroop test performance can predict decompensation events remains unknown.
Methods: This prospective cohort study included patients with cirrhosis admitted to Gifu University Hospital, Japan. CHE was assessed using the reference value of the Stroop test determined by the Japan Society of Hepatology. Decompensation events were defined as the development of overt hepatic encephalopathy (OHE), bacterial infection, gastrointestinal bleeding, or esophageal varices. Factors associated with decompensation were assessed using the Fine–Gray competing risk regression model.
Results: Of the 290 patients, CHE was present in 25 (9%). During a median follow-up period of 2.4 years, decompensation events occurred in 99 (34%), including 51 (18%) with bacterial infection, 49 (17%) with OHE, and 23 (8%) with gastrointestinal bleeding or esophageal varices. The incidence of decompensation events was significantly higher in patients with CHE than those without (60% vs. 32%; $p < 0.001$). Multivariable analysis revealed that CHE (subdistribution hazard ratio [SHR], 1.89; 95% confidence interval [CI], 1.09–3.28) was an independent factor for the development of decompensation events. Regarding each event, CHE was a significant factor for OHE (SHR, 3.47; 95% CI, 1.73–6.98) and bacterial infection (SHR, 2.57; 95% CI, 1.14–5.77).
Conclusion: The Stroop test is useful for predicting the development of decompensation events in patients with cirrhosis. In addition, the Stroop test stratifies the risk of not only OHE but also bacterial infection.

Poster Session 24
PF24-5 10227

Role of interleukin-6 as Risk Factor of Hepatic Encephalopathy Incidence Compared to Amonia in Liver Cirrhosis Patient

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Background: Hepatic Encephalopaty (HE) is serious complication of liver cirrhosis with high mortallity. Current available therapy mostly focused on amonia–decreasing, with varying efficacy. Beside hyperamonemia, inflammation is supposed to have important role in HE pathogenesis. This study aimed to analyze the role of IL–6 compared to amonia in HE incidence and severity.
Methods: This observational study involved 79 patients with liver cirrhosis divided into three groups: without HE, covert HE, and overt HE. Overt HE was defined using West Haven criteria, while covert HE was defined using the Psychometric Hepatic Encephalopathy Score (PHES). IL–6 and ammonia levels were measured. Logistic regression was used to compare the odds ratios (ORs) between IL–6 and ammonia on incidence and severity of HE.
Result: IL–6 correlated significantly higher to HE incidence (OR 12,92; 95% CI 3,44–48,50; p<0,001) than amonia (OR 7,00; 95% CI 0,32–150,72; p=0,21). For HE severity, IL–6 (OR 1,47; 95% CI 0,54–4,01; p=0,44) nor amonia (OR 1,04; 95% CI 0,85–1,28; p=0,08) did not show significant relationship. In the full adjustment model, there is an association between IL–6 and HE [per 1 unit increment; OR: 3.28; 95% CI 2.14–5.03]. Compared to the lowest tertile (IL–6<8), the ORs for the highest tertile (IL-6≥20) were 4.15 (95%CI: 2.28–7.53). Dose-response analysis showed P non-linear=0.71 and IL-6 AUC is 0.735.
Conclusion: IL–6 contributed significantly toward HE incidence in liver cirrhosis patients, demonstrating important role of inflammation in HE pathogenesis. Prospect of the use of therapeutic agent targeting IL–6 needed further investigation to confirm its efficacy and safety.

Poster Session 25

PF25-1 10108

PNPLA3 I148M Is Not Associated with HCC Risk but Correlates with Tumor Differentiation in MASLD Patients

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Background: The patatin-like phospholipase domain-containing protein 3 (PNPLA3) I148M I148M variant has been implicated in metabolic dysfunction-associated steatotic liver disease (MASLD), but its role in hepatocellular carcinoma (HCC) development is unclear. This study examines the association between the PNPLA3 I148M variant and HCC risk.
Methods: A total of 562 MASLD patients, with and without HCC, were prospectively and consecutively enrolled at a tertiary university-affiliated hospital between June 2024 and May 2025. Genomic DNA was extracted from buccal swabs or liver biopsy samples, and single nucleotide polymorphism (SNP) genotyping was performed to determine the rs738409 genotype at codon 148 of PNPLA3. The histological grade of HCC was assessed using the Edmondson-Steiner (ES) grading system in patients who underwent core-needle liver biopsy.
Results: Among 474 non-HCC patients, the GG genotype was found in 39.9%, GC in 37.1%, and CC in 23.0%. In 88 HCC patients, these frequencies were 45.5%, 36.4%, and 18.2%, respectively. No significant differences in GG genotype distribution were observed between HCC and non-HCC groups (P = 0.509), nor in subgroups by sex, age, cirrhosis status, Fibrosis-4 Index, or Liver Stiffness Measurement. However, among HCC patients with histological grading, the GG variant was significantly associated with higher ES grades (P = 0.0076).
Conclusions: The PNPLA3 I148M GG variant was not linked to increased HCC risk in MASLD patients, regardless of liver disease severity. Although the GG variant is known to play a role in development and progression of MASLD, further studies are warranted to clarify its contribution to tumor initiation and dedifferentiation.

PF25-2 10129

Latent Transforming Growth Factor-Beta Binding Protein 1 as A Molecular Diagnostic marker for Hepatocellular Carcinoma

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Background: The latent transforming growth factor-beta binding protein 1 (LTBP-1) is a secreted protein and considers as a part of the extracellular matrix (ECM). LTBP-1 expression was extremely strong in numerous malignant tumors. Therefore, the current study aims to evaluate the diagnostic role of LTBP-1 as a biomarker to distinguish HCC from Egyptian patients with liver cirrhosis.
Methods: The present study included 90 individuals; 40 HCC patients, 30 patients with cirrhosis, and 20 healthy volunteers as a control group. LTBP-1 and AFP were measured.
Results: The level of LTBP-1 was significantly higher in HCC patients than healthy and patients with cirrhosis. A significant (p 0.001) association between LTBP-1 level and CLIP and BCLC in HCC patients. ROC curve analyses revealed that LTBP-1 showed a better diagnostic performance (AUC=0.970,Sensitivity: 82.50%, Specificity: 96.67%, PPV: 97.06%, NPV: 80.56%) in distinguishing HCC from cirrhosis patients, compared to AFP (AUC=0.810, Sensitivity: 62.50%, Specificity: 93.33%, PPV: 92.59%, NPV: 65.12%).AFP was not significantly (p=0.098) associated with CLIP score. There was a significant (p 0.001) association between the serum level of LTBP- 1 and BCLC score in HCC patients. The LTBP-1 level was gradually increased with the progress in BCLC score, where, the level was 46.8 in score 4 against 26.6 in score 0. Conversely, AFP level was not significantly (p=0.172) associated with BCLC score. Taken together, serum LTBP-1might be a potential serum marker to discriminate HCC from liver cirrhosis patients due to its high sensitivity and specificity, compared to AFP. LTBP-1 might be a promising diagnostic biomarker for HCC.

Poster Session 25

PF25-3 10051

Steatotic Liver Disease: An Important Upstream Risk Factor for the Development of Metabolic Syndrome-related Diseases

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Background & Aims: Steatotic liver disease (SLD) is the most common chronic liver disease and is closely linked to obesity and metabolic risk factors. SLD is often seen alongside conditions such as type 2 diabetes (T2D), hypertension (HT), and dyslipidemia (DL), but its role as a risk factor for these diseases is not fully understood.
Methods: This study used longitudinal health examination data from 714 individuals who underwent health checks and abdominal ultrasounds at baseline and after 7 years. Data collected included demographics, physical findings, blood pressure, laboratory results, and lifestyle information. Logistic regression analysis was used to assess the impact of SLD on the development of metabolic syndrome-related diseases.
Results: At baseline, 60.9% of participants were diagnosed with SLD, with higher prevalence among men and those with higher BMI. The SLD group also had elevated liver enzymes, triglycerides, LDL cholesterol, uric acid, and fasting glucose, and lower HDL cholesterol. Individuals with SLD had higher rates of obesity, T2D, HT, and diabetic nephropathy at both baseline and follow-up. Baseline SLD was found to be an independent risk factor for developing T2D, HT, and diabetic nephropathy, but not for obesity. Conversely, baseline obesity and diabetic nephropathy independently predicted new cases of SLD after 7 years. Notably, improvement in SLD status was associated with a reduced risk of developing metabolic syndrome-related diseases.
Conclusions: These findings highlight the importance of early detection and intervention in SLD to prevent metabolic diseases.

PF25-4 10075

Short Term and Long Term Regression of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) in Older Adults

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most prevalent chronic liver disease worldwide, affecting over 30% of the global adult population. To reduce the global burden of MASLD, identifying patients likely to experience disease regression is essential. This study used data from the Korean National Health Insurance Service Senior Cohort. We included participants with both severe liver disease (SLD) and at least one cardiometabolic risk factor (CMRF) who underwent national health screening during three periods: baseline (2009 to 2010), short term (2011 to 2012), and long term (2016 to 2019). We used demographic data, lifestyle behaviors, socioeconomic status, disability status, death records, and health screening results. MASLD regression was defined as the absence of both SLD and CMRF. Logistic regression and decision tree models were used to predict this binary outcome. Among patients with MASLD, about 23% experienced regression in the short term and 18% in the long term. In short-term models, the area under the receiver operating characteristic curve (AUROC) was 0.788 for logistic regression and 0.760 for the decision tree. In long-term models, the AUROC was 0.756 and 0.722, respectively. Net reclassification improvement (NRI) analysis showed that the decision tree outperformed logistic regression in classifying non regression cases in the short term. The developed models for predicting short and long term MASLD regression may serve as useful tools for assessing liver health. Further prospective studies are warranted to validate their clinical utility.

Poster Session 26

PF26-1 10176

Establishment of a Mouse Model of Liver Tumorigenesis with Concurrent Steatotic Liver Disease

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Background and Aim: Non-viral liver cancers associated with metabolic dysfunction-associated steatotic liver disease (MASLD) are increasing worldwide. We aimed to establish a mouse model of liver tumorigenesis in the context of steatotic liver injury and to characterize the histopathological features of the resulting tumors, with the goal of elucidating mechanisms relevant to human hepatocarcinogenesis.
Methods: Two-week-old male C57BL/6N mice received a single intraperitoneal injection of diethylnitrosamine (DEN; 25 mg/kg body weight). After weaning, mice were assigned to one of three groups: (1) standard diet (control), (2) choline-deficient, methionine-restricted high-fat diet (CDAHFD), or (3) standard diet plus intraperitoneal carbon tetrachloride (CCl4) three times weekly. These regimens were continued for nine months. Liver tissues were collected at 6 and 9 months and subjected to histological evaluation.
Results: At 6 months, liver tumors were observed only in the CCl4 group. By 9 months, tumors were detected in all groups. Histopathological analysis revealed a range of lesions from adenomas to adenocarcinomas, characterized by increased cell density, elevated nucleus-to-cytoplasm ratios, and structural atypia. The incidence and histological features of tumors in the CDAHFD group were similar to those in the control group.
Conclusion: The combination of DEN and CDAHFD did not accelerate the time to tumor formation compared with DEN alone. These findings suggest that CDAHFD may be insufficient to promote liver carcinogenesis in this model. Further studies are underway to clarify tumor characteristics and underlying mechanisms in the context of MASLD.

PF26-2 10098

The Utility of Non-invasive Imaging Modalities for Diagnosing Cirrhosis in Metabolic-dysfunction Associated Steatotic Liver Disease: A Systematic Review

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Background: Cirrhosis remains a key prognostic milestone in the clinical course of metabolic dysfunction-associated steatotic liver disease (MASLD). Accurate identification of cirrhosis is essential for risk stratification, surveillance, and management. However, radiological features of cirrhosis are often subtle or non-specific, particularly in the absence of portal hypertension or significant fibrosis. As MASLD becomes the leading cause of chronic liver disease, this study aims to determine the diagnostic gaps in the imaging diagnosis of cirrhosis.
Methods: We systematically reviewed 2 key databases to identify studies consisting of basic imaging techniques and liver cirrhosis from 2015 till inception. Studies were then screened for imaging definitions of cirrhosis and features of cirrhosis which were classified into clear, indirect, and no definitions. The distribution of key features was identified across each imaging modality.
Results: We screened 6596 articles eventually including 115 articles utilizing basic imaging techniques in patients with cirrhosis. The most common imaging modality to evaluate cirrhosis was ultrasound, used in over half of the studies, followed by magnetic resonance imaging and computed tomography. Of these 115 studies, only 5 studies had a clear definition of cirrhosis, whilst 50 studies had no definition of cirrhosis. Of the remaining 60 studies that identified features of cirrhosis, liver surface nodularity was ubiquitous across all 3 major modalities. Other pertinent features include abnormal parenchymal echotexture, features of portal hypertension, and liver segmental redistribution.
Conclusion: Despite the widespread use of imaging in cirrhotic patients, this study highlights the crucial need for standardized imaging criteria for cirrhosis.

Poster Session 26

PF26-3 10017

Prognostic Significance of Bioelectrical Impedance Analysis in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

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The application of bioelectrical impedance analysis (BIA) in metabolic dysfunction-associated steatotic liver disease (MASLD) is gaining popularity due to inadequacy of BMI-based measurement. This study aims to evaluate the factors associated with advanced liver diseases with the utilisation of BIA.We enrolled 254 MASLD patients who had valid vibration-controlled transient elastography (VCTE) and BIA. Total body fat (kg), muscle mass (kg), total body fat percentage, total body muscle percentage, appendicular skeletal muscle mass percentage and visceral fat index were measured by BIA. Severe steatosis and advanced fibrosis/cirrhosis (F3/F4) were defined by VCTE parameters. Major adverse cardiovascular events (MACE) included acute myocardial infarction, cardiac revascularization procedure and stroke. Univariate and multivariate analysis were applied to calculate p-value, odds ratio (OR) and 95% confidence intervals (95%CI).Among 254 MASLD patients (mean age 53.8 +/-11.7 years; 51.2% male, mean BMI 28.2+/-4.6 kg/m2), 81.1% had severe steatosis and 14.2 % had F3/4. Visceral fat index was an independent predictor of F3/F4 (OR 1.088, 95%CI 1.005-1.178), severe steatosis (OR 1.080, 95%CI 1.007-1.157) and MACE (OR 1.193, 95%CI 1.042-1.364). Higher total body muscle percentage was associated with lower odds of severe steatosis (OR 0.956, 95%CI 0.917-0.996) and higher odds of MACE (OR 1.123, 95%CI 1.014-1.244). Other independent predictors of F3/4 included alanine transaminase level (OR 1.016, 95%CI 1.007-1.025), platelet count (OR 0.987, 95%CI 0.980-0.994) and hypertension (OR 3.076, 95%CI 1.299-7.284).Visceral fat index and total body muscle percentage by BIA demonstrated predictive value in MASLD. Increased utilization of BIA in MASLD assessment should be advocated.

PF26-4 10032

Impact of Hypothyroidism on Liver-related Events among People with Metabolic Dysfunction-associated Steatotic Liver Disease

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Background: Observational studies have reported that hypothyroidism increases risk of metabolic dysfunction-associated steatotic liver disease (MASLD) and its advanced subtype. This study expands on these findings by investigating longitudinal association between hypothyroidism and liver-related events (LREs) in MASLD.
Methods: Patients with MASLD who underwent thyroid function tests (TFTs) between 2000 and 2024 in Hong Kong were included. Baseline thyroid status was identified using ICD-9-CM diagnosis codes and TFTs, and thyroxine replacement treatment; time-varying thyroid status was determined by TFTs. LREs were defined as hepatocellular carcinoma and cirrhotic complications.
Results: In 20478 patients, 179 LREs occurred over a median follow-up of 4.8 years. The incidence of LREs did not differ significantly with baseline thyroid stimulating hormone (TSH) and free thyroxine (T4). Baseline hypothyroidism was only associated with a 1.11-fold increased risk of LREs in univariate model, but not hyperthyroidism. In contrast, time-varying TSH levels (adjusted cause-specific hazard ratio [aCSHR] 1.01, 95% CI 1.004-1.036) and TSH groups (4-10 mIU/L: aCSHR 2.36, 95% CI 1.42-3.92, p&It;0.001; >10 mIU/L: aCSHR 4.73, 95% CI 1.50-14.88, p=0.008) were associated with higher LRE risk. LRE incidence varied significantly by thyroid status over time (Figure 1). Time-varying hypothyroidism was associated with higher LRE rates (aCSHR 3.01; 95% CI, 1.94-4.67; p&It;0.001), with aCSHRs of 2.60 for subclinical hypothyroidism and 6.31 for overt hypothyroidism. No association was found for time-varying hyperthyroidism.
Conclusion: The significant association between time-varying hypothyroidism (both subclinical and overt) and LREs suggest dynamic TFT changes may be useful for monitoring outcomes in patients with MASLD.

Poster Session 26
PF26-5 10003

Association Between Sitting Time and Frailty in Patients with MASLD: A Survey Using the Global Physical Activity Questionnaire (GPAQ)

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Background: Frailty is influenced by sedentary behavior, including sitting time. The Global Physical Activity Questionnaire (GPAQ) is a validated tool that can assess sitting time. We aimed to investigate factors related to frailty in MASLD patients, including sitting time.
Methods: This prospective observational study included 68 MASLD patients who were assessed by the Liver Frailty Index (LFI) and GPAQ (51.5% male, mean age 56 years, BMI 27.8). All patients were classified into the robust or pre-frail/frail groups according to the results of LFI. Decision tree analysis was used to examine the profiles associated with pre-frail/frail.
Results: According to the results of LFI, 25.0% of patients were classified as robust, 73.5% as pre-frail, and 1.5% as frail. The median sitting time was 420 minutes/day. Age was significantly higher in the pre-frail/frail groups compared to the robust group. However, no significant difference was observed in sex, BMI, and liver stiffness between the two groups. FIB-4 index and HbA1c values were significantly higher in the pre-frail/frail groups compared to the robust group. However, no significant difference was observed in the sitting time between the two groups. Decision tree analysis revealed that sitting time >420 minutes/day was associated with pre-frailty in male patients aged <65 years.
Conclusion: This study demonstrated the sitting time in patients with MASLD. Additionally, sitting time was associated with pre-frailty in male patients with MASLD who were under 65 years old. Reducing sitting time may contribute to improving frailty in non-senior male patients with MASLD.

Poster Session 27

PF27-1 10044

Molecular Clustering of Metabolic Dysfunction-Associated Steatotic Liver Disease Based on Transcriptome Analysis

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Background: MASLD is a complex metabolic disorder with a diverse spectrum. This study aimed to classify patients with MASLD into molecular subtypes based on the underlying pathophysiology.
Methods: We performed high-throughput RNA sequencing on 164 liver tissue samples from healthy controls and patients with MASLD. The clustering was based on individual genes or pathways that showed high variation across the samples. Second, the clustering was based on single-sample gene set enrichment analysis.
Results: Optimal homogeneity was achieved by dividing the samples into four clusters (one healthy control and three MASLD clusters I-III) based on the top genes or pathways with differences across the samples. No significant differences were observed in waist circumference, blood pressure, glucose, ALT, or AST levels between cluster I patients with MASLD and the healthy controls. Cluster I showed the clinical features of lean MASLD. Cluster III of MASLD demonstrated hypertension and a T2DM prevalence of 57.1% and 50.0%, respectively, with a significantly higher fibrosis burden than clusters I and II. Cluster III was associated with severe fibrosis and abnormal glucose homeostasis. In MASLD cluster I, the sphingolipid and GPCR pathways were upregulated, whereas the complement and phagocytosis pathways were downregulated. In MASLD cluster II, the cell cycle and NOTCH3 pathways increased, whereas the PI3K and insulin-related pathways decreased. In MASLD cluster III, increased activity occurred in the IL-2/4 and ECM pathways, coupled with decreased serotonin 2A/B pathways.
Conclusion: MASLD can be divided into three distinct molecular phenotypes, wherein each is characterized by a specific molecular pathway.

PF27-2 10045

Cost-effectiveness Analysis of MASLD Screening Using FIB-4 Based Two-step Algorithm in the Medical Check-up

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Background and Aims: We tried to investigate whether advanced fibrosis screening in MASLD patients is cost-effective for adults aged 40-49 years during medical or health check-up.
Methods: The target group for analysis was adults who received medical check-ups for various reasons in the United States. We constructed a hybrid model of the decision tree model and Markov model to compare expected costs and quality-adjusted life-years (QALYs) between 'screening' and 'no screening' groups from healthcare system perspectives. Patients diagnosed MASLD with advanced fibrosis by FIB4 and VCTE were given intensive lifestyle intervention (ILI). The incremental cost-effectiveness ratio (ICER) was calculated for a 30-year horizon.
Results: Assuming effect of ILI is limited to regression of liver fibrosis, ICER of the FIB-4-based two steps algorithm was $103,405 per QALY in adults aged 40-49 years, which was slightly above the threshold value ($100,000/QALY). And in those in adults aged 50-59 and 60-69 years, the ICER was $137,593 and $197,901 per QALY, respectively. If we assume the effect of ILI can improve liver fibrosis as well as cardiovascular disease events, ICERs of screening in aged 40-49 and 50-59 years were $74,596, and $95,974 per QALY, respectively. In an analysis that included additional positive effect on extrahepatic cancer by ILI, estimated ICERs were below the threshold in those in aged 40-49 and 50-59 years.
Conclusions: Advanced fibrosis screening in MASLD patients using the FIB-4-based two-step algorithm and ILI was cost-effective for adults aged 40-49 years, taking into account both liver fibrosis and cardiovascular disease.

Poster Session 27

PF27-3 10084

Changes in ALT Levels Following Tirzepatide Initiation in Patients with MASLD

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Background and Aim: Tirzepatide, a dual GIP/GLP-1 receptor agonist, has shown promising metabolic benefits. We retrospectively evaluated the impact of tirzepatide on serum ALT levels and body weight in patients with metabolic dysfunction-associated steatotic liver disease (MASLD), to explore its potential effects on hepatic inflammation.
Methods: This study included 34 MASLD patients who initiated tirzepatide between June 2023 and December 2024 at our institution and affiliated centers. Inclusion criteria were BMI >23 and elevated ALT (>30 IU/mL for men, >23 IU/mL for women) at baseline. Changes in body weight and ALT levels over a 24-week period were analyzed.
Results: Baseline characteristics were: 17 males and 17 females, mean age 53.7±12.2 years, body weight 86.6±18.4 kg, BMI 32.5±5.92, ALT 54.0±24.9 IU/mL, and HbA1c 7.41±0.99%. Prior medications included GLP-1RA/DPP-4 inhibitors/biguanides/none (n=20/5/1/8). The lowest values during follow-up were 82.2±18.2 kg (body weight) and 34.1±17.2 IU/mL (ALT), both significantly reduced from baseline ($p<0.001$). Even in patients with <5% weight loss (n=18), ALT significantly decreased ($p=0.007$). Patients with cirrhosis (n=7) also exhibited significant reductions in body weight and ALT, comparable to non-cirrhotic patients. Those switched from GLP-1RA (n=20) experienced slower, but still significant, improvements in both parameters ($p<0.001$ and $p=0.005$, respectively). Only two patients discontinued tirzepatide due to adverse events.
Conclusion: Tirzepatide may exert hepatoprotective effects in MASLD patients regardless of the extent of weight loss, baseline fibrosis status, or prior antidiabetic therapy.

PF27-4 10104

Uncovering Patient Awareness of Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) in Singapore: Risk Factors, Complications and Management Strategies

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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of liver cirrhosis, with prevalence of up to 29.3% in Singapore and a projected 20% increase by 2030. As no approved pharmacotherapy is available locally, lifestyle modifications and risk factors management are crucial to prevent progression to liver cirrhosis and hepatocellular carcinoma (HCC).
Methods: A cross-sectional, descriptive survey was administered between September 2024 and May 2025 among patients with MASLD and/or their caregivers receiving follow-up care at the Singapore General Hospital MASLD Clinic. The survey collected demographic data and assessed awareness, perceptions, and knowledge of MASLD, its risk factors, complications (liver, cardiovascular, and mortality risk), and management strategies.
Results: 100 responses were collected. Respondents had a mean age of 61.6±14.6 years; 53% were female and 83% were Chinese, with a mean BMI of 25.2±4.4. Over half (53%) had at least pre-university education. Most had type 2 diabetes mellitus (61%), hypertension (72%), hyperlipidemia (70%), and liver cirrhosis (80%). While 85% had heard of MASLD, 39% answered less than half of the knowledge questions correctly, and only two achieved full scores. Less than half identified hypertension (43%) and hyperlipidemia (46%) as risk factors. Although 84% recognized MASLD as a cause of cirrhosis, only 47% knew of its progression to HCC, and 23% of its cardiovascular risks. 84% were willing to implement lifestyle changes. Face-to-face discussions were the preferred method for receiving information.
Conclusion: Substantial knowledge gaps in MASLD exist. Targeted education and specialised counselling are needed to support effective disease management.

Poster Session 27
PF27-5 10137

Differences in the Prevalence of NAFLD, MAFLD, and MASLD According to Changes in the Nomenclature in a Health Checkup Using MRI Derived Proton Density Fat Fraction

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Purpose: International expert panels proposed new nomenclatures, metabolic dysfunction-associated fatty liver disease (MAFLD) in 2020 and metabolic dysfunction associated steatotic liver disease (MASLD) in 2023, along with revised diagnostic criteria to replace non-alcoholic fatty liver disease (NAFLD). We aimed to investigate the differences in NAFLD, MAFLD, and MASLD prevalence with changing nomenclature in a health check-up using MRI-derived proton density fat fraction (MRI-PDFF) to assess hepatic steatosis. We also examined the prevalence of the subclassifications of steatotic liver disease (SLD) and the differences in characteristics among the sub-categories.
Methods: We included 844 participants who underwent liver MRI-PDFF at our health check-up clinic between January 2020 and November 2022. Hepatic steatosis was defined as MRI-PDFF > 5%. Participants were categorized according to NAFLD, MAFLD, MASLD, and sub-classifications of SLD.
Results: The prevalence rates of NAFLD, MAFLD, and MASLD were 25.9%, 29.5%, and 25.2%, respectively. 30.5% of the participants was categorized as SLD. The prevalence rates of the SLD sub-categories were 25.2% for MASLD, 3.7% for MASLD and alcohol associated liver disease (MetALD), 0.1% for alcohol-associated liver disease, 1.3% for specific etiology SLD, and 0.1% for cryptogenic SLD. Compared with patients in the MASLD group, those in the MetALD group were younger, predominantly male, and exhibited higher levels of serum aspartate aminotransferase, gamma-glutamyl transpeptidase, and triglycerides.
Conclusion: The prevalences of NAFLD and MASLD assessed using MRI-PDFF were similar, with MASLD accounting for 97.3% of the patients with NAFLD. The separate MetALD sub-category may have clinical characteristics that differ from those of MASLD.

Poster Session 28

PF28-1 10186

Gene Expression Analysis of Immune Rejection in a Mouse Liver Transplantation Model

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Background and Aim: Although immunosuppressive therapies have improved short term outcomes after liver transplantation, immune rejection, particularly chronic rejection remains a clinical challenge. The mechanisms underlying these processes are not fully understood, in part due to the limited availability of long-term observational data from experimental animal models. This study aimed to elucidate the dynamics of immune rejection and tissue remodeling using a murine model of orthotopic allogeneic liver transplantation. We focused longitudinal gene expression of infiltrating immune cells, parenchymal cells and non-parenchymal cells in grafted liver tissue, with the goal of characterizing the interplay between immune response and hepatic regeneration over time.
Methods: Orthotopic liver transplantation with hepatic artery reconstruction was performed using male BALB/c mice (donors) and male C57BL/6 mice (recipients), aged 11-13 weeks. Graft tissues were sampled at defined time points up to 16 weeks post-transplantation. Total RNA was extracted for transcriptomic analysis.
Results: Lymphocyte markers (CD4, CD8, CD19) and myeloid cell markers (Cd11c, Cd11b, Adgre1, Ly6c, Ly6g) showed peak expression at 2 weeks post-transplantation, followed by a gradual decline. Among epithelial markers, Krt19 (cholangiocytes) peaked at week 2 and declined, while Asgr1 (hepatocytes) was lowest at week 2 and subsequently increased. AFP expression remained relatively unchanged. Cd31, a marker of sinusoidal endothelial cells, peaked at week 4 before declining.
Conclusion: Immune rejection in this orthotopic allogeneic liver transplantation model peaks around 2 weeks postoperatively and diminishes by 8 weeks. Concurrently, regenerative responses of sinusoidal endothelial cells, hepatocytes, and cholangiocytes are observed, suggesting coordinated resolution and tissue repair.

PF28-2 10142

The Association between Metabolic Abnormalities and the Development of Fatty Liver: A Cohort Study Using a Large Scale Health Check-up Database in Japan

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Background: Although many studies have investigated the prevalence and incidence of fatty liver disease, most have focused only on health checkup participants. This raises concerns about selection bias, as those who do not participate in health checkups could not be included, potentially leading to misrepresentation of fatty liver. This study aimed to estimate the prevalence, incidence, and association between metabolic abnormalities and fatty liver in the entire cohort of insured individuals in Japan
Methods: We used data from the National Civil Engineering and Architecture Health Insurance database, covering annual health checkups conducted between 2017 and 2024. Fatty liver was diagnosed via abdominal ultrasound, and metabolic status was assessed using five cardiometabolic criteria. Cox proportional hazards models were applied to individuals without fatty liver at baseline. Inverse probability weighting (IPW) was used to adjust for the selection bias.
Results: A total of 91,737 individuals were analyzed; 73.6% were male, and ages ranged from 18 to 83 years. After IPW adjustment, the prevalence of fatty liver was 24% (men: 32%, women: 12%). The incidence rate was 4.34 per 100 person-years (men: 5.98, women: 2.46). All five criteria were significantly associated with fatty liver onset. High BMI showed a hazard ratio of 2.36 (95% CI: 2.22-2.50), and having all five abnormalities yielded a hazard ratio of 8.11 (95% CI: 6.74-9.76).
Conclusion: This study clarified the prevalence and incidence of fatty liver disease in Japan, as well as its cumulative association with metabolic abnormalities.

Poster Session 28

PF28-3 10155

Prevalence of Risk Factors for Non Alcoholic Fatty Liver Disease in Cryptogenic Cirrhosis : A Case Control Study

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Background: Non-alcoholic fatty liver disease (NAFLD) can progress silently to cirrhosis with loss of classical histological features, thus masquerading as cryptogenic cirrhosis. NAFLD has been deemed to be the commonest etiology of Cryptogenic cirrhosis (CC).
Aim: The study was designed to compare the prevalence of risk factors for NAFLD in patients of Cryptogenic cirrhosis and cirrhosis due to other etiologies. Methods - This cross-sectional study compared 50 NAFLD cases (CC) and 50 controls (cirrhosis due to known causes excluding NASH) on risk factors (obesity, diabetes, dyslipidemia, hypertension, metabolic syndrome) and metabolic biomarkers (Adiponectin, HOMA-IR) over the past 10 years.
Results: The average age (61.70 &plusmn 11.24 yrs vs 54.16 &plusmn 12.30 yrs;p=0.002) and proportion of females (48% vs 14%;p&lt0.001) in CC was significantly higher than controls. The prevalence of obesity (82% vs 38%;p&lt0.001), diabetes (72% vs 20%;p&lt0.001), dyslipidemia (16% vs 4%;p=0.046) and metabolic syndrome (66% vs 16% ;p&lt0.001) were higher in CC than in controls. Insulin resistance (HOMA-IR) was higher in CC (2.72 &plusmn 2.26) compared to controls (1.48 &plusmn 1.28)(p=0.003). Fasting Adiponectin levels were lower in CC group (11.80 &plusmn 11.18 &microg/ml) than controls (18.06 &plusmn 15.72 &microg/ml)(p=0.024). On multivariate logistic regression analysis, past obesity and higher HbA1c were independently associated with CC.
Conclusion: The prevalence of obesity, diabetes, dyslipidemia and metabolic syndrome is significantly higher in CC than cirrhosis due to other etiologies. Insulin resistance is higher and Adiponectin levels are lower in CC. All these findings suggest that NAFLD is the predominant etiology of cryptogenic cirrhosis.

PF28-4 10165

Changing Trends and Survival Outcomes in MASLD-related Hepatocellular Carcinoma: A Multicenter Retrospective Cohort Analysis

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a growing cause of hepatocellular carcinoma (HCC). Advances in imaging, surveillance, and therapy may have shifted how patients present and survive. We assessed temporal changes in clinical features, management, and survival in MASLD-related HCC over 20 years.
Methods: We retrospectively analyzed 441 patients with imaging- or histology-confirmed MASLD-related HCC treated at multiple tertiary centers. Patients were grouped into Era 1 (January 2005-December 2014; n = 102) and Era 2 (January 2015-June 2024; n = 342). We compared demographics, tumor characteristics, and treatment intent using Wilcoxon and Chi-square tests. Survival was evaluated by Kaplan-Meier analysis and restricted mean survival time (RMST) differences at 1, 5, and 9 years.
Results: Baseline age, sex, and comorbidities (diabetes, hypertension, hyperlipidemia) were similar between eras. Median BMI declined from 26.7 kg/m2 (IQR 23.0-29.4) to 24.2 kg/m2 (21.8-27.1; p = 0.004). The proportion of advanced tumors (BCLC C/D) decreased from 31% to 18% (p = 0.018), while curative-intent therapy (transplant, resection or ablation) rose from 15% to 28% (p < 0.001). RMST differences favored Era 2 by 14.8 days at 1 year (95% CI 4.8-24.9; p<0.001), 226.0 days at 5 years (163.7-288.2; p<0.001), and 603.8 days at 9 years (505.1-702.4; p<0.001).
Conclusion: Over two decades, MASLD-related HCC patients experienced stable tumor parameters with long-term survival gains, likely reflecting earlier detection and expanded curative modalities. These findings underscore the importance of continued research regarding HCC surveillance and multidisciplinary care.

Poster Session 28
PF28-5 10170

Incretin-Based Therapies for MASLD with Type 2 Diabetes: Results from Two Prospective Studies

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is frequently associated with type 2 diabetes mellitus (T2DM), which increases the risk of liver fibrosis and cardiometabolic complications. Incretin-based therapies, such as semaglutide (Sema) and tirzepatide (TZP), have shown promise in improving both metabolic and hepatic parameters; however, real-world data remain limited.
Methods: We evaluated two prospective studies in patients with MASLD and T2DM. Verification 1: a multicenter study of 80 patients receiving oral Sema, with 70 completing 48 weeks. Verification 2: a single-center pilot study of 16 patients receiving TZP, with 13 completing 48 weeks. In both studies, dose adjustments were determined by each physician while monitoring efficacy and adverse events.
Results: Both Sema and TZP treatment led to significant improvements in glycemic control, liver enzymes, and body weight throughout the 48 weeks. After 48 weeks, CAP value and non-invasive tests for liver fibrosis, including type IV collagen 7S, WFA+-M2BP, FIB-4 index, and liver stiffness, significantly decreased in both cohorts. ALT reduction was significantly correlated with weight reduction in both cohorts (Sema: r=0.37; TZP: r=0.57). Similarly, CAP changes were significantly correlated with weight reduction in the Sema group (r=0.44), and a similar trend was observed in the TZP group (r=0.45, p=0.12). The most common adverse events were transient gastrointestinal symptoms, such as grade 1-2 nausea (Sema: 28.8%; TZP: 31.3%).
Conclusion: Both oral Sema and TZP treatments demonstrated significant dual benefits in improving hepatic and metabolic parameters in patients with MASLD and T2DM, supporting their therapeutic potential in this high-risk population.

Poster Session 29

PF29-1 10175

The Mechanism of BGB324 and the Effect of AXL Family Inhibitors in MAFLD

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) fibrosis is a critical stage in the pathogenesis and progression of MAFLD to more severe conditions. Studies have reported that AXL and MerTK, two members of receptor tyrosine kinase, and their ligand-Gas6 show possible effects in reducing MAFLD fibrosis. However, the mechanism elaboration on the effect of AXL inhibitor (BGB324) is limited; and the conclusion for the MertK effect on MAFLD fibrosis is conflicting among studies.
Methods: Human hepatic stellate cells (LX-2) were treated with Transforming Growth Factor beta 1 (10 ng/ml) for 24 or 48 hours to induce fibrosis. Classical inhibitors were selected to investigate their anti-fibrotic effect by RT-qPCR and Western blotting, with inhibitor optimal doses validated via CCK-8 assays. Flow cytometry was utilized to analyse cell cycle arrest and apoptosis ratios after exposure.
Results: BGB324 increased the mRNA levels of senescence markers GLB1 and P16, but there was no change regarding the SA-beta-Gal staining. Meanwhile, BGB324 induced LX-2 arrest at the G2 stage and increased apoptosis in a dose-dependent manner. BGB324 and MerTK inhibitor UNC225 delivered a more anti-fibrotic effect than Gas6 inhibitor RU301.
Conclusions: The anti-fibrotic mechanism of BGB324 may involve regulating cell cycle arrest and cellular apoptosis, but not senescence; and BGB324 and UNC2250 showed more anti-fibrotic effect than RU301. These findings support further investigation of BGB324 and other AXL inhibitors as therapeutic agents for MAFLD fibrosis.

PF29-2 10178

Strain-Dependent Susceptibility to Diet-Induced Fatty Liver Disease in Mice

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Background and Aim: Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease linked to obesity and metabolic syndrome, with rising global prevalence. Its development is thought to involve complex interactions between genetic background and environmental factors such as diet and physical activity. However, the underlying mechanisms remain poorly understood, and suitable animal models are needed for therapeutic development. This study aimed to establish a dietary model of MASH across three mouse strains (BALB/c, C57BL/6, and PWK/PhJ) and to evaluate strain-specific differences in disease progression.
Methods: Male BALB/c, C57BL/6, and PWK/PhJ mice were maintained on a standard diet until 6 weeks of age, after which they received either a standard diet or a choline-deficient, methionine-restricted high-fat diet (CDAHFD) for six weeks. At 12 weeks of age, peripheral blood and liver tissue were collected for hematologic, biochemical, and histopathological analysis.
Results: CDAHFD feeding significantly reduced body weight in BALB/c and C57BL/6 mice, but not in PWK/PhJ mice. Hemoglobin levels, red blood cell counts, and platelet counts were unaffected across groups. In PWK/PhJ mice, the lymphocyte fraction increased with CDAHFD feeding. All CDAHFD-fed groups showed elevated GOT and GPT levels, with PWK/PhJ mice displaying markedly elevated transaminases (>1,000 IU/L). Histologically, severe hepatitis and liver fibrosis were evident only in CDAHFD-fed PWK/PhJ mice.
Conclusion: Under CDAHFD feeding, PWK/PhJ mice developed more severe liver injury and fibrosis than BALB/c or C57BL/6 mice, suggesting that genetic background strongly influences susceptibility to diet-induced steatohepatitis.

Poster Session 29

PF29-3 10187

Effect of the Emulsifier Polysorbate 80 on a Diet-Induced MASLD Mouse Model

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Background and Aim: The global prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is increasing, yet factors influencing its progression remain poorly understood. Establishing a mouse model that recapitulates the progression from MASLD to metabolic dysfunction-associated steatohepatitis (MASH) is essential for elucidating disease mechanisms and developing therapies. Recent studies suggest that dietary emulsifiers may contribute to fatty liver development. In this study, we evaluated the impact of polysorbate 80 (P80), a commonly used emulsifier, on the progression of MASLD in mice fed a choline-deficient, methionine-restricted high-fat diet (CDAHFD).
Methods: Six-week-old C57BL/6 male mice were fed CDAHFD for six weeks, with or without 2% P80 added to drinking water. At 12 weeks of age, peripheral blood, liver, small intestine, and large intestine samples were collected for biochemical, histopathological, and gene expression analyses.
Results: Sirius Red staining revealed pericellular liver fibrosis in all CDAHFD-fed mice; however, bridging fibrosis was not observed, even with P80 supplementation. Serum transaminases trended higher in the P80 group. In the small intestine, expression of mucosal barrier-associated genes (Muc2, Defa3, Lyz1) decreased with P80. In the large intestine, immune cell markers (Cd8, F4/80, Cd11c, Nk1.1) and proinflammatory cytokines (IL-6, IL-1β) were elevated with P80, indicating enhanced intestinal inflammation.
Conclusion: Polysorbate 80 impaired mucosal barrier function and exacerbated intestinal inflammation, contributing to a trend toward more severe liver injury. These findings highlight the role of dietary emulsifiers in MASLD progression and warrant further investigation in translational models.

PF29-4 10192

PNPLA3 I148M GG Variant Promotes Immune Cell Infiltration and is Linked to Metabolic Dysfunction-associated Steatotic Liver Disease Progression

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Background: Immune cells play a critical role in metabolic dysfunction-associated steatotic liver disease (MASLD) progression. The patatin-like phospholipase domain-containing protein 3 (PNPLA3) I148M variant has been linked to hepatic inflammation and fibrosis, but its effect on intrahepatic immune infiltration and activation is unknown.
Methods: Seventy MASLD patients were prospectively enrolled. Genomic DNA from buccal swabs or liver biopsies was genotyped for the PNPLA3 rs738409 SNP. Immunohistochemistry with CD3 and CD68 antibodies quantified T cells and macrophages, respectively. Total RNA from biopsy specimens underwent quantitative reverse transcription-PCR to assess expression of immune activation markers.
Results: Among the 70 patients with MASLD, 34 carried the GG genotype, 21 GC, and 15 CC. GG carriers trended toward higher rates of advanced fibrosis (F3/F4 vs. GC+CC; $P = 0.051$) and exhibited significantly increased periportal CD3+ and CD68+ cell densities compared with GC/CC carriers ($P < 0.05$). Transcriptomic analysis demonstrated upregulation of chronic antigen-stimulation and activation markers (CD8A, GZMB, CCL2, TIMP1) in GG carriers ($P < 0.05$). Correlation matrices revealed consistent positive associations among inflammatory, steatosis-related, and fibrosis-related markers.
Conclusions: These findings indicate that the PNPLA3 I148M variant is significantly associated with enhanced immune cell infiltration and activation in the MASLD liver. Further studies are warranted to elucidate the mechanistic links between this genetic variant and liver inflammation, which may provide insights into novel therapeutic targets for MASLD progression.

Poster Session 29
PF29-5 10219

Hepatocyte-specific (pro)renin Receptor Knockout Attenuated Diet-induced Steatosis in Mice with Improved Insulin Resistance and Metabolic Rates

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), defined as steatosis in the presence of cardiometabolic risk factors, is the most common cause of chronic liver disease. (Pro)renin receptor (PRR) is reportedly involved in lipid metabolism and PRR knockdown protects mice against hepatosteatosis and inflammation. However, the impact of hepatocyte-specific PRR knockout on MASLD remain unclear.
Methods: Hepatocyte-specific PRR knockout (PRRhepKO) mice were generated by crossing PRR floxed mice with albumin-Cre transgenic mice. MASLD was generated by high fat diet (HFD) feeding for 12 weeks. Primary hepatocytes isolated from wild-type (WT) and PRRhepKO mice were used for proteome analysis.
Results: PRRhepKO mice had decreased body weight and reduced total body fat weight on an HFD. In addition, PRRhepKO mice also displayed improved insulin resistance and increased metabolic rates. Hepatic steatosis was also attenuated by hepatocyte PRR knockout. The expressions of peroxisome proliferator-activated receptor-alpha, peroxisomal acyl-coenzyme A oxidase 1 (ACOX1) and cytochrome p450 4A14 (CYP4a14) were upregulated in PRRhepKO mice livers. In vitro, primary hepatocytes from PRRhepKO mice showed increased abundance of proteins regulating fatty acids oxidation in both proteomics and western blots. However, hepatocyte-specific PRR knockout mice showed increased hepatic inflammation on both normal diet and HFD, including increased inflammatory cell recruitment, and proinflammatory cytokines expression with autophagy impairment.
Conclusion: Our findings revealed that PRR knockout in hepatocytes attenuated steatosis and improved metabolism in mice with MASLD but caused liver inflammation on both normal diet and HFD by autophagy impairment. Accordingly, targeting PRR signaling in MASLD should be cautious.

Poster Session 30

PF30-1 10016

RNA Binding Protein TIA1 Protects Hepatic Lipid Homeostasis and Prevents Fibrotic Nonalcoholic Steatohepatitis through Stress Granule Assembly

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Background: NAFLD has emerged as a major global public health issue, while its etiology is complex and molecular mechanisms are unclear. TIA1, an RNA binding protein involved in the post transcriptional regulation of gene expression, is also a key molecule involved in the assembly of stress granules (SGs) under cell stress. However, the function and mechanism of TIA1 and SGs in the context of NAFLD are poorly understood.
Methods: We generated hepatocyte-specific TIA1 knockout mice to study in vivo effects of TIA1 on lipid metabolism under HFD, HFHC diet and MCD. Lipid deposition and metabolic homeostasis were analyzed in AML12 cells with multiple loss- and gain-of function studies. Additionally, the relationship of TIA1 with SREBP1 was explored via RNA immunoprecipitation and third-generation sequencing. The regulatory role of TIA1 in modulating SREBP1 translation was further elucidated using luciferase reporter assays and chromatin immunoprecipitation.
Results: Through RNA sequencing and GEO database analysis, we found that TIA1 is upregulated in NAFLD liver and is associated with poor prognosis of NAFLD/NASH. Hepatocyte-specific knockdown of TIA1 in mice significantly exacerbate liver steatosis and fibrosis. Additionally, we demonstrate that TIA1 expression and TIA1-assmbled SGs are elevated in palmitic acid (PA)-simulated AML12 cells and essential to maintain lipid homeostasis. Mechanistically, TIA1 can specifically bind to the mRNA 3'UTR region of SREBP1 and inhibit its translation.
Conclusion: These results reveal that TIA1 functions as an important regulator of hepatic lipid homeostasis, and its deficiency exacerbates hepatocyte lipotoxicity and injury, and promotes the development of fibrotic nonalcoholic steatohepatitis.

PF30-2 10042

Nintedanib Alleviates Metabolic Dysfunction-associated Steatohepatitis by Suppressing THBS1 Expression in Activated Fibroblasts

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Background and Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a global health burden, with activated fibroblasts playing a key role in its progression. Nintedanib, a tyrosine kinase inhibitor approved for idiopathic pulmonary fibrosis (IPF), has shown antifibrotic potential. This study aimed to investigate the therapeutic effects of nintedanib in MASLD by targeting activated hepatic fibroblasts.
Methods: Fibroblasts were isolated from MASLD patient liver tissues and treated with nintedanib or sorafenib. For in vivo analysis, fibrosis models were established using both a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) and a methionine- and choline-deficient diet with ethionine (MCDE). THBS1 inhibitor treatment was evaluated in the CDAHFD model. Protein expression was analyzed by Western blot, and transcriptional changes were assessed using bulk and single-cell RNA sequencing.
Results: THBS1 was upregulated in MASLD liver tissues. Nintedanib reduced fibroblast viability and decreased phosphorylation of AKT and ERK. In LX2 cells, nintedanib suppressed fibrosis-related genes, including TGFBI, FN1, Col1a1, and THBS1. In both CDAHFD and MCDE models, nintedanib eliminated FAP+PD-L1+ fibroblasts and reduced THBS1 expression. In the CDAHFD model, THBS1 inhibition led to suppression of fibrotic markers and a decrease in FAP+PD-L1+ fibroblast populations. THBS1 knockdown in LX2 cells also decreased FAP, a-SMA, and FN1, with minimal effect on phosphorylated signaling proteins.
Conclusions: Nintedanib and THBS1 inhibition effectively target activated fibroblasts and attenuate fibrosis in MASLD. These findings support nintedanib as a potential antifibrotic therapy in MASLD.

Poster Session 30

PF30-3 10100

Mitochondrial ROS Accumulation as a Key Pathogenic Driver in MASLD: Impact of Disrupted Mitochondrial Protein Processing of Antioxidant Enzymes

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by lipid accumulation, inflammation, and oxidative damage. A key pathological feature is mitochondrial reactive oxygen species (ROS) accumulation, which contributes to hepatocellular injury and fibrosis. In this study, we investigated the upstream mechanisms responsible for mitochondrial ROS increase in MASLD. Our findings highlight the role of disrupted mitochondrial protein processing, which impairs the maturation and activity of antioxidant enzymes. Among these, Peroxiredoxin V (Prx V), a mitochondria-localized thiol peroxidase, was notably affected. Using a methionine-choline-deficient (MCD) diet-induced MASLD mouse model, we observed that defective mitochondrial import and processing of antioxidant enzymes led to significant ROS accumulation and hepatic damage. In Prx V knockout (KO) mice, these effects were further exacerbated, with increased lipid deposition, inflammatory gene expression, and histological evidence of fibrosis compared to wild-type controls. The data suggest that the mitochondrial protein quality control system is impaired in MASLD, reducing the availability of functional antioxidant enzymes and enhancing susceptibility to oxidative stress. The vulnerability of Prx V to processing defects underscores its central role in maintaining mitochondrial redox homeostasis. These results identify mitochondrial protein processing dysfunction as a critical upstream event driving ROS-mediated liver pathology in MASLD and support the therapeutic relevance of preserving antioxidant capacity through mitochondrial protein regulation.

PF30-4 10106

Intestinal Epithelial Peroxisome Proliferator-activated Receptor γ Deficiency Deteriorates Insulin Resistance in Mice with Metabolic Dysfunction-associated Steatohepatitis

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Background: Peroxisome proliferator-activated receptor gamma (PPARγ) is highly expressed in the intestinal epithelium and has been shown to protect against intestinal inflammation in experimental colitis. Intestinal inflammation and bacterial translocation (BT) are known to contribute to the progression of metabolic dysfunction-associated steatohepatitis (MASH). We aimed to investigate the role of intestinal PPARγ in mice with MASH.
Methods: Mice with intestinal epithelial cell-specific PPARγ deficiency were generated using a villin-Cre transgene and floxed *Pparg* allele, designated $Pparg^{\delta IEC}$. Littermate mice carrying only the floxed *Pparg* allele without the Cre transgene, designated $Pparg^{fl/fl}$, served as controls. MASH was induced by feeding a fast food diet (FFD) for 24 weeks.
Results: Mice fed with FFD displayed characteristics of MASH, including obesity, insulin resistance, liver steatosis, inflammation and fibrosis. Although $Pparg^{\delta IEC}$ and $Pparg^{fl/fl}$ mice showed similar weight gain and severity of liver injury on FFD, $Pparg^{\delta IEC}$mice exhibited more severe insulin resistance. Intestinal epithelial PPARγ deficiency exacerbated intestinal inflammation with increased expression of proinflammatory cytokines. Additionally, $Pparg^{\delta IEC}$ mice displayed increased gut permeability and elevated serum lipopolysaccharide levels compared to controls. Downregulation of intestinal tight junction proteins with upregulation of inducible nitric oxide synthase and long myosin light chain kinase were observed in $Pparg^{\delta IEC}$ mice. Aggravated endotoxemia in $Pparg^{\delta IEC}$ mice led to increased adipose tissue inflammation and decreased phosphorylation of Akt and IRS-1 in skeletal muscle.
Conclusion: Intestinal PPARγ deficiency promoted intestinal inflammation, increased gut permeability and worsen insulin resistance in FFD-fed mice. Targeting intestinal inflammation may offer a therapeutic approach to metabolic dysfunction in MASH.

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PF30-5 10115

Maintenance of Mitochondria-driven Oxysterol Metabolism is a Key to Early MASLD Prevention

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Background: Hepatic insulin resistance (IR) in steatosis has been shown to cause CYP7B1 suppression with subsequent (25R)26-hydroxycholesterol (26HC) accumulation, leading to hepatocyte toxicity followed by subsequent inflammation. To provide a new model explaining how the dysregulation in hepatocellular oxysterols drives MASLD, hepatic oxysterol regulation in Cyp7b1 knockout (Cyp7b1-/-) and Cyp7b1 transgenic (CYP7B1hep.tg) overexpressing mice were studied.
Methods: Male Cyp7b1-/- or CYP7B1hep.tg mice were fed ad lib. either normal diet (ND), western diet (WD), or high cholesterol diet (HCD). Age/sex/body weight-matched wild type (WT) mice were used for control. Serum/liver biomarkers, lipids, oxysterols, bile acids, and gene expression were comprehensively analyzed.
Results: WD and HCD feedings in Cyp7b1-/- mice led to significant hepatic cholesterol accumulations, but only WD-fed mice demonstrated evidence of liver toxicity (i.e., serum ALT elevation). The calculated HOMA-IR demonstrated IR in WD-fed mice but not in HCD-fed mice. In WD-fed Cyp7b1-/- mouse livers, 26HC levels were found markedly elevated with suppression of insulin responsive Sult2b1. Meanwhile, 26HC levels in HCD-fed mice were unelevated, indicative of diminished cholesterol transport to mitochondria. Meanwhile, WD-fed CYP7B1hep.tg mice developed no significant hepatotoxicity as evidenced by liver histology and serum biomarker analyses. Hepatic 26HC levels were maintained at WT levels. Comparative oxysterol/RNA-sequence analyses revealed that WD-fed CYP7B1hep.tg mouse livers had a diminished 26HC translocation into hepatocyte nucleus, thereby attenuating LXR/PPAR-mediated fatty acid uptake lipogenesis, oxidation and consequent oxidative stress.
Conclusion: Enhanced oxysterol metabolism by maintaining Cyp7b1 and Sult2b1 can reduce 26HC-driven liver toxicity in steatosis, which are possible mechanistic targets for MASLD intervention.

Poster Session 31

PF31-1 10113

Evaluation of Non-Invasive Fibrosis Markers in HBV-Infected Pregnant Women from the Kyrgyz Republic

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Background: Chronic hepatitis B virus (HBV) infection remains highly prevalent in pregnant women in the Kyrgyz Republic. Despite the known risks of HBV-related complications during pregnancy, limited data exist on the frequency and progression of liver fibrosis in this population. This study aimed to evaluate non-invasive fibrosis markers and their association with HBV phases and hematological indices.
Methods: We conducted a retrospective cohort study of 354 pregnant women with confirmed HBV infection, observed in multiple regions of the Kyrgyz Republic from 2019 to 2024. Data were extracted from clinical records, including hematological and liver function tests. Non-invasive indices such as *APRI*, *RDW*, and *ALBI* were used to assess fibrosis risk. Patients were stratified by HBeAg status and HBV phase. Statistical analysis was performed using R Studio to compare fibrosis indices across subgroups and assess postpartum changes.
Results: Among the women studied, 83.5% were HBeAg-negative with chronic HBV infection, and 11.7% had HBeAg-negative chronic hepatitis. Higher *APRI* and *ALBI* scores were observed in patients with elevated *RDW* (above 14.5), especially in HBeAg-positive cases. Viral load was significantly higher in women with *APRI* of 0.5 or less. Postpartum follow-up showed an increase in *APRI* above 0.5 in 25% of HBeAg-positive and 19.7% of HBeAg-negative women with elevated *RDW*.
Conclusion: Non-invasive markers, particularly *APRI* and *ALBI* combined with *RDW*, may help identify pregnant women at risk for fibrosis progression. The postpartum rise in *APRI* suggests the need for continued monitoring.

PF31-2 10039

Wilson’s Disease in Adults in Vietnam from 2012-2022

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Introduction: The aim of this study was compare the clinical and laboratory features of Wilson's disease (WD) in adults at two major hospital in Vietnam (Bach Mai and Cho Ray Hospital).
Subject & Method: The patients with WD were diagnosed basing on standards of Ferenci criteria at Bach Mai Hospital (2012 to 2015, n = 60) and Cho Ray Hospital (2015 to 2020, n = 66).
Results: In Bach Mai hospital (n =50): Average age: 16.3 (3-53). Male/female = 1.2. The most common clinical symptoms were jaundice (51.7%), splenomegaly (18.3%), ascites 9/60 (15.5%). The neurological symptoms were: Hypertonia 68.3%, dysarthria: 61.7%, dysphagia 58.3%, sloppy handwriting: 56.7%, hand tremor: 40.0%. Three main features of WD were KF ring: 53.3%, low serum ceruloplasmin concentration: 100%, high 24-hour urine copper level: 100%. The ATP7B gene mutation detection rate is 44/60 (73%). There are 7 new mutations. In Cho Ray Hospital (n =66): Average age: 25.1. Female/male 1.6. The most common clinical symptoms were jaundice 53.0%, splenomegaly 45.5%, ascites 37.1%. The neurological symptoms were sloppy handwriting 43.9%, hand tremor 33.3%, dysarthria 28.8%. Hemolytic anemia, menstrual disorder, arthritis accounted for 35.7%, 35.5%, 25.7%, respectively. Three main features of WD were KF ring 78.8%, low serum ceruloplasmin concentration 92.4%, high 24-hour urine copper level 93.9%. The ATP7B gene mutation detection rate is 97%. There are 3 new mutations.
Conclusion: Neurological symptoms are more common in young patients (Bach Mai hospital). Hepatobiliary symptoms are more common in elderly patients (Cho Ray Hospital).

Poster Session 31

PF31-3 10031

Sanger Sequencing in the Diagnosis of Rare Liver Diseases in Southern Vietnam

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Background: Rare liver diseases, including inherited metabolic disorders, are often underdiagnosed due to nonspecific clinical manifestations and the lack of specific diagnostic tools. In Southern Vietnam, the application of advanced genetic technologies in clinical practice remains limited. Sanger sequencing, known for its high accuracy and ability to detect single-gene mutations, offers new prospects for identifying the genetic causes of rare liver diseases.
Objective: We report four cases of rare inherited liver diseases diagnosed by Sanger sequencing at Tam Anh General Hospital, Ho Chi Minh city.
Methods: This case series reports on patients presenting with chronic liver dysfunction of unclear etiology who underwent targeted Sanger sequencing. Genes analyzed included ATP7B (Wilson disease), HFE (hemochromatosis), and SLCO1B1/SLCO1B3 (Rotor syndrome), and ABCC2 (Dubin-Johnson syndrome)
Results: One female patient was diagnosed with Wilson disease based on a pathogenic homozygous mutation in ATP7B. Two middle-aged men with elevated serum ferritin and liver fibrosis was confirmed to have hereditary hemochromatosis with a compound heterozygous mutation in HFE. One young man patients with isolated conjugated hyperbilirubinemia were found to have biallelic mutations in SLCO1B1 (Rotor syndrome), respectively. In all cases, genetic confirmation facilitated specific therapeutic decisions and family screening.
Conclusion: Sanger sequencing is a feasible and effective diagnostic tool in the clinical setting of Southern Vietnam. Its application significantly improves diagnostic accuracy for rare liver diseases and supports individualized treatment strategies, genetic counseling, and preventive care for future generations.
Key words: Sanger sequencing, inherited liver disease.

PF31-4 10074

A Case of PFIC Type7, Demonstrating the Utility of Whole Exome Sequencing

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Background: PFIC is an autosomal occult genetic disorder, and low γ-GTP levels in spite of cholestatic liver damage should be used to differentiate this disease. Genetic testing is considered useful for diagnosis, but there are cases in which the diagnosis is difficult, despite a typical clinical presentation.
Case. A: 6-month-old girl. Born to Indian parents. She was transferred to our hospital for a thorough examination of her cholestatic liver disorder and hypocalcemia following the onset of afebrile convulsions.
Physical Examination: ocular conjunctival yellowing, liver palpated 2 lateral finger palpations, spleen palpated 1 lateral finger palpation. Blood tests showed biliary stasis with AST 183 U/L, ALT 96 U/L, TB 6.8 mg/dL, DB 5.1 mg/dL, γ-GTP 68 U/L and TBA 177.7 μmol/L. Liver biopsy showed decreased interlobular bile ducts, enhanced expression of CK7 in hepatocytes and bile duct epithelialization. Gene panel analysis showed no significant genetic mutations, but the clinical course and laboratory findings did not exclude a new PFIC, and whole exome analysis showed a homozygous variant in ubiquitin-specific protease 53 (USP53) in the affected child.
Discussion/Conclusion: Although USP53 is now established as an associated gene for PFIC type 7, it was difficult to detect by gene panel testing in this case. On the other hand, PFIC was considered based on the pathological and clinical picture and was diagnosed by whole exome analysis. Comprehensive genetic analysis for cholestatic disease is useful for diagnosis, but it is important to provide detailed clinical information in collaboration with the research and analysis system.

Poster Session 31
PF31-5　10152

Frailty is an Independent Predictor of Mortality in Patients with Chronic Liver Disease: A Multicenter Retrospective Cohort Study

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Background: Frailty is emerging as a prognostic factor in chronic liver disease (CLD). However, its clinical impact remains underexplored, particularly in Japan. This study aimed to evaluate the prognostic significance of frailty in Japanese patients with CLD. In addition, the prevalence and clinical characteristics of frailty in this population were assessed.
Methods: This multicenter retrospective study included patients with CLD who were admitted to three institutions in Japan. Frailty was diagnosed based on a Clinical Frailty Scale score of > 4. Factors associated with prognosis and frailty were evaluated using Cox proportional hazards regression and logistic regression models, respectively.
Results: Of 715 patients (median [interquartile range] age, 67 [56-74] years; 354 [49.5%] of male; 227 [38.7%] with viral hepatitis), frailty was identified in 137 (19.2%). During the median follow-up of 2.9 years, 221 patients (28%) died. Patients with frailty had significantly shorter survival than those without frailty (median 2.4 vs. 10.6 years, $p < 0.001$). Multivariable Cox regression analysis showed that frailty was an independent adverse factor for mortality (hazard ratio 1.75; 95% confidence interval, 1.25-2.45, $p = 0.001$) in patients with CLD. Regarding determinants of frailty, multivariable logistic regression analysis showed that older age, hepatic encephalopathy, hypoalbuminemia, thrombocytopenia, and prolonged international normalized ratio were associated with frailty.
Conclusions: Frailty is prevalent in patients with CLD and independently predicts poor survival. Given its prognostic significance, frailty assessment should be incorporated for risk stratification, early intervention, and outcome improvement in patients with CLD.

Poster Session 32

PF32-1 10048

Evaluation of the Efficacy of Lusutrombopag in Chronic Liver Disease: Impact of Liver Disease Etiology and Pretreatment Platelet Count

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Background: Lusutrombopag, an oral thrombopoietin receptor agonist, is used to manage thrombocytopenia in patients with chronic liver disease undergoing invasive procedures. This study aimed to investigate how the cause of liver disease influences the hematologic response to lusutrombopag.

Methods: A multicenter retrospective study was conducted across nine hospitals, enrolling patients treated with lusutrombopag between December 2015 and December 2023. Efficacy was evaluated based on the proportion of patients achieving a platelet count ≥50,000/μL and the degree of platelet count increase, with subgroup analysis according to liver disease etiology and baseline platelet counts.

Results: Seventy patients were included in the analysis. Patients with viral cirrhosis exhibited a significantly greater increase in platelet count compared to those with non-viral etiologies (29,100/μL vs. 19,200/μL, P=0.012). While patients with a pretreatment platelet count of 40,000–50,000/μL had a higher success rate in reaching ≥50,000/μL than those with <40,000/μL (84.2% vs. 62.5%, P=0.038), the absolute increase in platelet count was comparable between the two groups (25,700/μL vs. 24,400/μL, P=0.972). Among patients receiving repeated treatment, the second course showed a reduced platelet response compared to the first (26,900/μL vs. 20,800/μL, P=0.041). Thrombosis occurred in 2.9% of patients as the main adverse event.

Conclusion: The efficacy of lusutrombopag is influenced not only by baseline platelet count but also by the underlying liver disease etiology. These findings highlight the importance of considering liver disease etiology, in addition to platelet count, when selecting and optimizing thrombocytopenia management strategies in chronic liver disease.

PF32-2 10136

Integrated Surgical Approach for Hepatic Cystic Echinococcosis: Experience from the Syzganov National Scientific Center of Surgery

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Background: Kazakhstan remains a highly endemic region for hepatic cystic echinococcosis (CE). Minimally invasive techniques combined with antiparasitic therapy are increasingly replacing open surgery as the treatment of choice.

Purpose: To assess the effectiveness and safety of an integrated surgical approach in the treatment of hepatic CE.

Methods: A retrospective analysis of 634 patients treated between January 2017 and June 2025 at the Syzganov National Scientific Center of Surgery was performed. Cysts were staged according to the WHO-IWGE classification (2003). Albendazole monotherapy was used in 32 patients with CE1/CE3a cysts less 5 cm. In patients with cysts diameter more 5 cm underwent laparoscopic pericystectomy (n=53), open surgery (n=390), or PAIR (n=159).).

Results: Albendazole monotherapy achieved 88.5% effectiveness. The PAIR group had the shortest operative time (mean 55.4 min) and no intraoperative blood loss, compared to laparotomy and laparoscopy (225.2 and 215.3 min, respectively). Hospital stay was significantly shorter in the PAIR group (3.8 days) than in laparotomy (7.5 days) or laparoscopy (6.4 days) (p=0.0001). Mean follow-up was 39.8 months. Recurrence rates were similar across groups (3.6% in laparotomy vs. 5.1% in PAIR).

Conclusion: Albendazole is effective for CE1/CE3a cysts less 5 cm. For cysts from 5 to 10 cm, PAIR with neoadjuvant therapy offers a safe and efficient alternative to surgery, with shorter recovery and comparable recurrence rates. Laparoscopic pericystectomy remains a valid option in selected patients.

Poster Session 32
PF32-3 10220

Integrated Liver Care in Indonesia: A Model Study of Collaboration in the Management of Chronic Liver Disease in Communities

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Background: The prevalence of chronic liver diseases such as MASLD, hepatitis B/C, and cirrhosis is increasing in Indonesia, in line with sedentary lifestyles and high rates of metabolic syndrome. Successful management of these diseases requires ongoing interventions that prioritize patient education, medication adherence, and lifestyle changes. At the community level, the involvement of nurses and pharmacists is key in a promotive-preventive and rehabilitative approach. This study aims to examine and assess the effectiveness of a community-based collaborative nursing and pharmacy model in improving clinical outcomes and behavior of chronic liver disease patients in Indonesia.
Method: A systematic review of 18 national and regional quantitative studies (2018-2024). Evaluation parameters included changes in ALT/AST levels, medication adherence, weight control, and patient participation in educational programs.
Results: The Prolanis BPJS Health study in several provinces showed an increase in service visit adherence to 76% and an average weight loss of 1.4 kg in patients with liver comorbidities. Educational interventions by community pharmacists in Surabaya for hepatitis C patients increased medication adherence from 52% to 81% over six months. In Makassar, nurses' roles as patient companions for cirrhosis patients through home visits reduced hospitalization frequency by 40% compared to the control group (p=0.05).
Conclusion: The integrated liver care model based on collaboration between nurses and pharmacists has proven effective in Indonesia. Systematic implementation in primary care and community settings has the potential to reduce the burden of chronic liver disease and improve patients' quality of life sustainably.

PF32-4 10201

Impact of Partial Splenic Embolization on Pancreatic Congestion with Portal Hypertension

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Aim: Pancreatic congestion in patients with portal hypertension (PH) has been reported. We aimed to investigate the impact of partial splenic embolization (PSE) on pancreatic congestion and glucose tolerance in patients with PH.
Methods: This retrospective study evaluated 125 patients with PH who underwent PSE to control PH. The pancreas volume index (PVI), the ratio of pancreas volume to body weight, was measured before and 3 months after PSE. Glucose tolerance was categorized as follows: normal type, fasting plasma glucose (FPG)< 110 mg/dL; impaired fasting glucose (IFG), FPG between 110-125 mg/dL; and diabetes mellitus (DM) type, either DM under treatment or FPG 126 mg/dL or more.
Results: Fouty two patients were identified as having the DM type, 35 with IFG, and 48 with the normal type. PVI exhibited a significant reduction compared with baseline (p<0.001). When defining the improvement group in pancreatic congestion as those with a PVI reduction rate of 4.62% or higher, this group demonstrated significantly higher baseline PVI and FPG than the non-improvement group (p<0.001 and p=0.005, respectively). In a multivariate analysis of factors associated with improvement, a PVI 0.061 or more and DM type were independent factors (odds ratio [OR] 8.36, p<0.001; OR 2.42, p=0.039, respectively). An improvement in DM was defined as a 10% reduction in FPG or a 0.2% reduction in HbA1c levels. In multivariate analysis, DM type was an independent factor related to DM improvement (OR 2.81, p=0.013).
Conclusion: PSE effectively reduced the volume of an enlarged pancreas and enhanced glucose control.

Poster Session 32
PF32-5 10033

Evaluation of Chemotherapy-associated Fatty Liver Disease in Epithelial Ovarian Cancer: The Clinical Significance

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Introduction: Epithelial ovarian cancer (EOC) is one of the most lethal gynecologic malignancies. A body of evidence indicates the plausibility of drug-induced liver injury, a common cause of mortality in cancer patients. Therefore, in this study, we evaluated whether chemotherapy for epithelial ovarian cancer (EOC) is associated with the risk of developing fatty liver disease (FLD).
Method: A prospective study was conducted on EOC patients for the development of FLD following chemotherapy.
Result: The patient's age ranged from 17 to 72 years. Of 154 cases, 28 developed FLD, while it was absent in 126 cases. The mean age of these two groups was 48.8 and 49, respectively. The cases that developed fatty liver were aged 36-72 years. We correlated fatty liver with different clinical parameters, which included age, CA125, HE4, CEA, CA19-9, age at menopause, first childbirth, last childbirth, menarche, tumor size (cm), weight, height, GFR, BSA, and TFI (months). Most of them did not show any significant correlation except weight ($p=0.006$), neuropathy ($p=0.001$), mucositis ($p=0.003$), and diarrhea ($p=0.001$). Parameters including TFI and p53 expression were found to be nearly significant ($p=0.08$ for each).
Conclusion: While managing EOC, the impending complications should be considered. The significant risk factors for developing FLD are higher weight and therapy-related complications like diarrhea, mucositis, and neuropathy, including p53 expression and treatment-free survival. In order to improve overall survival, preventive interventions should be implemented based on the risk factors listed above.
Keywords: Fatty liver disease, epithelial ovarian cancer, chemotherapy, weight

Poster Session 33

PF33-1 10035

Comparison of Noninvasive Test for Histological Cirrhosis in Primary Biliary Cholangitis

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Background: Primary biliary cholangitis (PBC) is an autoimmune cholestatic liver disease. Liver cirrhosis diagnosed by biopsy is a robust predictor of poor prognosis, but it needs invasive procedure. We analyzed the association between the noninvasive tests and histological cirrhosis in patients with PBC.
Methods: In this retrospective study, we included PBC patients who underwent liver biopsy. Cirrhosis was diagnosed by histological findings. ALBI score, FIB-4 index, FIB-3 index, AST to platelet ratio index, the AST/ALT ratio, and pretreatment GLOBE score were analyzed as noninvasive test for liver cirrhosis. The pretreatment GLOBE score was calculated using baseline values of age, bilirubin, alkaline phosphatase (ALP), albumin, and platelet count.
Results: A total of 183 PBC patients were analyzed. The median age was 58 years, and 19% were male. The numbers of patients with Scheuer stage 1, 2, 3, and 4 were 76, 47, 21, and 39, respectively. The pretreatment GLOBE score significantly increased according to histological stage: stage 1, 0.25; stage 2, 0.53; stage 3, 0.68; and stage 4, 2.11 ($P<0.001$). The area under the receiver operating characteristic curve of the pretreatment GLOBE score, the ALBI score, FIB-4 index, FIB-3 index, AST to platelet ratio index, and the AST/ALT ratio were 0.872, 0.844, 0.828, 0.798, 0.776, and 0.744, respectively. The optimal cutoff value of the pretreatment GLOBE score for predicting histological cirrhosis was 1.27 (AUROC: 0.868; sensitivity: 0.84; specificity: 0.84).
Conclusion: The pretreatment GLOBE score may be a useful noninvasive test for predicting liver cirrhosis in PBC patients.

PF33-2 10226

Body Mass Index as a Predictor of Liver Fibrosis and Steatosis Grades in Patients with Chronic Liver Disease

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Background: Non-invasive assessment of chronic liver disease severity is essential in modern clinical practice, particularly for evaluating the risk of fibrosis and hepatic steatosis progression. Body Mass Index (BMI) is a simple anthropometric parameter, yet its role as an independent predictor of liver damage requires further scientific validation.
Methods: This cross-sectional study involved patients with chronic liver disease in Makassar. Variables included age, sex, BMI, fibrosis grade based on Liver Stiffness Measurement (LSM, grades 0-4), and steatosis grade based on Controlled Attenuation Parameter (CAP, grades 0-3). Statistical analyses were conducted using Kruskal-Wallis, Spearman correlation, and multivariate ordinal logistic regression to evaluate the association between BMI and liver fibrosis and steatosis, adjusted for age and sex.
Results: Among 394 subjects (63.7% male), the mean age was 47 years and the mean BMI was 23.79 kg/m^2, with various liver disease etiologies. A significant association was found between higher BMI categories and increasing fibrosis ($p<0.001$) and steatosis grades ($p<0.001$). In multivariate models, BMI independently predicted fibrosis (OR = 2.03; 95% CI: 1.65-2.50) and steatosis (OR = 1.94; 95% CI: 1.55-2.41). Age was also significantly associated with fibrosis (OR = 1.02; 95% CI: 1.01-1.04), while sex showed no significant association with either parameter.
Conclusion: BMI serves as an independent clinical predictor for both hepatic fibrosis and steatosis, and may be useful in non-invasive monitoring and risk stratification in chronic liver disease management.

Poster Session 33
PF33-3 10193

Dengue-Induced Coagulopathy Presenting with Hemorrhagic and Ischemic Stroke: A Rare but Life-Threatening Complication

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Background: Dengue fever is a common mosquito-borne viral disease in tropical regions such as Indonesia. While typically self-limiting, severe forms may present with life-threatening complications due to coagulopathy. Neurological manifestations, including stroke, are extremely rare and may result from both hemorrhagic and thrombotic mechanisms.
Case Presentation: A 51-year-old male presented with fever, headache, and cough for 3 days. Laboratory results confirmed dengue infection (positive NS1 antigen), leukopenia, and thrombocytopenia. No neurological deficits were observed at admission. On the second day of hospitalization, the patient developed right-sided hemiparesis and dysarthria. Neurological examination revealed right upper motor neuron facial palsy. MRI of the brain showed hyperacute bilateral cerebellar hemorrhages and a subacute infarct in the left thalamus. Laboratory tests showed elevated D-dimer, prolonged aPTT, and persistent thrombocytopenia. The patient received intravenous mannitol, platelet apheresis, fresh frozen plasma, and empiric antibiotics. Antiplatelet therapy was initiated after platelet count exceeded 100,000. Neurological symptoms gradually improved, and the patient was discharged in stable condition after 15 days with ongoing rehabilitation.
Discussion: Dengue-associated stroke is an uncommon but severe complication. The pathophysiology includes systemic inflammation, endothelial dysfunction, thrombocytopenia, and coagulopathy. In this case, the coexistence of hemorrhagic and ischemic stroke suggests a complex interplay of prothrombotic and bleeding tendencies. Early recognition and multidisciplinary management were critical for favorable outcomes.
Conclusion: Although rare, stroke should be considered in dengue patients with new neurological symptoms. Prompt imaging, supportive care, and a multidisciplinary approach are essential to reduce morbidity and prevent long-term disability.
Keywords: Dengue, Coagulopathy, Stroke, Hemorrhagic

PF33-4 10135

Endoscopic Ultrasound (EUS)-guided Portal Pressure Gradient Measurement Assessment of Acute Hemodynamic Response to Intravenous Propranolol

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Background: Hepatic venous pressure gradient (HVPG) is the gold-standard method to diagnose and quantify portal hypertension and the hemodynamic response to drug therapy. Acute hemodynamic response to intravenous propranolol assessed with HVPG predicts adverse liver-related events. Non-invasive tests (NITs) are used in daily clinical practice to stratify the risk of clinical significant portal hypertension. Nevertheles, NITs are not recommended in assessing hemodynamic changes in portal hypertension. Endoscopic ultrasound (EUS)-guided portal pressure gradient (EUS-PPG) measurement has been accurated compared to HVPG and can directly obtain the real portal vein pressure.
Methods: We report our experience in assessing the acute hemodynamic response to intravenous propranolol with EUS-PPG measurement in a case series of four patients. The procedure was performed as previously reported, with a 25-gauge dedicated needle with prophylactic antibiotherapy and deep sedation. Following baseline EUS-PPGm, 0.15 mg/kg of body weight, propranolol was administered intravenously by a continuous infusion in 10 minutes. The second EUS-PPGm was repeated 15 minutes later.
Results. There was observed a significant reduction of PPG in 2 patients treated with intravenous propranolol [10.5 mmHg to 4.75 mmHg (22%) and 10 mmHg to 2 mmHg (20%), respectively]. In the other two patients, the first EUS-PPG measurement was normal. So, a second EUS-PPG measurement was not performed avoiding unnecessary chronic use of beta-blockers. No adverse events were observed.
Conclusion: EUS-PPG measurement was safe in this case series and can assess acute hemodynamic changes after intravenous administration of propranolol.

Poster Session 33
PF33-5 10132

The Role of Serum Kallistatin Level in Comparison to Other Non-Invasive Panels for Evaluating Portal Hypertension in Egyptian Cirrhotic Patients

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Background: Esophageal Varices are considered an important complication of portal hypertension so the Baveno VI consensus recommend the use of non- invasive tests to stratify patients and role out highrisk esophageal varices (HREV) in whom endoscopic evaluation is needed.
Aim: To investigatethe role of serum Kallistatin level and other different panels for evaluating portal hypertension in Egyptian patients with liver cirrhosis.
Methods: This prospective study evaluated a total number of 90 Cirrhotic Patients admitted to Hepatology and Gastroenterology department & Endoscopy Unit at National Liver Institute, Menoufia University by measuring serum Kallistatin level and compare it to other different panels to evaluate Portal Hypertension by grading esophageal varices in correlation to GI endoscopy findings.
Results: A total 90 patient were enrolled with mean of age of 59.8 (9.8) years, 57.8% were male and 42.2% were female. The mean level of serum kallistatin was significantly lower in patients with varices. It also shows a significant decline in patients with large varices. Kallistatin can predict the presence of EV at cut off values of 23.1, with sensitivity and specificity of 76.5% and 98.6%, respectively.
Conclusion: Serum kallistatin is a promising marker along with other non-invasive panels can be used to predict the presence of esophageal varices especially when they are large and risky. Endoscopy is still the gold standard for the diagnosis of esophageal varices in cirrhotic patients, but the use of the non-invasive predictors, especially Kallistatin will help physicians to restrict endoscopy to those patients who are highly suspected of having esophageal varices.

Poster Session 34

PF34-1 10094

Prognostic Value of Circulating cfDNA in Patients with Unresectable HCC Receiving Atezolizumab and Bevacizumab

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Background: Atezolizumab plus bevacizumab (Atezo/Bev) combination therapy has emerged as the standard first–line treatment for unresectable hepatocellular carcinoma (HCC), demonstrating promising survival benefits in clinical trials. However, real–world data suggest only a subset of patients derive sustained benefit. The identification of noninvasive prognostic biomarkers is crucial for optimizing treatment strategies in clinical practice.
Methods: This retrospective analysis included 55 patients with unresectable HCC who received Atezo/Bev therapy between October 2020 and August 2023. Plasma cell–free DNA (cfDNA) concentrations were measured from pre–treatment blood samples. Patients were stratified into high and low cfDNA groups based on the median value. Associations between cfDNA levels and clinical outcomes–including overall survival (OS), objective response rate (ORR), disease control rate (DCR), and duable response (DR)–were examined. DR was defined as a complete or partial response, or stable disease maintained for at least six months.
Results: Patients with high baseline cfDNA concentrations showed significantly shorter OS compared to those with low levels (median OS: 13.0 vs. 33.1 months; $p = 0.0015$). No significant differences were observed in ORR, DCR, or DR. Multivariate Cox regression analysis revealed that AFP > 100 ng/mL (HR = 2.15, 95% CI: 1.00–4.60, $p = 0.049$) and elevated cfDNA levels (HR = 3.26, 95% CI: 1.41–7.54, $p < 0.01$) were independently associated with poorer OS.
Conclusion: Baseline plasma cfDNA concentration may serve as a valuable, non–invasive biomarker to predict overall survival in patients with unresectable HCC undergoing Atezo/Bev treatment.

PF34-2 10195

A Rare Case of Hepatogastric Fistula Induced by Radiofrequency Ablation Combined with Atezolizumab plus Bevacizumab in the Treatment of Hepatocellular Carcinoma

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Hepatogastric fistula is a rare but serious complication in hepatocellular carcinoma (HCC) treatment. Atezolizumab plus bevacizumab (Atezo/Bev) and radiofrequency ablation (RFA) are both established modalities, and in the context of conversion therapy, their sequential use is sometimes employed. A 65-year-old male with BCLC stage B HCC (maximum tumor diameter 45 mm; 9 nodules) received Atezo/Bev as first-line therapy. After 11 cycles, most lesions had regressed, leaving a shrunken main tumor in the right lobe and two small residual tumors in the left lobe. The 12th cycle included bevacizumab administration, followed by RFA targeting both left lobe lesions. Combination therapy was resumed 11 days after RFA. No immediate complications were noted; however, contrast-enhanced CT after the 14th cycle revealed a fistula between the ablation site in segment 2 and the stomach. The patient remained asymptomatic, and endoscopy showed no perforation or abscess. A conservative approach was chosen, continuing atezolizumab monotherapy while withholding bevacizumab. To our knowledge, this is the first reported case of hepatogastric fistula induced by RFA in combination with bevacizumab. When performing RFA during Atezo/Bev therapy, especially for lesions close to the gastrointestinal tract, clinicians should be cautious of potential delayed fistula formation.

Poster Session 34

PF34-3 10110

High Proximity of Treg-CD4T Cell Interactions in Spatial Omics Analysis Regulating Cancer Progression in Patients with Hepatocellular Carcinoma

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Background: Tumor immune microenvironment influences clinical outcome, but spatial relationships between immune cells in hepatocellular carcinoma (HCC) are not elucidated.
Methods: Multiplex immunohistochemistry (OPAL™, CD3, CD4, CD8, Foxp3, CD68, CD163, CD11c, CD56, CD66b, CD20, CD11b, DAPI) was performed on 72 resected HCC tissues, and 4 areas of tumor/tumor border/non-tumor border/non-tumor were obtained with Mantra™. Immune cell phenotypes were analyzed by inForm™ and Interaction variable (Interact. Var.; the percentage of target immune cells with an intercellular distance of less than 25 μm) was evaluated by phenoptr™. In addition, RNA of the tumor/non-tumor areas was extracted from formalin-fixed paraffin-embedded samples and targeted RNA sequencing of 629 genes related to tumor immunity was analyzed by Miseq (Illumina).
Results: In the distribution of immune cells in the 4 areas, recurrence free survival (RFS) and overall survival (OS) were worse in cases with a high number of regulatory T cells (Treg: CD3+CD4+Foxp3+) in the tumor border/non-tumor border area($p<0.05$). In the proximity analysis between immune cells, RFS and OS were worse in cases with high Interact. Var. of Treg-CD4T cell (CD4T:CD3+CD4+) in the tumor border/non-tumor border area ($p<0.05$). Gene set enrichment analysis in RNA-NGS data showed that T cell receptor, EGFR and MAPK signaling and EMT pathway were enhanced in cases with high Interact. Var. of Treg-CD4T in the tumor border area.
Conclusion: Spatial omics and NGS analysis in HCC tissues revealed that patients with higher proximity of Treg-CD4T in the tumor border/non-tumor border area had poor clinical outcomes and increased expression of cancer progression genes.

PF34-4 10117

A Case of Immune-related Adverse Event Arthritis during Atezolizumab plus Bevacizumab Therapy for Hepatocellular Carcinoma

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Background: Immune checkpoint inhibitors (ICI) have improved outcomes in hepatocellular carcinoma (HCC). However, immune-related adverse events (irAE), including arthritis, may occur. Reports of irAE-associated arthritis remain limited, and its clinical features remain poorly understood. We present a case of irAE arthritis during atezolizumab plus bevacizumab (Atezo/Bev) therapy.
Case: An octogenarian man with steatotic liver disease and asthma managed with inhaled corticosteroids had a history of multiple HCC resections and radiologic interventions. Due to multifocal HCC recurrence, Atezo/Bev therapy was initiated. Three months later, he developed fever and malaise and was hospitalized. Infectious workup was negative. Laboratory tests showed low ACTH and cortisol levels, raising suspicion for relative adrenal insufficiency. Hydrocortisone (10 mg/day) was started, leading to temporarily resolution of fever. On day 7, fever with new-onset right shoulder pain. Imaging showed no structural abnormalities, but symptoms improved with increased hydrocortisone and NSAIDs. By day 14, hydrocortisone was discontinued. However, bilateral shoulder pain persisted. MRI of the left shoulder demonstrated high signal on fat-suppressed T2-weighted and low signal on T1-weighted images, findings consistent with inflammatory arthritis. He was diagnosed with Grade 2 irAE arthritis. Prednisolone was initiated on day 17, resulting in rapid symptom resolution. Prednisolone was tapered successfully without recurrence. Atezo/Bev therapy was resumed without further adverse events.
Conclusion: This case highlights that irAE arthritis can occur during Atezo/Bev therapy. Early recognition and steroid treatment can enable safe symptom control and continuation of ICI therapy. Clinicians should consider irAE arthritis in patients with new joint symptoms during immunotherapy.

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Pre-treatment GLIM-defined Malnutrition Predicts Poor Prognosis in Patients with Unresectable Hepatocellular Carcinoma Undergoing Systemic Therapy

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Background: The Global Leadership Initiative on Malnutrition (GLIM) criteria provide a standardized framework for diagnosing malnutrition. However, evidence regarding their application in patients with hepatocellular carcinoma (HCC) is limited. We aimed to evaluate the prevalence and prognostic impact of GLIM-defined malnutrition in patients with unresectable HCC undergoing systemic therapy.
Methods: We retrospectively included patients with HCC who initiated first-line systemic therapy at our institution between 2009 and 2024. Malnutrition was screened using the Malnutrition Universal Screening Tool and diagnosed according to the GLIM criteria. Overall survival (OS), progression-free survival (PFS), and post-progression survival (PPS) were analyzed using the log-rank test and Cox proportional hazards models.
Results: Of the 153 patients (median age, 73 years; 124 males [81%]), Child-Pugh class A/B were 142 and 11, and BCLC stages A/B/C were 10, 58, and 85 patients, respectively. Initial regimens were combination immunotherapy (n=39), lenvatinib (n=45), and sorafenib (n=69). Malnutrition was diagnosed in 30 patients (19.6%) and associated with higher Child-Pugh scores, elevated PIVKA-II, and more extrahepatic metastases. Median OS, PFS, and PPS were significantly shorter in patients with malnutrition than those without (9.0 vs. 22.5, 6.0 vs. 8.6, 3.5 vs. 7.3 months; all $p<0.05$). In multivariable analyses, GLIM-defined malnutrition independently predicted shorter OS (HR 2.00, 95% CI 1.16-3.46) and PPS (HR 1.72, 95% CI 1.01-2.92).
Conclusions: GLIM-defined malnutrition was prevalent and independently associated with poor prognosis in patients with HCC undergoing systemic therapy. Pre-treatment nutritional assessment using GLIM should be considered in clinical practice.