Emerging Topic Conference 2025

MASLD, MetALD and ALD: Challenges and Opportunities

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Poster #: 1

Abstract Title: Clinically Distinct Metabotypes of Pediatric Metabolic Dysfunction-Associated Steatotic Liver Disease: An Unsupervised Machine Learning Analysis of Children Enrolled in NASH CRN Studies

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Abstract Background:

Phenotypic heterogeneity among children with MASLD is poorly understood. This study aimed to identify metabolic phenotypes (metabotypes) among pediatric patients with MASLD based on clinical, histological, and high-resolution metabolomics data.

Methods:

We analyzed the clinical and untargeted metabolomics data of 517 children ages 5-18 years with biopsy-proven MASLD from three NASH Clinical Research Network (NASH CRN) studies. The following predictors informed an unsupervised machine learning algorithm (k-means clustering): age, BMI percentile, waist circumference (WC), systolic blood pressure (SBP), uric acid, alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting triglycerides, very low-density lipoprotein (VLDL), LDL, and homeostatic model of insulin resistance (HOMA-IR). Integrative network analysis of the metabolomics and clinical data was performed using xMWAS software (v.0.552) to examine metabolic features associated with each metabotype.

Results:

We identified three pediatric MASLD metabotypes: 1) Early-mild (49.7%, younger with lowest levels of lipids, liver enzymes, and insulin resistance), 2) Adipo-lipid-SBP (35.8%, highest BMI percentile, WC, lipids, and SBP), 3) Inflammatory-fibrotic (14.5%, highest levels of liver enzymes, and advanced fibrosis). Network analysis within the Inflammatory-fibrotic metabotype revealed a positive association between ALT and several glycerophospholipids (LysoPC(20:2), PE(32:0), CL(68:5)) as well as bile acid species (3-oxocholadienoic acid). The Adipo-lipid-SBP metabotype network demonstrated a positive association between fasting triglycerides and various glycerophospholipid species (PC(28:7), LysoPC(14:0)), while in the Early-mild metabotype network, age was negatively associated with monoacylglycerol and PC species.

Conclusion:

Our findings reveal significant heterogeneity among children with MASLD, identifying three clinically distinct metabotypes characterized by unique metabolic profiles and varying disease severity. These metabotypes could inform targeted interventions and management strategies, enhancing precision healthcare for children with MASLD. Further research is needed to validate our novel findings.

Research Type: Translational

Additional Authors:

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Poster #: 2

Abstract Title: Impact of Glucagon-like Peptide-1 Receptor Agonists on the Risk of Adverse Liver Outcomes among Patients with Alcohol-associated Liver Disease and Type 2 Diabetes.

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Abstract Background:

Pathways involved in glycemic control and aversion to drinking alcohol can be a common target for glucagon-like peptide-1 receptor agonists (GLP-1RA). Therefore, we sought to study the impact of GLP-1RA on adverse liver outcomes (ALO) among patients with alcohol-associated liver disease (ALD) and type 2 diabetes mellitus (T2DM).

Methods:

Patients with T2DM who were newly diagnosed with ALD between 2013 and 2020 were identified using the IBM-Marketscan database. Patients were categorized based on GLP-1RA exposure, treated as a time-varying factor. To account for confounders, Overlap Propensity Score Weighting (OPSW) was utilized. Poisson regression models were used to analyze the adjusted risk of ALO, a composite endpoint defined by the first occurrence of any hepatic decompensation (HD), portal hypertension (PH), hepatocellular carcinoma (HCC) or liver transplantation (LT) relative to GLP-1RA.

Results:

Among 14,730 patients, the majority was male (n= 9,752, 66.2%) with a median age of 57 (IQR 52-61) years; 2.2% (n=317) had GLP-1RA exposure. Overall, 32.0% (n=4,717) of patients experienced HD, 15.9% (n=2,345) had features of PH, 3.8% (n=563) developed HCC, and 2.5% (n=374) received a transplant. Patients taking GLP-1RA were less likely to experience HD (22.4% vs. 32.2%) and HCC (0.3% vs. 3.0%) compared with individuals not taking GLP-1RA (both $p<0.001$); there was no association of GLP-1RA with the incidence of PH and LT (both $p>0.05$). After OPSW matching, 46 patients taking GLP-1RA had ALO over 379 person-years, with an absolute incidence rate difference of -9.0% (95% CI -15.0% to -3.0%) and an adjusted incidence rate of 0.57 (95%CI 0.39-0.82; p=0.003) compared with non-GLP-1RA patients. In examining the composite ALO, patients exposed to GLP-1RA had lower HD with 33 events over 400 person-years and a lower adjusted incidence rate of 0.56 (95%CI 0.36-0.86; p=0.008) relative to non-GLP-1RA group (Figure).

Conclusion:

GLP-1RA can potentially mitigate the risk of adverse liver outcomes, particularly decompensation, among patients with alcohol-associated liver disease. Future trials are needed to further investigate the role of GLP-1RA among patients with liver disease.

Research Type: Clinical

Additional Authors:

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Poster #: 3

Abstract Title: Population Based Screening For Alcohol Associated Liver Disease Using the Electronic Health Record

Presenter Name: Allison Kwong, MD

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Affiliation / Institution: Stanford

Abstract Background:

A screening modality that identifies patients with alcohol-associated liver disease (ALD) prior to symptom onset could improve outcomes and prognosis. As part of a clinical trial in partnership with Ria Health (NCT05747703), we deployed an EHR-wide screening program based on elevated liver enzymes, with linkage to care via the Ria Treatment Platform — a telehealth approach for alcohol use disorder (AUD) that incorporates medical assessment, medications, education, and coaching. Here, we evaluate the demographic yield of patients responding to this population-based screening effort for ALD.

Methods

Patients were identified through the STAnford Research Repository (STARR), if they were ≥18 years old and had ALT, AST, or GGT greater than 45, 45, or 100 respectively within 90 days. Invitations were sent to potential participants via Epic MyHealth, explaining that their test results may be attributed to alcohol and providing a link to complete a screening questionnaire to enter a study to reduce alcohol use. Demographics and clinical data of respondents were extracted by chart review.

Results

In the first phase of the study, 17,739 invitations were sent, and identifiable data were available for 39 of 93 patients who completed screening, with mean age of 46 years (SD 16), 23% female; 33% AST >45 U/L, 67% ALT >45 U/L, 11% GGT >100 U/L; and AUDIT-C score 4 (IQR 3-7). The average BMI was 29.4 kg/m2 (SD 5.8); 33% had hypertension, 31% diabetes, and 82% hyperlipidemia; median FIB-4 0.83 (IQR 0.49-2.10). Eligible patients with AUDIT-C ≥3 (n=30) proceeded to structured MINI interview and TLFB; 83% met criteria for AUD (9% mild, 39% moderate, 35% severe), self-reporting a median 5 standard drinks per week (IQR 3-15) and PETH 41 ng/mL (IQR 14-160). Although steatosis was not confirmed by imaging, 89% would meet criteria for metALD based on reported amount of alcohol consumption (≤350 gm/week for women and ≤420 gm/week for men) rather than ALD.

Conclusion

The population-based screening strategy based on elevated liver enzymes detected 93 patients with a desire to reduce their alcohol use. The majority of those with AUDIT-C ≥3 would classify as metALD rather than ALD on further alcohol intake history. Quantification of alcohol use would help to clarify

thresholds for metALD vs ALD and enable treatment to be tailored appropriately. This is a promising strategy to detect early steatotic liver disease with linkage to timely and appropriate subspecialty care.

Additional Authors:

Kristina Folta, John Mendelson, Judith Prochaska, Kevin Hallgren, Weiyu Wu, Allison Kwong

Poster #: 4

Abstract Title: Novel Lipotoxicity Influenced Enhancer regulates increased S100A11 alarmin expression in Steatohepatitic Livers

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Abstract Background:

Metabolic dysfunction associated steatohepatitis (MASH) is a complex liver disease in which endoplasmic reticulum (ER) stress and the release of endogenous alarmins are key mediators. Studies indicate that epigenetic regulation governs individual susceptibility and risk of MASH progression. Yet the crosstalk between lipotoxic ER stress and epigenetic regulation is understudied.

Methods:

Extracellular vesicles (EVs) were isolated by differential ultracentrifugation from palmitate treated hepatocytes. Proteomics was performed by mass spectroscopy. Mice were fed Choline-deficient, Amino acid-defined high-fat diet (CDAHFD) to induce steatohepatitis and high Fat, Fructose, and Cholesterol (FFC) diet to induce MASH. Chromatin immunoprecipitation (ChIP), histone acetylation studies, and dCas9-KRAB mice were employed to determine the functional consequences of the Lipotoxicity Influenced Enhancer (LIE) domain.

Results:

Proteomics of hepatocyte-derived lipotoxic EVs identified S100A11 enrichment. Transcript level analyses of S100A11 demonstrated 3-fold enrichment in FFC-fed mouse livers and 2-fold increment in human MASH livers compared to respective controls. Functionalized Surface Plasmon Resonance chip based quantification of S100A11 on hepatocyte specific EVs (ASGR-2+ and CYP2E1+) demonstrated increased S100A11 signals in MASH patient plasma. Examination of the genomic location of S100A11 indicated clustering of several S100 family genes; however, only S100A11 was upregulated in lipotoxic conditions. Interrogation of publicly available human liver ChIP-Seq GEO datasets identified a putative H3K27acetylated region, upstream to the S100A11 promoter. ChIP-qPCR studies demonstrated a direct correlation between lipotoxic ER stress and H3K27acetylation of the putative domain, which we termed LIE. dCas9-KRAB mediated repression of LIE activation in Huh7 cells alleviated palmitate-induced S100A11 upregulation. Transient LIE repression in thapsigargin treated Huh7 cells showed no attenuation of S100A11 transcripts, demonstrating LIE specificity to lipotoxicity. Introduction of hepatotropic AAV8 encoding LIE-sgRNAs in dCas9-KRAB mice attenuated diet induced hepatic S100A11 upregulation in two steatohepatitis models; 3 weeks of CDAHFD and 6 weeks of FFC diet (recapitulates human MASH). We observed significant reduction of inflammatory foci in the LIE-sgRNA injected mice livers.

Conclusion:

Our studies define a novel LIE and demonstrate lipotoxicity dependent epigenetically upregulated hepatic-S100A11 signaling as a potential therapeutic target in MASH.

Research Type: Basic

Additional Authors:

Feda H Hamdan, Amy S. Mauer, Yasuhiko Nakao, Daheui Choi, Gyanendra Puri, Yeriel Yoon, Alexander Revzin, Harmeet Malhi*

Poster #: 5

Abstract Title: Fecal proteomics links neutrophil degranulation with mortality in patients with alcohol-associated hepatitis

Presenter Name: Henriette Kreimeyer, MD

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Abstract Background:

Patients with alcohol-associated hepatitis (AH) have a high mortality. Alcohol exacerbates liver damage by inducing gut dysbiosis, bacterial translocation and inflammation, which is characterized by increased numbers of circulating and hepatic neutrophils. We aimed to characterize the fecal proteome of patients with AH and to elucidate its clinical importance.

Methods:

We performed high-quantitative fidelity Tandem Mass Tag proteomics analysis using LC/MS to characterize the fecal proteome in patients with AH (InTeam cohort; n=80), alcohol use disorder (AUD, n=19), and controls (n=20). Overrepresentation Analysis using Reactome Pathway and Gene ontology were performed. A fecal biomarker and its prognostic effect were validated by ELISA in fecal samples from patients with AH, who were recruited in a second and independent multicenter cohort (AlcHepNet; n=70).

Results:

Fecal proteomic profiles showed distinct patterns between controls, patients with AUD and AH (Bray-Curtis: P=0.001). Overrepresentation Analysis demonstrated that 22.5 - 40% of all upregulated proteins belong to the neutrophil degranulation pathway across all three groups (Fig. 1A). The neutrophil degranulation pathway may also be associated with disease severity, as it was the most upregulated pathway in AH patients that died during follow-up (P=0.002). We then performed a focused analysis including proteins that showed significant differences between all three groups, between patients with AH and AUD patients and a progressive increase or decrease in accordance with disease severity. Twelve proteins, including myeloperoxidase (MPO), fulfilled these criteria. The majority of proteins showing a progressive increase in accordance with ALD severity are expressed in neutrophils, while proteins that are decreased are expressed in muscle. Fecal MPO, a protein which is released from azurophilic granules upon neutrophil activation, predicts 60-day survival in patients with AH (high MPO level HR: 2.84, logrank: P=0.035). These results were confirmed by fecal ELISA in a validation cohort of patients with AH (Fig. 1B, high MPO: HR: 2.86e+08, logrank: P=0.037). There is no correlation of fecal MPO with serum leukocytes or hepatic neutrophil infiltration (R=-0.023, P=0.85; R= 0.082, P=0.62).

Conclusion:

Proteins linked to neutrophil degranulation are more abundant in patients with AH compared to AUD and controls and are associated with disease severity. MPO can predict survival and can serve as a prognostic noninvasive marker. Proteins linked to neutrophil degranulation are more abundant in patients with AH compared to AUD and controls and are associated with disease severity. MPO can predict survival and can serve as a prognostic noninvasive marker.

Research Type: Translational

Additional Authors:

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Poster #: 7

Abstract Title: VALIDATION OF THE MASEF SCORE FOR ITS DIAGNOSTIC ENRICHMENT UTILITY FOR AT-RISK MASH IN THE NIMBLE PROJECT

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Abstract Background:

There is an unmet need for non-invasive tests (NITs) to identify those with metabolic dysfunction associated steatotic liver disease (MASLD) who are at risk of increased liver and all-cause mortality. This has been defined as metabolic dysfunction associated steatohepatitis (MASH) with NAFLD activity score (NAS) >= 4 and fibrosis stage >= 2 (at-risk MASH). The MASEF score is a multi-analyte (12 lipids, BMI, AST, ALT) proprietary test for this purpose. Aims: To independently evaluate the diagnostic performance of the MASEF score for at-risk MASH and its histological components.

Methods:

A retrospective evaluation of prospectively collected samples from a curated population from the NASH CRN with a relatively even distribution of fibrosis stages was performed. Blood samples were collected within 90 days of a liver biopsy in over 90% and within 180 days in all. Liver histology was scored by the CRN pathology committee using its validated protocol masked to clinical and laboratory data. Lipidomic analyses were performed by One-Way Lipidomics (OWL) and raw MASEF scores were provided. Data analysis was performed by NIMBLE investigators without involvement of OWL. Our goal was to define the AUROC, sensitivity and specificity for at-risk MASH and its components MASH, NAS >= 4, fibrosis stage >= 2, >= 3 and 4 (cirrhosis). The MASEF score was compared to ALT for the diagnosis of MASH and FIB-4 for fibrosis cutoffs noted above.

Results:

A total of 1073 individuals were studied (mean age 52.5 yrs, BMI 34.8 kg/m2, T2DM n=490, MASH n=835, NAS >=4 n=574, fibrosis stage >=2 n=737, >= stage 3 n=475 and cirrhosis n=198). The AUROC, sensitivity, specificity at Youden cut-point for at-risk MASH were 0.78 (p< 0.0001 vs AUROC 0.5), 72%, and 70%, respectively. At 90% sensitivity the specificity was 45%, while at 90% specificity, the sensitivity was 36%. The AUROC/sensitivity/specificity for activity markers were as follows: MASH (0.81/71%/78%, p< 0.0001), NAS >= 4 (0.77/81%/60%, p< 0.0001). The AUROC, sensitivity, specificity for fibrosis cutoffs were: stage >= 2 (0.77, 70%, 70%p< 0.0001), >= stage 3 (0.71, 80%, 53% p< 0.0001), cirrhosis (0.72, 70%. 66%, p< 0.001). MASEF score outperformed ALT for MASH and NAS >= 4 and FIB-4 for fibrosis stage >= 2 but not for advanced fibrosis or cirrhosis.

Conclusion:

The MASEF score enriches the probability of having 'at risk' MASH in a population with MASLD. Its performance is weighted toward stage 2 fibrosis rather than cirrhosis.

Research Type: Clinical

Additional Authors:

Gowthami Kanagalingam, MD; Sudha Shankar, MD; Katherine P. Yates, ScM; Roberto A. Calle, MD; Alex Pasek, MD; Clayton Dehn; Claude Sirlin, MD; Anthony Samir, MD MPH; Michael Middleton; Theodore T. Pierce; Kathryn Fowler; sarah sherlock; Tania N. Kamphaus, PhD; Mohammad S. Siddiqui, MD; Kris V. Kowdley, MD, FACP, FACG, AGAF, FAASLD; Anna Mae Diehl, MD; Bryce S. Hatfield; Rohit Loomba, MD, MHSc, FAASLD; Arun J. Sanyal, MD, FAASLD

Poster #: 10

Abstract Title: Absence of intestinal Mucin-2 Promotes Goblet Cell-associated Antigen Passages Formation to Prevent Ethanol-induced Steatohepatitis in mice.

Presenter Name: Maria Fernanda Raya Tonetti, PhD

Presenter Email: mrayatonetti@ucsd.edu

Affiliation / Institution: University of California San Diego

Abstract Background:

Goblet cells secrete mucins, cytokines, and antimicrobial peptides and participate in the education of the immune system through goblet cell-associated antigen passages (GAPs). The major mucin expressed in the intestine is Mucin-2 (Muc2). Chronic ethanol disrupts goblet cells function. Notably, Muc2 deficiency and small intestinal GAP formation protects against ethanol-induced liver disease. Our previous work showed that expression of glycoprotein 130 (gp130) receptor on intestinal epithelial cells mediates GAP formation via induction of the muscarinic acetylcholine receptor 4 (mAChR4) receptor on goblet cells promoting protection from ethanol-induced liver disease. The aim of our study was to determine the relative contributions of Muc2 and mAChR4 to GAP formation.

Methods:

Female mice with either selective deletion of mAChR4 on goblet cells (mAChR4ΔGC), Muc2 deficiency (Muc2-/-), Muc2 deficiency and gp130 deficiency in intestinal epithelial cells (Muc2-/-gp130ΔIEC) and wild-type littermates were subjected to the NIAAA model of ethanol feeding. Human SI organoids were used.

Results:

We confirmed that ethanol promotes the formation of a thicker mucus layer, and inhibits small intestinal GAP formation in mice and humans. Compared with wild-type mice, mAChR4ΔGC mice had fewer small intestinal GAPs, leading to an impaired small intestinal immune response, with reduced expression of CD11b and CD11c. They also showed reduced small intestinal antibacterial defense via Reg3g, leading to bacterial overgrowth and increased bacterial translocation to the liver. Thus, GAP inhibition exacerbated ethanol-induced steatohepatitis, evidenced by elevated plasma transaminase levels, increased steatosis, and more hepatic inflammation (Cxcl1 and Cxcl2), despite normal ethanol metabolism.Muc2-/-gp130ΔIEC lost the protective effect against ethanol-induced steatohepatitis observed in Muc2-/- mice. Notably, Muc2-/- mice presented increased small intestinal GAP formation compared with wild-type mice. However, GAP formation was inhibited in Muc2-/-gp130ΔIEC mice leading to a reduced expression of CD11b and interleukin-22 (Il-22). Lower SI Il-22 expression resulted in diminished Reg3b expression and increased bacterial translocation to the liver. Consequently, Muc2-/-gp130ΔIEC had higher plasma transaminase levels, and increased hepatic mRNA expression of Tnf, Ccl5, and Tgf-β1. Thus, GAP closure in Muc2-/- mice resulted in the loss of protection against ethanol-induced steatohepatitis

Conclusion:

Absence of intestinal Mucin-2 promotes GAP formation to prevent ethanol-induced steatohepatitis in mice. Inhibition of mAChR4-mediated GAP formation exacerbates steatohepatitis and impairs the small intestinal immune response, even in Muc2-deficient mice. Thus, targeting goblet cells function via mAChR4 signaling holds promise for mitigating alcoholic liver disease progression.

Research Type: Basic

Additional Authors:

Maria Fernanda Raya Tonetti, PhD; Noemi Cabre, PhD; Marcos Fernandez Fondevila; Alvaro Eguileor; Bernd Schnabl, MD, FAASLD; Cristina Llorente, MS, PhD.

Poster #: 11

Abstract Title: Novel DGAT2 antisense inhibitor demonstrates significant histological benefit in biopsy-proven MASH patients with advanced liver fibrosis stage F3: Subset analysis of a 51-week multicenter randomized double-blind placebo-controlled phase 2 trial

Presenter Name: Keyvan Yousefi, Pharm.D., R.Ph., Ph.D.

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Affiliation / Institution:

Abstract Background:

ION224 is an investigational ligand-conjugated antisense inhibitor of diacylglycerol acyltransferase 2 (DGAT2), an enzyme that catalyzes the final step in hepatic triglyceride synthesis. We previously reported the first clinical evidence that reduction of hepatic fat after DGAT2 inhibition in patients with F2 and F3 fibrosis leads to MASH resolution and the ION224-CS2 study (NCT04932512) met the primary endpoint of >=2-point reduction in NAS with >=1-point improvement in hepatocellular ballooning or lobular inflammation without worsening of fibrosis. The current analysis focuses on the effects of ION224 in patients with advanced liver fibrosis (stage F3) from the study.

Methods:

This subset analysis conducted in patients with advanced fibrosis stage F3 included 39 patients treated with 90 or 120mg ION224 (n=26) or placebo (n=13). Biopsy proven MASH patients with MASLD activity score (NAS)>=4 and MRI-PDFF>=10% received monthly subcutaneous injections of ION224 or placebo during a 49-week treatment period followed by a subsequent biopsy evaluation.

Results:

Baseline characteristics were: age 57+-10 years (mean+-SD), body weight 109.7+-27.6 kg, female 51%, type 2 diabetes 59%, MRI-PDFF 21+- 7.0%. The primary endpoint of >=2-point reduction in NAS score was met in 61.5% of ION224-treated patients, compared to 15.4% for placebo (p=0.006). Histological benefit was further supported by a higher proportion of ION224-treated patients demonstrating improvement in both hepatocellular ballooning and lobular inflammation combined (46.2% vs 15.4% in placebo). Also, a higher proportion of ION224-treated patients showed MASH resolution without worsening of fibrosis (30.8% versus 15.4% for placebo) as well as >=1 stage improvement in fibrosis without worsening steatohepatitis (46.2% vs 30.8% for placebo). A significantly higher proportion of ION224-treated patients showed a post-baseline relative reduction in MRI-PDFF of >=30% (88.5% vs 38.5% in placebo, p=0.002) or >=50% (53.8% vs 7.7% in placebo, p=0.005). ION224 was safe and well-tolerated with no treatment-related SAEs, no GI side effects or change in body weight and showed a 0.5% placebo-adjusted improvement in HbA1c at the 120mg dose.

Conclusion:

The current analysis provides evidence of clinical benefit of ION224 in patients with advanced fibrosis independent of changes in body weight. These data support the potential for ION224 treatment to provide benefit to MASH patients with advanced liver fibrosis.

Research Type: Clinical

Additional Authors:

Rohit Loomba, MD, MHSc, FAASLD; Erin Morgan; Keyvan Yousefi, PharmD, PhD, RPH; Dan Li; Richard S. Geary, PhD; Sanjay Bhanot, MD, PhD.

Poster #: 17

Abstract Title: GLP-1 Receptor Agonists have a potential to improve disease activity in Pediatric Metabolic Dysfunction-Associated Steatotic Liver Disease

Presenter Name: Andrea Tou, MD

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Affiliation / Institution: Children's Hospital of Philadelphia

Abstract Background:

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is the most common chronic liver disease in children and is characterized by hepatic steatosis with >= 1 cardiometabolic risk factor. In adults, Glucagon-Like-Peptide-1 Receptor Agonists (GLP-1 RAs) are used to not only treat Type 2 Diabetes Mellitus (T2DM) and obesity, but have also been shown to promote histologic resolution of metabolic dysfunction-associated steatohepatitis (MASH). There is a paucity of studies evaluating the use of GLP-1 RAs in pediatric MASLD. Our objective was to determine the effect of GLP-1 RAs in pediatric patients with MASLD by using an alanine aminotransferase (ALT) reduction of >= 17 U/L as a marker of improved disease activity per AASLD guidance. Secondary outcomes included changes in body mass index (BMI) z-score, weight, blood pressure, and serum markers of metabolic dysfunction associated co-morbidities.

Methods:

An IRB-approved single center retrospective study was performed in patients < 21 years old who had a diagnosis of NAFLD / MASLD and were started on a GLP-1 RA at the Children's Hospital of Philadelphia from 1/1/2018 - 1/10/2024. ALT and secondary endpoint values were collected at baseline, 6 months into treatment, and at the end of treatment. Demographics and medication start / end dates were also obtained. A Wilcoxon signed-rank test assuming independent observations was used for statistical analysis.

Results:

111 patients met our inclusion criteria. 51% were male, 40% were White, and median age at GLP-1 RA initiation was 15 years old. Mean treatment duration was 13 months, with Semaglutide (41%) being the most frequently prescribed. Notably, there was a mean reduction in ALT by 18 U/L (p=0.01) post-GLP-1 RA, and by 23 U/L (p =0.02) 6 months into therapy. ALT fully normalized in 58% of patients. BMI z-score decreased by a mean of 0.06 (p<0.01) with no significant changes in weight post-GLP-1 RA, but there were statistically significant improvements in GGT, HbA1c, and triglycerides. When stratifying for patients started on a GLP-1 RA for the indication of obesity (51%) versus T2DM (49%), the T2DM cohort had a significantly greater change in ALT, still without significant weight reduction in either group.

Conclusion:

This is the largest dedicated pediatric study evaluating the effects of GLP-1 RAs on MASLD to date. Our data supports the potential use of GLP-1 RAs in the treatment of pediatric MASLD with the greatest impact in patients with T2DM. The mechanism by which this may occur does not seem exclusive to weight loss given no significant changes in weight, and only minimal changes in BMI z-score post-GLP-1 RA. This is hypothesized to be due to improvements in hepatic and whole-body insulin resistance, among other mechanisms. Further data with standardization of medication dosing and duration, and comparison of serum biomarkers with imaging is required to better understand the impact of GLP-1 RAs on the treatment of pediatric MASLD.

Research Type: Clinical

Additional Authors:

Andrea M. Tou, MD; Jennifer Panganiban, MD;

Poster #: 18

Abstract Title: AHEAD, A NOVEL VALIDATED MACHINE LEARNING MODEL FOR CLINICAL DIAGNOSIS OF ALCOHOL-ASSOCIATED HEPATITIS

Presenter Name: Hanna Blaney, MD

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Abstract Background:

Alcohol-associated hepatitis (AH) is a unique clinical syndrome, with new onset or worsening of jaundice, with 90-day mortality of up to 90% in most severe forms. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has proposed clinical criteria for AH diagnosis (AST>50 and <400 IU/L, serum bilirubin [SB] >3 mg/dl, presentation within 60 days from last alcohol use) for management and for enrollment in clinical trials. However, these criteria are not evidence-based. We performed this multicenter study with the aim of validating NIAAA clinical criteria for diagnosis in patients with alcohol- associated liver disease (ALD).

Methods:

Seven centers with liver biopsy data for ALD were included in the study. To ensure external validity, centers were randomized into Training and Test Sets, such that each set comprised data from different centers. The outcome of interest was biopsy-proven AH defined by the presence of Mallory-Denk Bodies, lobular inflammation, and ballooning degeneration. Three machine learning algorithms-Random Forest (RF), Gradient Boosting Machine (GBM), and XGBoost (XGB)-were developed using the Training Set (Figure, A-C). The final ensemble model, termed the Alcohol Hepatitis Ensemble Algorithm Development (AHEAD), was constructed as the geometric mean of the three individual models. The GME model was compared against the NIAAA criteria.

Results:

The Training Set included 263 patients from 4 centers, with 60 diagnosed with AH. The Test Set comprised 204 patients from 3 centers, with 30 diagnosed with AH. In the Test Set, RF had an AUC of 0.682 (95% CI 0.591-0.773), GBM had an AUC of 0.690 (95% CI 0.597-0.782), and XGB had an AUC of 0.684 (95% CI 0.594-0.774). The AHEAD model achieved an AUC of 0.695 (95% CI 0.608-0.782), demonstrating superior performance compared to the NIAAA model, which had an AUC of 0.590 (95% CI 0.494-0.685) (Bootstrap p = 0.049). Using a 50% probability cutoff, the AHEAD Score achieved a specificity of 61.5% (107 out of 174 non-cases correctly identified) and a sensitivity of 63.3% (19 out of 30 cases correctly identified). In contrast, the NIAAA model showed a specificity of 54.6% (95 out of 174)

and the same sensitivity of 63.3% (19 out of 30). The higher specificity of the AHEAD model suggests an improved ability to identify true non-cases compared to the traditional NIAAA criteria.

Conclusion:

AHEAD, a novel validated model based on AST, AST/ALT ratio, and serum bilirubin is more accurate compared to the currently used NIAAA clinical criteria for clinicaldiagnosis of AH and for recruitment of patients into clinical trials. Additional variables may further improve the accuracy of the model.

Research Type: Clinical

Additional Authors:

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Poster #: 19

Abstract Title: Initiation of naltrexone is associated with lower rates of AKI, SBP, and mortality in patients with decompensated alcohol-associated cirrhosis and ascites

Presenter Name: Vinay Jahagirdar, MBBS

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Affiliation / Institution: University of Missouri Kansas City School of Medicine

Abstract Background:

Naltrexone is an FDA-approved medication for the treatment of alcohol use disorder (AUD). It has been shown to reduce heavy alcohol consumption and prevent relapse. However, concern for hepatotoxicity in patients with underlying liver disorders is a likely barrier to its widespread use. Data regarding its use in patients with decompensated alcohol-associated cirrhosis (AC) are scarce and emerging. We aimed to compare outcomes in patients with decompensated cirrhosis with or without the use of naltrexone.

Methods:

We queried the TriNetx US Collaborative Network-a research consortium of 60 healthcare organizations, to identify patients with AC with ascites, and ongoing alcohol use. The population was divided into two cohorts - those on naltrexone (Cohort A) and those not on naltrexone or acamprosate (Cohort B). Outcomes were assessed 30 days to 5 years after the initiation of pharmacotherapy or ascites. Propensity Score Matching (PSM) was used to create matched cohorts for age, sex, race and ethnicity. Risk estimate was reported as percentages. Estimates of odds ratios (OR) and 95 % confidence intervals (CI) were used to describe associations.

Results:

A total of 40,623 patients were identified, including 2,274 patients on naltrexone, and 38,349 patients not on naltrexone/acamprosate. After PSM, 2,269 patients were included in each group. A similar proportion of patients with (108/1056, 10%) and without naltrexone therapy (n=16/1486, 11%) developed a new episode of alcohol-associated hepatitis (OR 0.91, 95% CI 0.71, 1.18, p=0.482). Naltrexone was associated with a lower risk of esophageal varices (OR 0.79, 95% CI 0.6-1.0, p=0.050) compared to no naltrexone. Further decompensations including acute kidney injury (AKI) (OR 0.68, 95% CI 0.57-0.81; p<0.001) and spontaneous bacterial peritonitis (SBP) (OR 0.57, 95% CI 0.45-0.71], p<0.001) were significantly less common after initiation of naltrexone. Approximately 50% of each group was hospitalized

during the follow-up period, with 10 median admissions per patient in each group (p=0.992). One in 4 patients died, and naltrexone was associated with 20% lower odds of death compared to no naltrexone (OR 0.82, 95% CI 0.72-0.94, p=0.005).

Conclusion:

Patients with AC and active drinking have significant healthcare utilization and are at high risk of mortality. In this study, we observed naltrexone to be associated with reduced AKI, SBP, and death in patients with AC and ascites and ongoing alcohol use. These data suggest that naltrexone is not only safe in patients with decompensated liver disease but may also prevent further decompensation and reduce mortality.

Research Type: Clinical

Additional Authors:

Vinay Jahagirdar, MBBS; Katherine M. Cooper; Deepika Devuni, MBBS;

Poster #: 20

Abstract Title: Variable Treatment and Access to Liver Transplantation for Alcohol Associated Liver Disease: The California Liver Network

Presenter Name: Ashley Jowell, MD

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Affiliation / Institution: Duke University Medical Center

Abstract Background:

Alcohol associated liver disease (ALD) is now the most common indication for liver transplantation (LT), with greater acceptance of LT for alcohol associated hepatitis - however, significant practice variation exists and criteria for transplantation remain non-standard. We evaluated predictors of access to LT for ALD in a large representative state-based cohort.

Methods:

The California Liver Network is a consortium of six major LT centers in California, comprising >75% of the adult liver transplant volume in the state. Sociodemographic, clinical, and outcomes data were retrospectively collected for adults referred for LT at these centers between 2018 and 2020. We evaluated predictors of listing for patients with ALD, using a multivariable mixed effects model with center as a random effect.

Results:

Among 6856 patients referred during the study timeframe, there were 2084 (31%) with a specified indication of ALD. The median age was 55 years (IQR 48-62); 72% male; 40% White, 38% Hispanic; 3% Asian, and 2% Black; 22% reported a primary language other than English; and 34% had private insurance, 40% Medi-cal, and 21% Medicare. Median MELD at referral was 21 (IQR 14-30); 27% met NIAAA criteria for AH or had <6 months of sobriety; and 40% of evaluations were inpatient. Of the patients with AH, 36% were treated with steroid, which varied by center (range 10-58%). Ultimately, 45% were listed (MELD 21, IQR 18-29), and 26% were transplanted (MELD 33, IQR 31-39); 10% had a documented return to alcohol use during the referral/evaluation process. Primary reasons for decline included psychosocial reasons (36%; range 21-49%); medically too sick or unsuitable (28%; range 19-46%); and medically too well (16%; range 3-25%) (Figure). In the mixed effects model, women (p=0.01) and those with public insurance (vs private; p<0.001 for Medi-cal, p=0.001 for Medicare) were less likely to be listed. Adjusted for age, sex, race/ethnicity, insurance, MELD, and HCC status, center remained a significant predictor of listing (p<0.05). Results were similar when examining the subgroup of patients with <6

months of sobriety at the time of referral. 126 (6.0%) of patients were also evaluated, and 40 (1.9%) waitlisted, at another US transplant center.

Conclusion:

Referral and selection practices for LT have been suboptimally characterized. This comprehensive study of LT referrals in the state of California, which performs the most liver transplants in the country, highlights the need for standardized medical and psychosocial criteria for ALD to promote and ensure equity in the LT selection process.

Research Type: Clinical

Additional Authors:

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Poster #: 21

Abstract Title: Resmetirom effects on NASH with liver fibrosis in patients with NASH genetic risk alleles

Presenter Name: Julie Dubourg, MD

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Affiliation / Institution: Madrigal

Abstract Background:

MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating the efficacy of resmetirom in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH) and fibrosis. 966 patients with biopsy-confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo administered once daily. Histologic endpoints were assessed after 52 weeks. Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or >=1-stage reduction in fibrosis with no worsening of NAS (FI). In this analysis, we examined the impact of baseline PNPLA3, TM6SF2 and MBOAT7 genotypes on the response to resmetirom on serial liver biopsy and MRI-PDFF (magnetic resonance imaging proton density fat fraction).

Methods:

In the Phase 3 study (MGL-3196-11), PNPLA3 rs738409, TM6SF2 rs58542926 and MBOAT7 rs6141738 were genotyped in patients consenting to DNA collection and genetic testing for the response to resmetirom on serial liver biopsy and MRI-PDFF. The NASH resolution and fibrosis improvement responses on liver biopsy and the MRI-PDFF (median percent change from baseline at Week 52) response were analyzed within each treatment arm, comparing wild type, heterozygote and homozygote for each genetic risk allele.

Results:

Across three treatment arms, 740 patients had genotyping and serial liver biopsy data. The frequency of PNPLA3 GG (wild type), PNPLA3 CG (heterozygous), and GG (homozygous) genotypes across 3 treatment arms were 30-32%, 45-50% and 20-24% respectively. The frequency of TM6SF2 CC (wild type), TM6SF2 CT (heterozygous), and TM6SF2 TT (homozygous) genotypes were 79-82%, 15-21% and 0-3%

across 3 treatment arms. The frequency of MBOAT7 CC (wild type), MBOAT7 CT (heterozygous) and MBOAT7 TT (homozygous) genotypes were 28-29%, 47-50%, and 21-24% across 3 treatment arms. There were no differences observed in the level of response on biopsy or MRI-PDFF to resmetirom or placebo treatment in patients with genetic risk alleles for PNPLA3 and TM6SF2 (Table) or TMC4 (not shown).

Conclusion:

NASH risk alleles were prevalent in the MAESTRO-NASH population and did not influence the treatment response to resmetirom

Research Type: Clinical

Additional Authors:

Naga P. Chalasani, MD, FAASLD; Dominic Labriola; Rebecca Taub, MD; Quentin M. Anstee, MBBS, PhD, FRCP;

Poster #: 22

Abstract Title: Effects of Timely Treatment on Outcomes of Larsucosterol for Severe Alcohol-associated Hepatitis (AHFIRM Trial)

Presenter Name: Norman Sussman, MD FAASLD

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Abstract Background:

Previously, we reported findings in the Phase 2b AHFIRM trial evaluating efficacy of larsucosterol in patients with severe alcohol-associated hepatitis (sAH). Full data (ex-US+US data) of 90-day death or liver transplant did not meet statistical significance, but US data of larsucosterol vs. Placebo showed p=0.0265 for 30-mg and p=0.1308 for 90-mg groups. Full data showed 90-day mortality was reduced by 41% (p=0.068) in the 30-mg and 35% (p=0.124) in the 90-mg groups. The reduction of 90-day mortality of US data was 57% (p=0.014) and 58% (p=0.008) for 30-mg and 90-mg groups, respectively. Here we report the importance of timely treatment in outcomes of larsucosterol.

Methods:

AHFIRM, a phase 2b randomized, double-blind, placebo-controlled, global study, evaluated the safety and efficacy of larsucosterol in 307 enrolled patients with sAH (MDF <u></u>32 and MELD 21-30). Patients were randomized 1:1:1 to receive 1 or 2 intravenous infusions (72 hours apart) of 30-mg or 90-mg larsucosterol or Placebo. All patients received standard of care per investigators' discretion. If prescribed, Placebo patients received 32 mg methylprednisolone, while larsucosterol-treated patients received matching placebo capsules.

Results:

In the trial, the median time from hospital admission to the 1st dose (hospitalization-to-treatment days) was 5 days in US, 13 days in EU, 11 days in UK, and 7 days in AU, presenting considerable regional variation. Among all patients, 75% (upper quartile) were treated <10 days of hospitalization. Re-analysis of outcomes of those receiving treatment <10 days of hospitalization showed enhanced efficacy of 30-mg larsucosterol: less 90-day death or transplant from both full and US data (p=0.053 and p=0.015, respectively), and less 90-day mortality from full and US data (p=0.010 and p=0.002, respectively). However, the same re-analysis of timely treatment with the 90-mg group did not improve the efficacy as shown with the 30-mg group.

Conclusion:

AHFIRM showed a compelling signal of mortality reduction with both doses of larsucosterol. Re-analysis of the study outcomes for patients receiving treatment <10 days of hospitalization greatly improved efficacy of mortality reduction by 30-mg larsucosterol, suggesting the importance of timely treatment.

Research Type: Clinical

Additional Authors:

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Poster #: 23

Abstract Title: Analysis of Non-Invasive Liver Biomarkers in a Phase II Trial of the Glucagon and GLP-1 Receptor Dual Agonist Survodutide in People with Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Fibrosis

Presenter Name: Lorri Nacey, AD, Medical Science Liaison

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Affiliation / Institution:

Abstract Background:

We evaluated non-invasive liver biomarkers from a phase II trial of survodutide, a novel glucagon receptor/glucagon-like peptide-1 receptor dual agonist for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis.

Methods:

In this multinational, double-blind, phase II trial (NCT04771273), 295 people aged 18-80 years with biopsy-proven MASH (Non-alcoholic fatty liver disease Activity Score >=4), liver fibrosis (stage F1-F3) and body mass index >=25 kg/m2 were randomized to once-weekly subcutaneous injections of placebo (PBO) or survodutide 2.4, 4.8 or 6.0 mg (escalated over up to 24 weeks). In this analysis, we evaluated percentage of participants with >30%, >50% and >70% reduction in liver fat content (LFC; magnetic resonance imaging proton density fat fraction [MRI-PDFF] assessed; restricted to paired MRI data), resolution of steatosis (LFC <5%; MRI-PDFF assessed) with or without >17 U/L reduction in alanine transaminase (ALT; restricted to paired MRI data), absolute change in enhanced liver fibrosis (ELF) score, relative change in propeptide of type III collagen (Pro-C3), >30% reduction in LFC (controlled attenuation parameter [CAP; FibroScan] assessed), and absolute and relative change in liver stiffness (transient elastography [VTCE; FibroScan] assessed) from baseline (BL) to week 48. These biomarkers were analyzed according to the actual dose received at the start of the maintenance period.

Results:

The number of participants with significant >30%, >50% and >70% reduction in LFC (MRI-PDFF) was met in up to 87.0%, 78.2% and 52.7% with survodutide vs. 19.7%, 3.0% and 0.0% for PBO, respectively. LFC <5% with an ALT reduction of >17 U/L was met in up to 45.7% vs. 0.0% and without ALT reduction in up to 54.3% vs. 0.0% with survodutide vs. PBO, respectively. Absolute change in ELF score was up to -0.619 with survodutide vs. -0.003 with PBO; relative change in Pro-C3 was up to -26.32% vs. 5.47%,

respectively. >30% reduction in LFC (CAP) was met in up to 20.3% with survodutide vs. 0.0% with PBO. The absolute (relative) change in liver stiffness (VCTE) was up to -5.09 kPa (-32.99%) with survodutide vs. -1.18 kPa (3.44%) with PBO, respectively.

Conclusion:

Participants that received survodutide had significant improvements in LFC (MRI-PDFF and CAP assessed), liver stiffness (VCTE assessed), liver enzymes and other markers of fibrosis (ELF, Pro-C3) which was correlated with improvements in histological endpoints.

Research Type: Clinical

Additional Authors:

Mazen Noureddin, MD, MHSc; Corinna Schoelch; Elisabetta Bugianesi; Naim Alkhouri, MD; Mandy Fraessdorf; Jörn M. Schattenberg, MD; Philip N. Newsome, MD, PhD; Quentin M. Anstee, MBBS, PhD, FRCP; Guy W. Neff, MD; Harvey O. Coxson, PhD; Eric Lawitz, MD, FAASLD; Vlad Ratziu, MD; Atsushi Nakajima; Azadeh Hosseini-Tabatabaei; Arun J. Sanyal, MD, FAASLD; Ramy Younes.

Poster #: 25

Abstract Title: Incidence and prognosis of psychiatric intervention of alcoholic liver disease in Korea: a nationwide standard cohort study

Presenter Name: Hyundam (Dami) Gu, MD

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Affiliation / Institution: Johns Hopkins School of Public Health

Abstract Background:

Alcohol consumption is a major global concern leading to significant social and economic losses, yet its consumption remains high. Alcohol is a major cause of chronic liver disease. However, the co- occurrence of psychiatric conditions in patients with alcoholic liver disease and its impact on survival have not been adequately addressed in Korea.

Methods:

To investigate the medical utilization related to psychiatric problems in patients with alcoholic liver disease, we utilized data from the National Health Insurance Service–National Sample Cohort in Korea between 2002 and 2019. We defined psychiatric intervention as being claimed for outpatient clinics more than twice or hospitalized for psychiatric diseases such as depression, bipolar disorder, and anxiety. We further examined death and suicide attempts between those with and without psychiatric intervention.

Results:

Among total number of 46,340 patients who were enrolled, 37,155 were male (80.1%). 7,527 patients received psychiatric intervention. Baseline characteristics demonstrated that patients who received the intervention were older (55.60 ± 13.70 years vs 49.52 ± 12.92 years), had a higher prevalence of females (23.9 % vs 19.03%), and had more comorbidities (Charlson comorbidity index; 2.65±2.12 vs 2.21±1.58) than patients without psychiatric intervention. After adjustment, patients in the psychiatric intervention group exhibited a higher incidence of suicide attempts (adjusted HR: 3.343, 95% CI: 2.298 - 4.862) and death (adjusted HR: 1.568, 95% CI: 1.448 - 1.669) compared to their counterparts. Factors such as male sex and low socioeconomic status were also found to be associated with suicide attempts.

Conclusion:

This study underscores the importance of addressing psychiatric approaches, with a special focus on suicide attempts in patients with alcoholic liver disease.

Research Type: Clinical

Additional Authors: Yeonjoo Seo, Jihey Lim

Poster #: 26

Abstract Title: Assessing Steatosis-Associated Fibrosis Estimator (SAFE) score accuracy for Predicting Advanced Hepatic Fibrosis in Patients Undergoing Bariatric Surgery

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Abstract Background:

Metabolic-associated steatotic liver disease (MASLD) affects approximately a quarter of the global adult population and is the second leading cause of end-stage liver disease and liver transplantation in developed countries. Identifying patients at high risk for advanced fibrosis (F≥2) is crucial for early intervention to prevent progression to cirrhosis, particularly in primary care settings. The Steatosis-Associated Fibrosis Estimator (SAFE) score, which relies on widely available clinical variables, offers a non-invasive method to estimate liver fibrosis. We aim to externally validate the SAFE score in patients undergoing bariatric surgery.

Methods:

We performed a single center retrospective study of 147 adult patients undergoing liver biopsy during bariatric procedures at MedStar Georgetown - Washington Hospital Center between January 2019 and June 2024. We included patients with history of MASLD, age >18 with or without medical comorbidities (DM, HTN, dyslipidemia). We excluded patients who are undergoing repeat procedures or have history of liver disease secondary to etiologies other than MASLD. We collected demographics, laboratory data and liver biopsy data. Liver fibrosis stages were assessed based on the METAVIR scoring system. The SAFE score was calculated for each patient using the published formula, incorporating age, BMI, diabetes status, and laboratory values. We analyzed the diagnostic performance of the SAFE score (with cutoff>100) for excluding advanced fibrosis (F≥2) by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results:

We included 147 patients with a median age of 49 [IQR 41–58], 84% females, 82% non-Hispanic African Americans, median weight of 130 kg [IQR 115.7–149.45], median BMI of 46.37 [IQR 41.27–54.26], median AST of 18 U/L [IQR 15–25], median ALT of 18 U/L [IQR 13–30], median albumin of 4.2 g/dL [IQR 4–4.4], and median platelets of 280 × 10^9/L [IQR 229.5–318.5]. Among the cohort, 98 patients had hypertension and 59 had diabetes. The SAFE score demonstrated the following diagnostic performance for excluding advanced fibrosis (F≥2) at a cutoff >100: sensitivity of 0.333 (95% CI: 0.091–0.705), specificity of 0.841 (95% CI: 0.772–0.898), positive predictive value (PPV) of 0.120 (95% CI: 0.031–0.329), and negative predictive value (NPV) of 0.951 (95% CI: 0.897–0.980).

Conclusion:

The SAFE score demonstrated high specificity and negative predictive value for excluding advanced fibrosis (F≥2) in patients undergoing bariatric surgery, suggesting it may be a useful tool for identifying low-risk patients in clinical practice. However, the low sensitivity and positive predictive value indicate that it should be used cautiously and in conjunction with other clinical assessments, particularly for identifying high-risk individuals. Further studies in diverse populations are warranted to enhance its applicability and accuracy.

Research Type: Clinical

Additional Authors:

Kiandokht Bashiri, Ahmed Abdulraheem, Salwan AlSaadallah, Nadera Altork, Ghaith Almahanai, Usman Afzal, Jennifer Tran

Poster #: 27

Abstract Title: Enhanced Liver Fibrosis Outperforms Transient Elastography in Discordant Cases Validated by MRE or Liver Biopsy

Presenter Name: Adily Elmi, MD, MPH

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Affiliation / Institution: University Hospitals/Case Western Reserve University

Abstract Background:

Metabolic dysfunction–associated steatotic liver disease (MASLD), is characterized by hepatic steatosis of 5% or greater accompanied by hepatocellular damage and inflammation, with 20-25% of affected individuals at risk for steatohepatitis and fibrosis. In March 2024, Resmetirom became the first FDA-approved treatment for at-risk MASLD in adults with moderate to advanced fibrosis (F2-F3). Current guidelines recommend utilizing multiple non-invasive liver tests (NITs) to identify patients likely to have stage 2 or 3 fibrosis. However, a significant limitation of NITs is their variable accuracy in precisely staging fibrosis, which can result in diagnostic uncertainty and often necessitates a third, more definitive test, such as liver biopsy or MR Elastography. Our study aimed to evaluate the accuracy of NITs, specifically Enhanced Liver Fibrosis (ELF) and Vibration-Controlled Transient Elastography (VCTE), in a cohort of MASLD patients. The primary objective was to assess how frequently NITs concordantly stage at-risk MASLD versus how often they yield discordant results. Secondary objectives included determining the frequency of third-test utilization and evaluating whether ELF or VCTE was more accurate in fibrosis staging when a third test was required.

Methods:

Patients attending our liver clinic with MASLD were tested with NITs (ELF and VCTE) in an effort to identify at risk MASLD patients for potential treatment. We collected clinical variables including age, gender, body mass index (BMI), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, platelet count, and type 2 diabetes status for each patient. Only patients with current ELF and VCTE within the preceding 12 months were included.

Results:

We identified 45 patients who met the criteria of current ELF and VCTE within the last year. Patients were categorized according to whether non-invasive tests were concordant or disconcordant. The average age was 61 years, majority were females (60%) and white (77.8%) (Table 1). NITs were more likely to be discordant (56%) than concordant (44%), and a third test was required more than half the time to reliably stage liver fibrosis. ELF was the more accurate test in predicting fibrosis stage (43.5%) when compared to VCTE (21.7%) in our cohort (Table 2).

Conclusion:

Non-invasive liver tests (NITs) have become invaluable tools for excluding advanced fibrosis, but their limitations in precisely staging fibrosis remain a challenge. Our study revealed frequent discordance when NITs were used in combination, underscoring the need for cautious interpretation and the potential role of additional diagnostic strategies to enhance accuracy in fibrosis assessment.

Research Type: Clinical

Additional Authors: Seth Sclair, MD

Poster #: 28

Abstract Title: Semaglutide exposure is associated with lower odds of cirrhosis in non-obese, non-diabetic patients with steatotic liver disease: a global database study

Presenter Name: Katherine Cooper, MD

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Abstract Background:

Semaglutide is a GLP-1 receptor agonist that is approved for type 2 diabetes (DM), obesity, and cardiovascular disease. It has shown promise in liver disease by improving steatohepatitis in patients with metabolic dysfunction associated steatotic liver disease (MASLD). However, most data related to MASLD is derived from patients with comorbid DM and/or obesity, and data on long-term outcomes are limited. In this study, we assessed liver-related outcomes in non-obese, non-diabetic MASLD patients initiated on semaglutide therapy compared to no semaglutide therapy.

Methods:

Using the TriNetX Research Network, we conducted a multi-center retrospective cohort study using data from 98 healthcare organizations in five countries. Patients diagnosed with MASLD between Jan/2014–Jan/2024 with a body mass index (BMI) ≤30 kg/m² and no diagnosis of DM were included. Two cohorts were created: 1) those prescribed semaglutide after diagnosis of MASLD and 2) those not prescribed semaglutide. Groups were propensity-matched for demographic factors (age, sex, race), aminotransferases (ALT), and baseline comorbidities (hypertension, dyslipidemia, sleep apnea, ischemic heart disease, alcohol-related disorders). Liver outcomes (cirrhosis, decompensation, death) were assessed over 5 years.

Results:

A total of 183,237 patients were identified, including 2,178 who received semaglutide. Patients prescribed semaglutide were older (48.0 ± 10.5 vs. 44.0 ± 12.6. $p<0.001$).

Conclusion:

In this large multi-center study, semaglutide was associated with improved liver-related outcomes in patients with MASLD in the absence of DM and obesity. More research is needed to understand the benefits of GLP-1 medications in patients with non-standard indications at risk for developing chronic liver disease.

Research Type: Clinical

Additional Authors:

Katherine M. Cooper, Vinay Jahagirdar, Deepika Devuni, Juan Pablo Arab