AASLD Nov. 4-8, 2022

The Liver Meeting®

WASHINGTON D.C.

The Best of The Liver Meeting®

ALCOHOL ASSOCIATED LIVER DISEASE

About the program:

Best of The Liver Meeting 2022 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

Use of these slides:

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An artificial intelligence-generated model from a global cohort to predict 90-day survival in alcohol-associated hepatitis

Objective

To derive and test a new prognostic model for 90-day mortality in severe alcohol-associated hepatitis (AH) using a machine learning model.

Methods

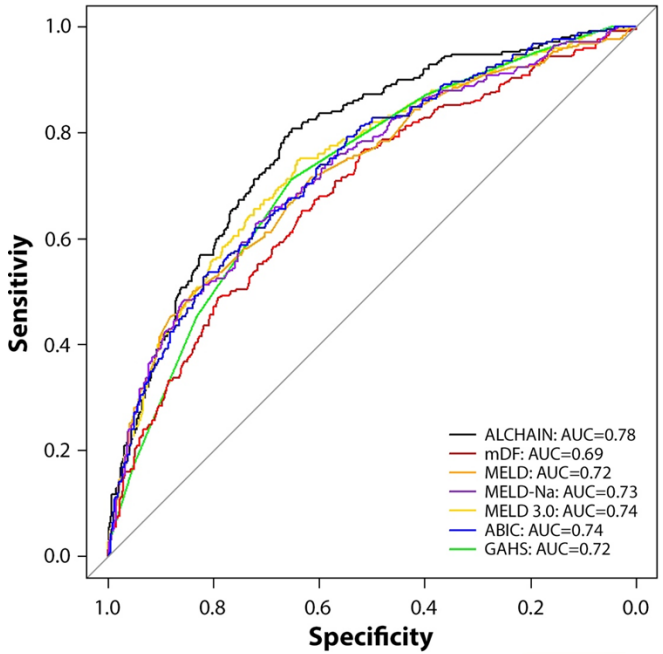
- 860 and 859 patients with AH based on NIAAA criteria included in the derivation and validation cohorts, respectively.
- All pairwise interactions were analyzed using the glinternet method.
- The ALCoholic Hepatitis Artificial INtelligence (ALCHAIN) score is a probability score that ranges from 0 to 1 corresponding to 90-day mortality, whether 0 corresponds to 0% and 1 to 100%.

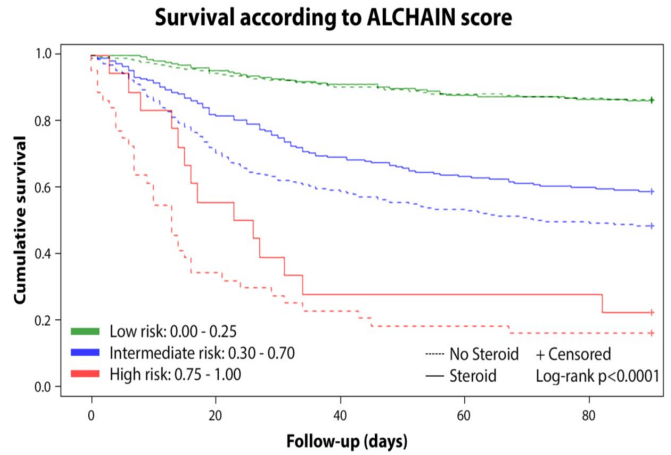
Main Findings

- The ALCHAIN score is statistically superior to mDF, MELD, MELD, MELD-Na, MELD 3.0, ABIC, and GAHS in the validation cohort.
- Steroid use was significantly associated with a lower hazard ratio of 30-day mortality in those with an ALCHAIN score between 0.30-0.70.

Conclusions

The ALCHAIN score is superior to existing scores and could be clinically useful for clinical trials and for personalizing steroid treatment.





Dunn W, et al., Abstract 125.

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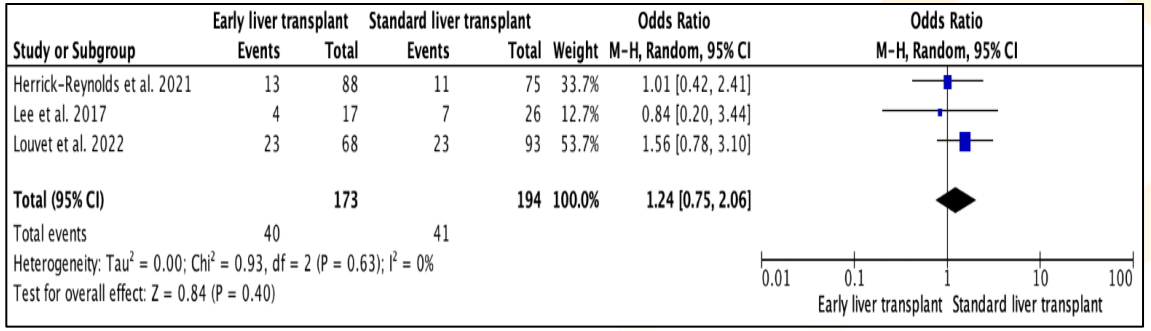
Alcohol relapse after early liver transplantation in patients with severe alcoholic hepatitis: A systematic review and meta-analysis

Aim

We conducted a meta-analysis to evaluate the alcohol-relapse rate in patients with severe alcoholic hepatitis (sAH) undergoing Liver Transplantation (LT) with or without an extensive sobriety period.



Methods

- MEDLINE and SCOPUS were queried for randomized controlled trials (RCTs), prospective or retrospective observational studies, and case-control studies.
- Studies assessing post-transplant outcomes (ie, alcohol relapse in patients undergoing standard vs early liver transplant) were incorporated.

Main Findings

- The average duration of pre-transplant abstinence was 225 ± 44 days for the early transplant group compared to 550 ± 12 days in the standard group.
- The pooled analysis demonstrates that there was no statistically significant difference in alcohol relapse between the groups (OR=1.24, 95% CI: 0.75-2.06, P=0.40).

Conclusions

Our findings demonstrate that early LT in patients with sAH was not associated with increased risk of alcohol relapse post-LT when compared with patients with extensive sobriety period.

Zafar Y, et al., Abstract 1572.

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Microbiota associated with butyrate synthesis are necessary to reduce alcohol preference transmission from AUD patients that received FMT

Aim

Determine the impact of sterile fecal supernatants and potential metabolites that impact microbiota-related alcohol behavior.

Methods

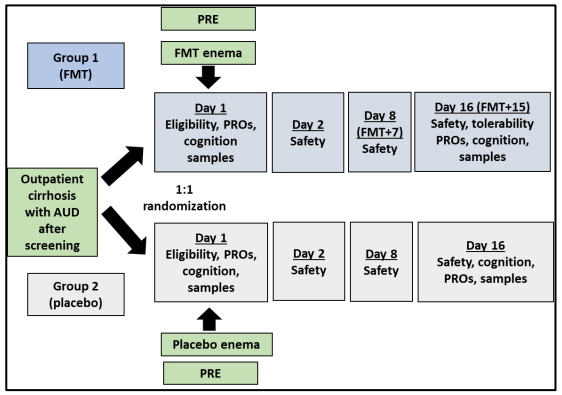
Germ-free mice were colonized with stools from patients from an RCT (pre-FMT, post-FMT, or supernatants) and initial ethanol acceptance (2-hr binge), intake and preference using two days of two-bottle choice drinking were measured.

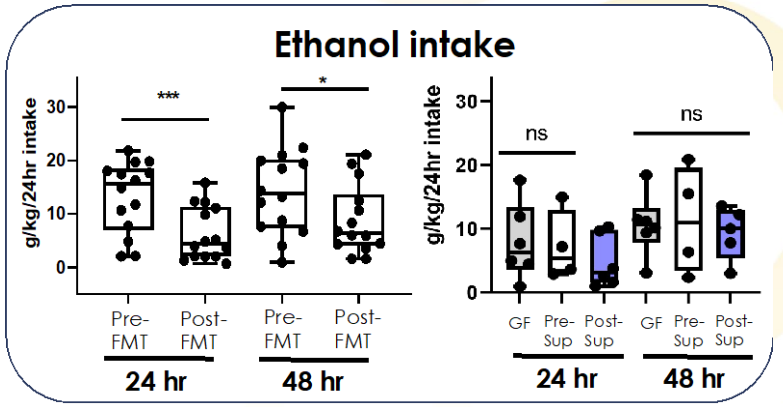
Main Findings

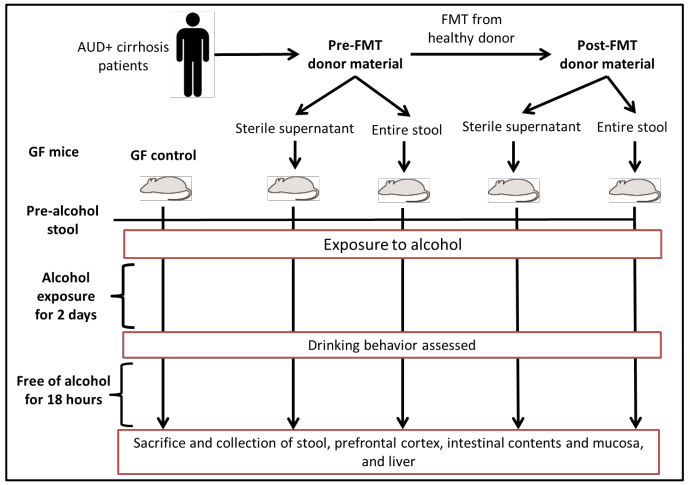
- Pre-FMT mice had greater initial acceptance, alcohol intake than post-FMT mice.
- GF control, pre- or post-FMT supernatants did not alter ethanol intake.
- Fecal metabolites showed a significantly higher butyrate levels in post-FMT compared to pre-FMT mice.

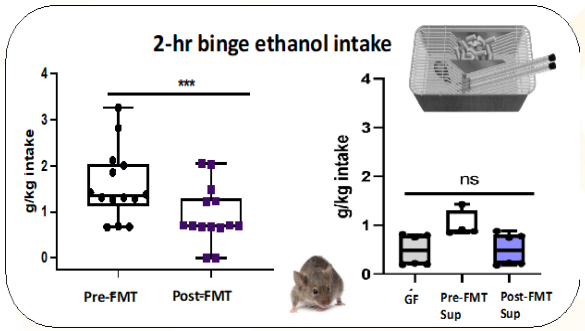
Conclusions

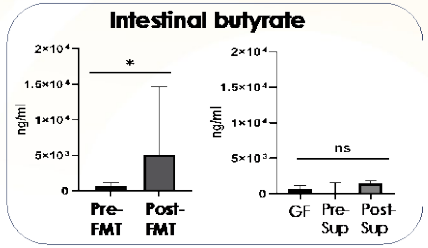
- Microbiota associated with butyrate production, but not their germ-free supernatants, are necessary to reduce alcohol preference transmission from AUD patients that received FMT.
- Strategies to increase these microbial populations in humans with AUD may be helpful for reducing alcohol consumption.











Wolstenholme JT, et al., Abstract 3102.

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Anakinra plus zinc versus prednisone for treatment of severe alcohol-associated hepatitis: A randomized controlled trial

Aim

Severe alcohol-associated hepatitis (SAH) has a 90-day mortality of up to 30%. Treatment with corticosteroids improves 30-, but not 90-day survival. The IL-1 receptor antagonist anakinra demonstrated efficacy signals in a phase 2 study, but there are no large trials comparing anakinra with standard of care.

Methods

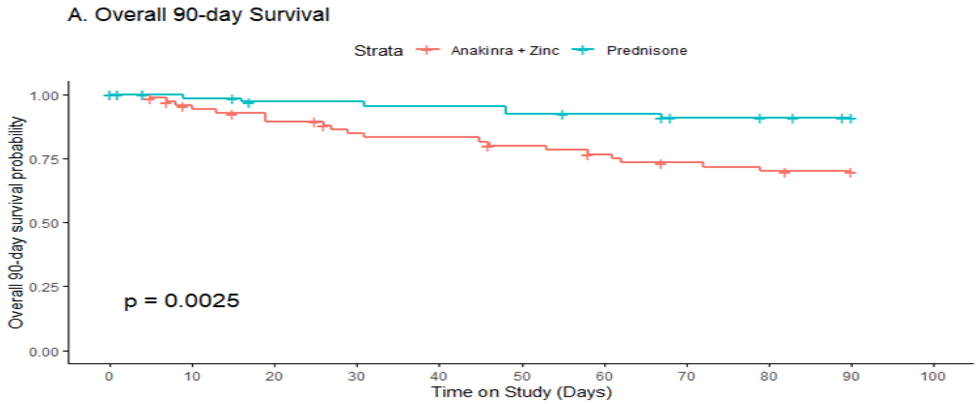
- A double-blind randomized placebo-controlled trial of anakinra 100 mg subcutaneously daily for 14 days plus ZnSO4 220 mg orally daily for 90 days (A+Z) vs prednisone 40 mg orally daily (pred) for 30 days in adults with SAH and MELD 20-35.
- The primary endpoint was overall survival at 90 days.

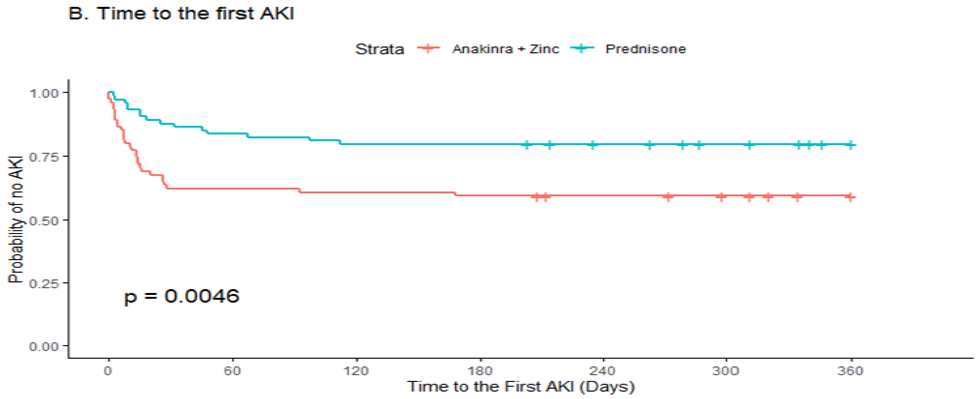
Main Findings

- 74 participants were randomized to A+Z vs 73 to pred.
- The study was stopped early after a planned interim analysis showed a significant difference in 90-day overall survival (69.9% in A+Z vs 91% in pred) (**Fig A**).
- 30 (41%) participants in A+Z developed AKI vs 15 (21%) in pred (**Fig B**).

Conclusions

Participants with SAH treated with A+Z had a significantly lower 90-day survival and higher incidence of AKI than those treated with pred.





Gawrieh S, et al., Abstract LO7.

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Clinical and laboratory scores can predict long-term cirrhosis in patients presenting with alcohol use disorder, data from large healthcare network

Objective

To outline the long-term incidence of AdvLD in patients initially presenting with AUD and no pre-existing liver disease; To explore the impact of certain comorbid conditions predicting the risk of AdvLD and mortality in AUD patients; To assess the accuracy of fibrosis-4 (FIB-4) score to predict the long-term risk of AdvLD in AUD patients with no pre-existing liver disease.

Methods

- Adults ≥18 years old with initial diagnosis of AUD based on ICD-9 and -10 codes. AdvLD was defined by a diagnosis of alcoholic hepatitis, cirrhosis (compensated or decompensated), or hepatocellular carcinoma (HCC).
- January 2006-December 2016; followed until 2021. University of Pittsburgh Medical Center (UPMC) health network clinics, hospitals, or ERs.

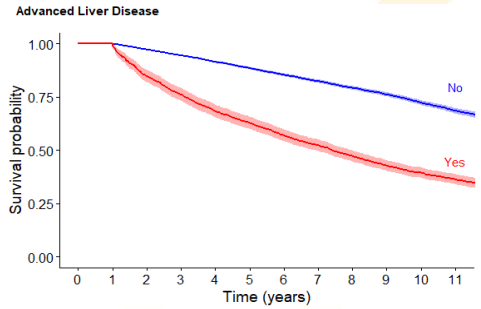
Main Findings

- History of DM, concurrent Hep C, and African-American race were major predictors of AdvLD development in AUD patients.
- Development of AdvLD doubled the risk of mortality with HR, 2.5 (2.3-2.7); DM increased the risk of mortality by 54%; History of Hep C increased mortality by 20%; AUD patients with AA race had lower mortality (HR, 0.7).
- DM, Hep C, and AA race showed additive effect to modify risk of mortality (similar to their effect on AdvLD incidence).

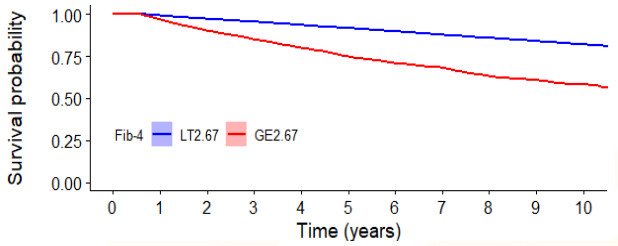
Conclusions

- Incidence of AdvLD in patients presenting with any alcohol-related problem to healthcare centers are alarmingly high.
- History of DM and hep C are strong contributors of AdvLD development in AUD patients. History of DM, Hep C, and race have additive effect modifying the risk of AdvLD in AUD patients. Elevated FIB-4 score should raise concern for high risk of AdvLD in 1 year, but not a reliable screening test due to low sensitivity.
- AUD patients exhibit a high mortality rate, and the development of AdvLD is the strongest risk factor.

Predictors of Mortality



Fibrosis-4 Score



	Sensitivity	Specificity	AUC
FIB-4 >2.6	0.37	0.86	0.62
FIB-4 ?5	0.18	0.95	0.56

AdvLD, advanced liver disease; AUD, alcohol use disorder, DM, diabetes mellitus; AA, African American; HR, hazard ratio.

Gougol, A, et al., Abstract LO11.

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Alcohol-associated Liver Disease

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