AASLD Nov. 12-15, 2021

The Liver Meeting®

DIGITAL **EXPERIENCE**

# The Best of The Liver Meeting®

## PORTAL HYPERTENSION/CIRRHOSIS

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## About the program:

Best of The Liver Meeting 2021 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.

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# AI-Cirrhosis-ECG (ACE) score predicts hepatic decompensation and liver-related mortality

## Aim

- To use the deep learning-based AI-Cirrhosis-ECG (ACE) score to predict hepatic decompensation and liver-related mortality in patients with cirrhosis

## Methods

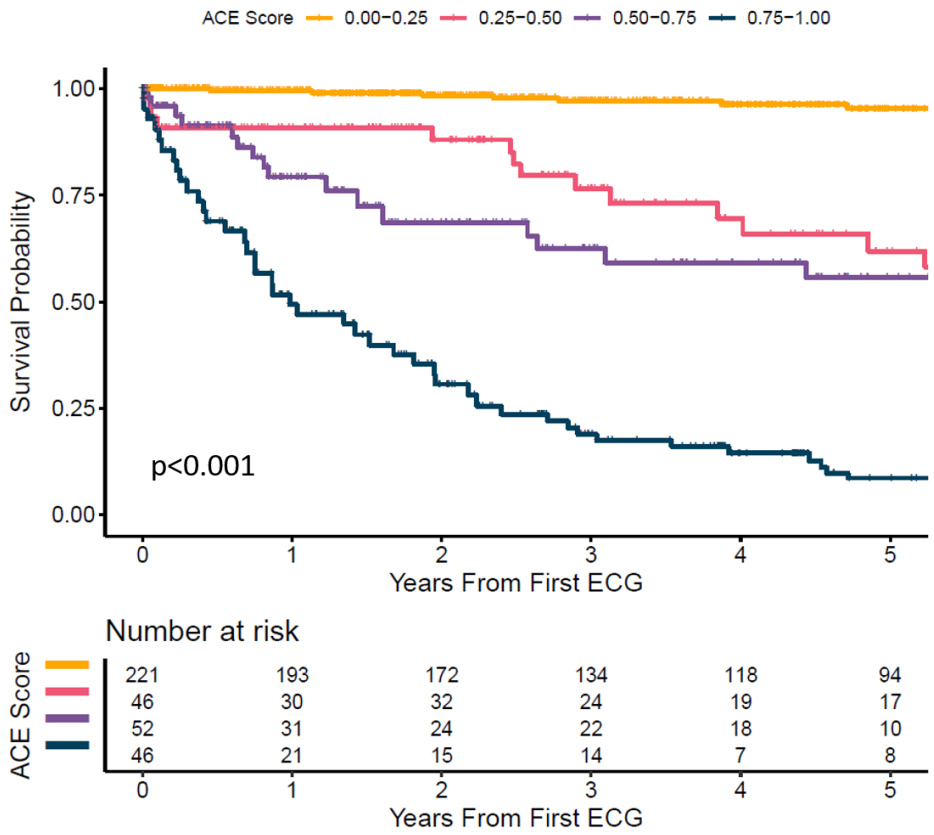
- The ACE score was applied to digitized 12-lead ECGs of 352 patients with cirrhosis and used to predict presence of hepatic decompensation and liver-related mortality.

## Main Findings

- AUC of 0.925, 87.1% sensitivity, and 83.2% specificity for prediction of hepatic decompensation.
- Independently associated with liver-related mortality (HR=1.40, p<0.001 for each 0.1 increase in ACE score).

## Conclusions

- Deep learning-based AI-ECG models may be useful for prediction of clinical outcomes in patients with cirrhosis.

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Ahn JC, et al., Abstract 163.

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# High versus low target mean arterial pressure in septic shock in critically ill cirrhotics: a prospective randomized controlled trial NCT03145168

## Aim and Objectives

**Primary** To assess the efficacy of high (80-85 mm of Hg) versus low (60-65 mm of Hg) in patients with cirrhosis and septic shock in improving 28-day survival

**Secondary**

- Reversal of shock and acute kidney injury (AKI) at day 5
- Incidence of intradialytic hypotension (IDH)
- Adverse effects
- Duration of mechanical ventilation & intensive care unit

## Methods

- Open-label single-center randomized controlled trial
- Patients with cirrhosis and septic shock (n=150)

## Main Findings

| | Intention-to-treat analysis (n=150) | | | Per-protocol analysis (n=124) | | |
|---|---|---|---|---|---|---|
| | Low MAP (n=75) | High MAP (n=75) | P value | Low MAP (n=67) | High MAP (n=57) | P value |
| 28-day mortality | 56% | 65% | 0.54 | 60% | 61% | 0.06 |
| AKI reversal at day 5 | 31% | 45% | 0.064 | 21 (31%) | 30 (53%) | 0.018 |
| Intradialytic hypotension | 25% | 8% | 0.008 | 18 (27%) | 2 (4%) | <0.001 |
| Length of stay in the intensive care unit | 6.2 ± 3.9 | 7.4 ± 5.2 | 0.11 | 6.3 ± 4.0 | 6.6 ± 4.7 | 0.71 |
| Reversal of shock at day 5 | 53% | 47% | 0.41 | 40 (53%) | 35 (48%) | 0.86 |
| Adverse events | 11% | 24% | 0.03 | | | |

## Conclusions

- Targeting a higher MAP strategy of 80 to 85 compared 60 to 65 mm of Hg in patients with cirrhosis with septic shock is associated with lower incidence of intradialytic hypotension, higher recovery of renal functions but more adverse effects.

Maiwall R, et al., Abstract 164.

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# Home-based, tunneled peritoneal drainage (PeKa) system as an alternative treatment option for patients with refractory ascites (RA)

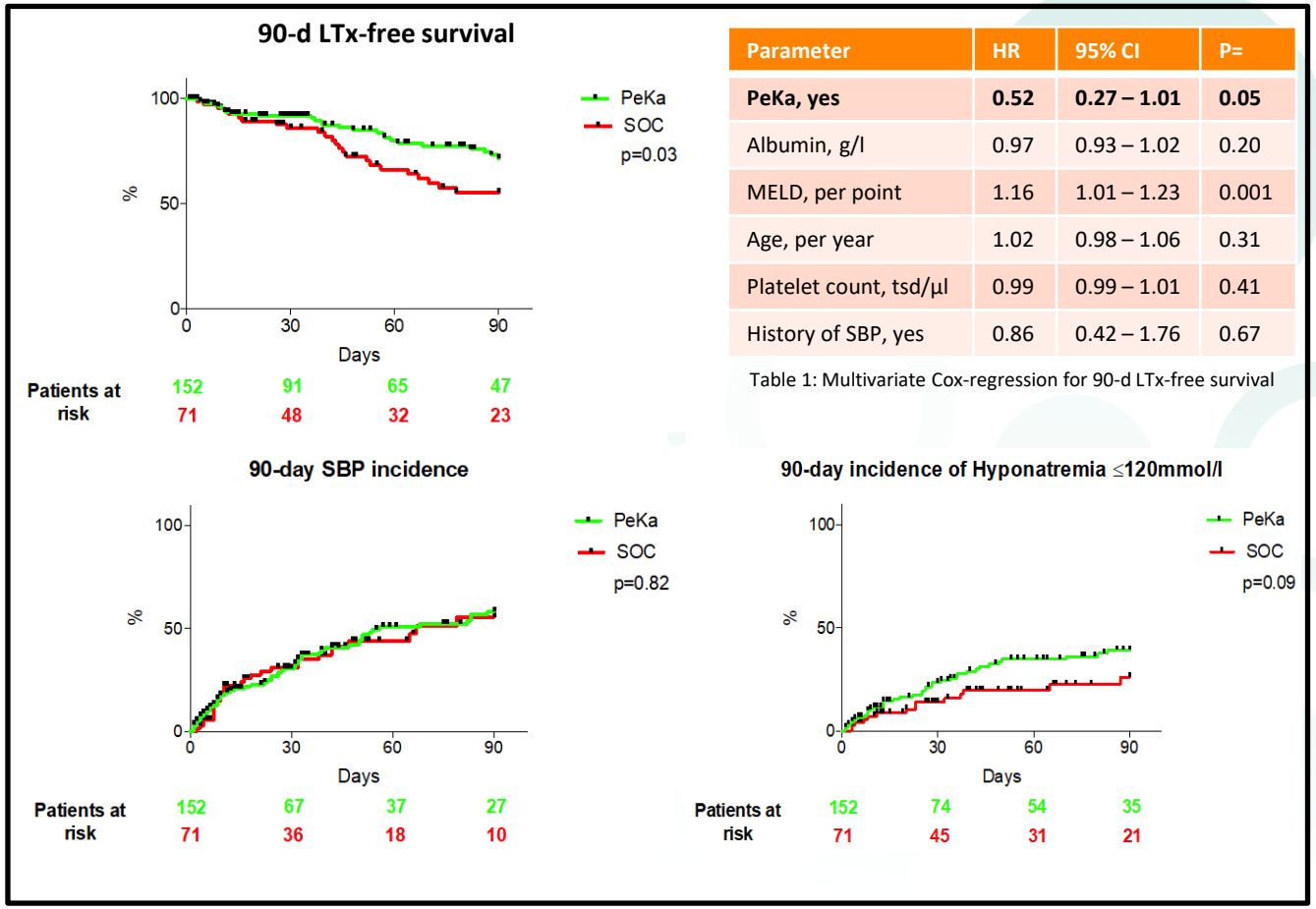
**Aim:** To evaluate the safety of PeKa in a large well-defined cohort of patients with decompensated liver cirrhosis and RA with a TIPS contraindication

**Methods:** Overall, 152 patients with a PeKa and 71 patients with repeated large volume paracentesis (SOC) were included and followed up regarding LTx-free survival, SBP incidence, and incidence of severe hyponatremia (≤120mmol/l)

**Main Findings:**

1. A number of 52 PeKa explants were recorded, median time to explant as 74 days. The most frequent reason for explant was infection (n=28).
2. Patients with PeKa had a higher 90-day LTx-free survival (p=0.03). However, after adjusting for potential confounders, this closely failed to achieve statistical significance (p=0.05).
3. SBP incidence was comparable between patients with SOC and patients with a PeKa (p=0.82).
4. There was a numerical higher incidence of hyponatremia in patients with a PeKa (p=0.09).

**Conclusions:** PeKa is an alternative treatment option in patients with RA and a contraindication for TIPS.




| Parameter | HR | 95% CI | P= |
|---|---|---|---|
| **PeKa, yes** | **0.52** | **0.27 – 1.01** | **0.05** |
| Albumin, g/l | 0.97 | 0.93 – 1.02 | 0.20 |
| MELD, per point | 1.16 | 1.01 – 1.23 | 0.001 |
| Age, per year | 1.02 | 0.98 – 1.06 | 0.31 |
| Platelet count, tsd/µl | 0.99 | 0.99 – 1.01 | 0.41 |
| History of SBP, yes | 0.86 | 0.42 – 1.76 | 0.67 |

Table 1: Multivariate Cox-regression for 90-d LTx-free survival

Tergast TL, et al., Abstract 167.

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# Genetic risk score stratifies risk of cirrhosis and hepatic decompensation in patients with liver disease

## Aim

Examine the impact of a previously published genetic risk score (GRS) upon fibrosis progression and development of decompensated disease across a chronic liver disease (CLD) cohort

## Methods

*Study population:* Collected from Indiana Biobank and includes 4,347 patients with 1,107 CLD cases confirmed by chart review.

*Endpoints:* Cirrhosis was identified at enrollment and at last clinical follow up with Mittal criteria, and decompensation was defined as varices, ascites, encephalopathy, jaundice or MELD>14.

*Statistical considerations:* Logistic regression was used to test the association between a GRS, including the summation of risk alleles from *PNPLA3, TM6SF2, HSD17B14* (0-6), and risk of endpoints. Cox proportional hazard model was used for survival analysis for incident decompensation. Adjusted for age, sex, BMI and 10 principal components.

## Main Findings

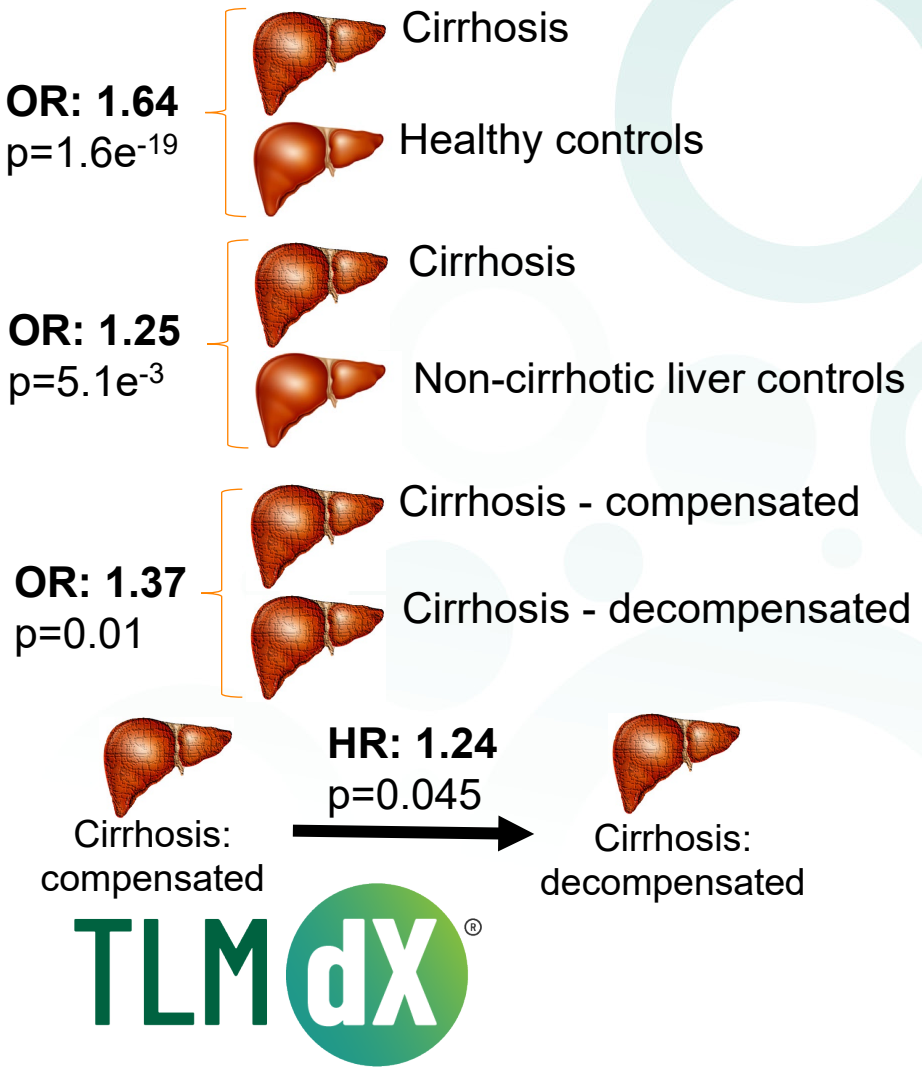
| | Liver Cases and controls (N=4,347) | Liver Cases (N=1,107) | Cirrhosis (N=653) |
|---|---|---|---|
| sex, %male | 41.6% | 50.1% | 56.5% |
| current age, years (mean, sd) | 56.3 (15) | 56.4 (12.1) | 57.2 (10.3) |
| BMI (mean, sd) | 30.9 (7.2) | 31.1 (7.2) | 30.6 (6.9) |
| Mediun follow up, days (Q1, Q3) | N/A | 1,647 (662, 3029) | 1,099 (475, 2278) |
| Compensated, enrollment | N/A | N/A | 41.7% |
| Decompensated, follow-up | N/A | N/A | 55.1% |

## Conclusions

A GRS is associated with risk of cirrhosis and decompensation in a US-based CLD cohort

Lammert C, et al., Abstract 193.

## Main Findings (cont'd)

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# Statins are associated with reduced risk of developing acute-on-chronic liver failure

## Objective

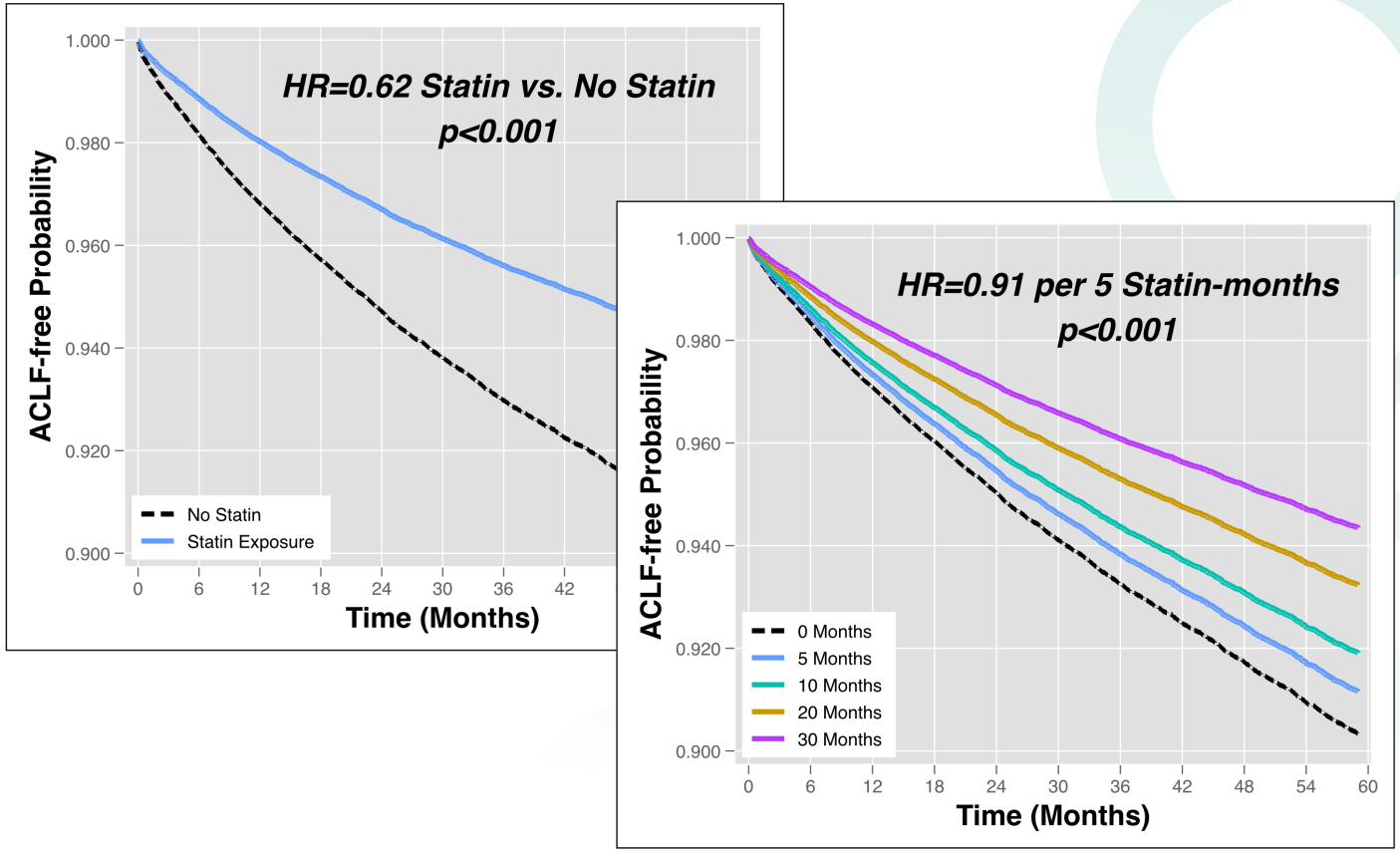
- To evaluate the association between statin exposure and risk of developing acute-on-chronic liver failure

## Methods

- *Design:* retrospective cohort study of patients with cirrhosis in a large Veterans Affairs cohort (VOCAL)
- *Exposure:* time-updating statin exposure over 5 years of follow-up from cirrhosis diagnosis
- *Outcome:* high-grade ACLF (EASL grade 2 or 3)
- *Analysis:* inverse probability weighted Cox proportional hazards regression and marginal structural models

## Conclusions

- Cumulative statin exposure associates with reduced risk of developing acute-on-chronic liver failure




Mahmud N, et al., Abstract 205.

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# Admission microbially-derived metabolites predict while thyroxine levels protect against brain failure: a multi-center metabolomics analysis in inpatients with cirrhosis

## Objective

- Determine admission serum metabolomic profiles to predict the development of grade 3-4 HE (brain failure) in patients admitted without this complication

## Methods

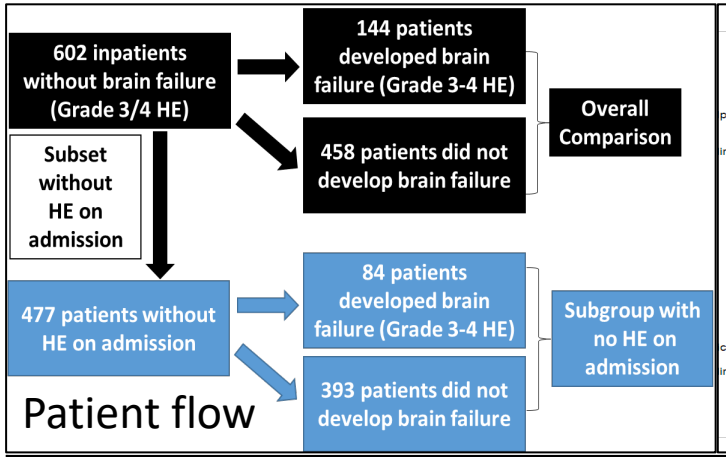
- Admission serum metabolomics from 602 inpatients from 11 centers without grade 3-4 HE were analyzed and adjusted for clinical covariates using ANOVA and Random Forest analysis (RFA).

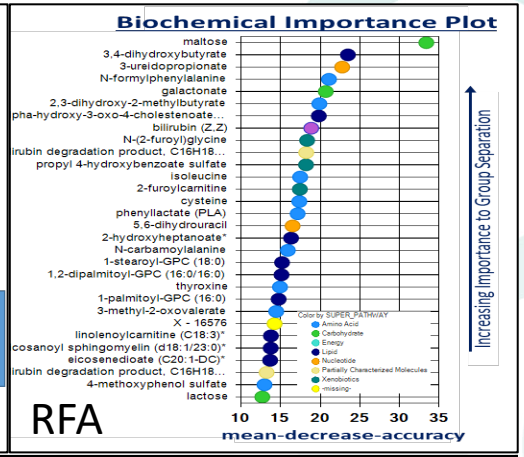
## Main Findings

- 20% patients developed grade 3-4 HE and higher microbially-derived metabolites and lower serum thyroxine predicted grade 3-4 HE development independent of clinical parameters (Figure and Table).

## Conclusions

- Serum metabolites including low thyroxine can predict grade 3-4 HE independent of clinical biomarkers in a multi-center cohort of inpatients with cirrhosis.




**Serum Metabolites Significantly higher on Clinical Variable-Adjusted ANCOVA**

| *: microbially derived metabolites | All Patients (n=602) Developed Brain Failure? | | Without admission HE (n=477) Developed Brain Failure? | |
|---|---|---|---|---|
| | No (n=458) | Yes (n=144) | No (n=393) | Yes (n=85) |
| Aromatic Amino acids (AA) | ↑ thyroxine | ↑3-(4-hydroxyphenyl)lactate*↑ phenyllactate* ↑ N-formylphenylalanine,↑4-methoxyphenol sulfate* | ↑ thyroxine | ↑3-(4-hydroxyphenyl)lactate*, ↑phenyllactate*,↑1-carboxyethylphenylalanine,↑4-methoxyphenol sulfate* |
| Branched chain AAs | ↑Isoleucine | ↑2,3 dihydroxy-2-methyl butyrate | | ↑2,3 dihydroxy-2-methyl butyrate |
| Benzoate metabolism | | ↑Propyl & methy-4-hydroxybenzoate sulfate* | | ↑Propyl & methy-4-hydroxybenzoate sulfate* |
| SCFA/ Carbohydrate | ↑3-4 dihydroxy butyrate | ↑ maltose, ↑ lactose, ↑galactonate | ↑3-4 dihydroxy butyrate | ↑ maltose, ↑galactonate |
| Lipids | ↑1-Stearoyl & palmitoyl-GPC | ↑ 7-HOCA | ↑1-Stearoyl/palmitoyl-GPC | ↑ 7-HOCA |

Bajaj J, et al., Abstract 206.

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# Portal Hypertension/Cirrhosis

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