RNA sequencing (scRNAseq) data from liver biopsies, we previously identified hepatocyte and neutrophil subpopulations enriched in AH. In this study, we focused on the interplay between hepatocytes and neutrophils subpopulations in AH to gain insight into the pathogenesis, with particular emphasis on the via of serum amiloid A - formyl peptide receptor 2 (SAA-FPR2).

Method: scRNAseq data from liver biopsies of patients with ALD at different stages (healthy n = 3; early ALD n = 3; AH n = 6) were analysed using CellChat to identify cellular interactions. The expression of SAA in liver biopsies was assessed by immunofluorescence (IF). SAA expression was assessed in a previously generated in vitro liver organoid model derived from liver biopsies of ALD patients treated with an AH medium containing a mixture of pro-inflammatory mediators (IL1b, TNFa, LPS, ethanol) using IF. SAA secretion in the liver organoid model was measured by ELISA. Human plasma levels of SAA were measured by ELISA in a cohort of patients with different stages of ALD (healthy n = 9; early ALD (F0/F1, F2, compensated cirrhosis) n = 34; AH n = 43) and the association with disease stage, survival (1, 3 and 12 months) and bacterial infections was analysed.

Results: scRNAseq analysis identified two hepatocyte subpopulations enriched in AH and overexpressing SAA, and a neutrophil subpopulation with high expression of IL1R1 and FPR2, the latter identified as a receptor for SAA. In silico analysis revealed a strong interaction between these subpopulations via SAA-FPR2 axis. IF of liver biopsies showed overexpression of SAA in hepatocytes and of IL1R1 and FPR2 in neutrophils from patients with AH. In liver organoids, SAA expression increased notably at the transcriptomic and protein levels in response to stimuli with AH medium. In human plasma, SAA levels increased significantly with ALD progression (healthy: 8782 ng/mL; early ALD: 19285 ng/mL; severe AH: 37710 ng/mL, p = 0.051). In patients with AH, SAA levels were higher in those who died at 1, 3 and 12 months compared to survivors (1 month: 48703 vs. 34885 ng/mL, p = 0.036; 3 months: 46034 vs. 36924 ng/mL, p = 0.038; 1 year: 53990 vs. 20361 ng/mL, p = 0.009). In addition, plasma SAA levels were increased in patients with active bacterial infections (47061 vs 33195 ng/mL, p = 0.053).

Conclusion: This study highlights the pivotal role of SAA-FPR2 in mediating interactions between hepatocytes and neutrophils, two of the most relevant cell populations in AH pathogenesis. We show how SAA increases its expression in response to inflammation, resulting in an intense interaction with neutrophils in the liver and in secretion into the general circulation, showing its utility as a biomarker of disease progression, patient survival and development bacterial infections.

OS-032

Comparative perioperative morbidity and mortality of transplantation for alcohol-related hepatitis or liver disease: data from the QuickTrans study

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Background and aims: Early liver transplantation (LT) improves term survival in patients with severe alcohol-related hepatitis (sAH) who do not respond to medical management, but few perioperative data are available. The aim of this study was to compare the perioperative morbidity outcomes and mortality of patients transplanted for sAH or decompensated alcohol-related cirrhosis.

Method: In the prospective multicenter QuickTrans study (19 centers), perioperative data (up to 90 days post-LT) of patients transplanted for sAH or decompensated alcohol-related cirrhosis were collected retrospectively. Pre-LT, perioperative, postoperative data and survival at 90 days and 2 years were compared between the 2 groups.

Results: Between 2012 and 2016, 68 patients with sAH were transplanted (group A) and 93 patients underwent standard LT for decompensated alcohol-related cirrhosis (group B). The Charlson index (with a median of 4, p = 0.3) and the median age of the donor (61 years in group A *vs.* 59.5 in group B, p = 0.46) were similar. Median cold ischemia time was also similar: 467 (A) *vs.* 465 minutes (B), p = 0.95. Patients transplanted for sAH tended to receive more transfusions during LT (median of 6 vs. 4 packed red blood cells, p = 0.08). During LT, patients with sAH had more often hemodynamic instability or bleeding (39.7 *vs.* 24.7%, p = 0.04). Patients transplanted for sAH had a trend toward being still intubated after 24 hours (79.4 *vs.* 65.9%, p = 0.07) and being on vasopressive support (32.1 vs. 20.2%, p = 0.12). After LT, 31.3% of patients with sAH needed renal replacement therapy *vs.* 19.1% in group B, p = 0.08. The length of stay in ICU after LT was two times longer in group A (10 vs. 5 days, p = 0.0002) and the total length of stay after LT was longer in group A (32 *vs.* 22.5 days, p = 0.0006). In univariate analysis, being transplanted for sAH and the MELD score at LT were associated with the risk of being still hospitalized 30 days after LT. In multivariate analysis, only sAH was independently associated with this risk (p = 0.04), whereas the MELD score was not (p = 0.22). After LT, 80.9% of patients (group A) *vs.* 76.3% (group B) had complications (p = 0.5), with infections or surgical complications being the most frequent, with no difference between the two groups (respectively 35.3 *vs.* 31.2%, p = 0.58 and 36.8 *vs.* 32.3, p = 0.55). Survival in the 2 groups was identical at 90 days (94.1 ± 2.9 *vs.* 94.6 ± 2.4%, p = 0.9) and 2 years after LT (89.6 ± 3.7 *vs.* 88 ± 3.4%, p = 0.77).

Conclusion: While patients transplanted for sAH have similar survival and complication rate after LT as patients transplanted for cirrhosis, their ICU and hospital stays are longer. These patients also have a more frequent need for renal replacement therapy and a trend toward postoperative delayed extubation and discontinuation of vasopressors. These results underline the need for adapting perioperative management of patients transplanted for alcohol-related hepatitis.

OS-033

Liver injury induced by CDK4/6 inhibitors for metastatic breast cancer: characterization and management. Data from a multicenter study

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