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**Serum bile acid profiles distinguish severe alcoholic hepatitis from decompensated alcohol-related cirrhosis**

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**Background and aims:** Alcoholic hepatitis (AH) is characterised by recent onset jaundice in patients with ongoing alcohol misuse. Distinguishing AH from decompensated alcohol-related cirrhosis (DC) guides rational use of prednisolone but can be challenging. Demonstration of steatohepatitis on liver biopsy remains the gold standard. Liver biopsy is not universally available and both biopsy and prednisolone are associated with complications. Differences in the serum bile acid (BA) profiles of patients with AH and DC have been reported. The aim of this study was to determine whether serum BAs can non-invasively discriminate between AH and DC.

**Method:** Serum BAs were measured by ultraperformance liquid chromatography-mass spectrometry in exploratory and validation cohorts. Patients with AH had a Maddrey’s Discriminant Function (DF) > 32 and steatohepatitis on liver biopsy. The exploratory cohort comprised 68 patients with AH (median Model for End-stage Liver Disease score, MELD, 23) and 21 with DC (defined as MELD > 18; median 26); the validation cohort comprised 65 patients with AH (median MELD 25) and 40 with DC and jaundice (defined as bilirubin > 80 micromol/L and DF > 32; median MELD 30). Mean age was 49 years; 69% were male. Data was analysed by orthogonal projection to least squares discriminant analysis (OPLS-DA) and area under the receiver operating curve (AUROC) analysis.

**Results:** OPLS-DA accurately discriminated AH from DC in both exploratory and validation cohorts. The AUROC for the full BA profiles was 0.93 (95%CI 0.87-0.99) and 0.93 (95%CI 0.88-0.98) respectively. Model diagnostics identified glycocholic (GCA) and taurocholic (TCA) acid as dominant metabolites. The AUROC for serum GCA was 0.90 (95%CI 0.83-0.97) in the exploratory and 0.85 (95%CI 0.77-0.92) in the validation cohorts. The AUROCs for TCA were 0.87 (95%CI 0.77-0.97) and 0.83 (95%CI 0.74-0.92). Both performed better than bilirubin (AUROC 0.79 (95%CI 0.67-0.91) and 0.65 (95%CI 0.54-0.76) respectively. In the validation cohort, TCA concentration more than or equal to 8300 nM had a sensitivity and specificity for AH of 83% and 85%.

**Conclusion:** AH has a serum BA profile distinct from patients with DC and similar liver dysfunction and jaundice. The discriminatory performance of both the entire bile acid profile and individual bile acids (GCA and TCA) indicates that they are promising non-invasive biomarkers for severe AH and may reduce the need for liver biopsy.

**Figure:**
Area under the receiver operating characteristic analyses for serum bile acids and bilirubin

Validation Cohort

Diagonal segments are produced by ties.