PTH-105 HOSPITAL ADMISSION IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE DUE TO NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction Individuals with non-alcoholic fatty liver disease (NAFLD) often have multiple medical comorbidities. The development of advanced chronic liver disease is considered a defining point in the natural history of NAFLD. The aims of this study were to pilot the use of electronic health record (EHR) follow-up of patients with NAFLD and to assess the frequency of clinical events due to both complications of liver disease and also non-liver related causes.

Methods Transient elastography data was collected from St James's University Hospital in Leeds between 2012–2017. Patients were defined as having advanced chronic liver disease based on liver stiffness measurement (LSM) >10 kPa and were analysed in two strata: ≥10–15 kPa, and >15 kPa. Hospital admissions and mortality were recorded from data submitted to NHSDigital, and sub-divided into liver-related and non-liver related causes.

Results The study included 486 patients: 303 (62%) male, mean age 56 years. Median follow-up interval was 24 months. Data regarding admissions is summarised in table 1. Four patients (all with LSM >20 kPa) were admitted on eight occasions with decompensation as a primary diagnosis code (5 admissions with hepatic encephalopathy, 2 variceal bleeding and 1 ascites). Four patients had primary diagnosis codes for hepatocellular carcinoma. Overall, liver-related events accounted for a minority of admissions. Considering inpatient admissions, only 1 in 5 admissions were for complications of liver disease, even amongst those individuals with LSM >15 kPa (table 1). The most common causes of non-liver related admission according to ICD-10 code were gastrointestinal (14%), cardiovascular (11%), musculoskeletal (10%) and respiratory (9%). Overall 17/486 individuals (3.5%) had died (5 patients ≥10–15 kPa; 12 patients >15 kPa). Liver disease was listed as a contributing factor in a minority of cases (5/17, 29%).

Abstract PTH-105 Table 1 Number of patients with liver and non-liver related admissions

Admissions	Patients TE _{≥10–15} kPa LSM n=252	Patients TE _{>15} kPa LSM n=234
Type of admission	Inpatient n=58	Inpatient n=89
Liver related	8	18
Non-liver related	50	71

Conclusions EHR can be used to accurately define outcomes in patients with advanced chronic liver disease due to NAFLD. The finding that liver related morbidity and mortality accounts for only 1 in 5 clinical events for patients with NAFLD and advanced chronic liver disease will significantly reduce the effectiveness of novel therapeutics in development for this patient group.

PTH-106 PLASMA S100A8/A9: A NOVEL MECHANISTIC BIOMARKER IN INNATE IMMUNE ACTIVATION IN ACUTE-ON-CHRONIC LIVER FAILURE

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Introduction Acute-on-chronic liver failure (ACLF) is driven by systemic inflammation but lacks reliable diagnostic or prognostic biomarkers. Circulating S100A8/A9 heterodimer (calprotectin) is secreted by activated myeloid cells to activate and propagate innate immune responses and organ dysfunction. This study aims to evaluate circulating levels of S100A8/A9 in ACLF and determine its effect on myeloid cell function.

Methods Plasma S100A8/A9 concentration of 92 patients at admission was analysed using enzyme-linked immunosorbent assay (ELISA) in ACLF (n=62), cirrhosis without organ failure (n=28) and healthy control (n=30) groups. Baseline plasma cytokines were measured by multiplex immunoassay. Indices of disease severity and survival was evaluated with Kaplan Meier analysis. Phenotype (CD11b, HLA-DR, Mer tyrosine kinase [MerTK], CD163 and CD206) of healthy CD14⁺ monocytes cultured with S100A8/A9 *in vitro* for 24 hours at 0, 1000 and 2500 ng/ml was assessed using flow cytometry (n=6).

Results Admission plasma S100A8/A9 was higher in ACLF (median 2000 ng/ml) compared with cirrhotics without organ failure (934.8 ng/ml p=0.007) and healthy control (963 ng/ml p=0.003) (figure 1). S100A8/A9 was higher in patients with systemic inflammatory response syndrome (SIRS) (p=0.045) and non-survivors (p=0.01). Baseline interleukin-1β (IL-1β) was elevated in ACLF compared to healthy (0.07 vs. 0.36 pg/ml p=0.009), correlating with S100A8/A9 concentration (r=0.508 p=0.01). Area under the receiver operating characteristic curve (AUROC) for S100A8/A9 to detect the presence of ACLF was 0.681 (p=0.009). For 90 day mortality in ACLF, AUROC was 0.694 (p=0.014) but highest for the CLIF-ACLF score (0.767, p=0.001). S100A8/A9 >1406 ng/ml (sensitivity 0.73 specificity 0.61) was associated with decreased transplant-free survival (log rank p=0.02) (figure 2). S100A8/A9 predicted 90 day mortality (p=0.018) on univariate analysis, remaining significant in a multivariate logistic regression model (OR 1.0 p=0.04). In flow cytometric analysis, activated CD11b⁺HLA-DR^{high}MerTK^{low} myeloid cells (%) significantly increased (p=0.01, Friedman's ANOVA) as S100A8/A9 concentration increased from 1000 to 2500 ng/ml with a trend to reduction in CD206 (p=0.13) (figure 3).

Abstract PTH-106 Figure 1