Conclusion We have identified and characterized a rare causal variant in MTTP and homozygosity for MTTP p.I564T is associated with progressive NAFLD without any other manifestations of abetalipoproteinemia.

P041 TANDEM MASS TAG-BASED QUANTITATIVE PROTEOMIC PROFILING IDENTIFIES NOVEL PUTATIVE SERUM BIOMARKERS FOR THE DIAGNOSIS OF DRUG-INDUCED LIVER INJURY IN PATIENTS

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Background Diagnosis of drug-induced liver injury (DILI) remains a significant challenge in interventional clinical trials during drug development and in clinical practice. We aimed to discover novel diagnostic biomarkers using proteomics and to evaluate their performance characteristics in distinguishing DILI from acute and chronic liver injury from other etiologies.

Methods Adults with idiosyncratic DILI and acute non-DILI liver disease controls were recruited to the Prospective European DILI Registry. Case definitions and causality assessment were performed according to European Association for the Study of the Liver recommendations. Tandem Mass Tag (TMT) labelled quantitative proteomics was performed in serum samples from a discovery set of healthy volunteers (HV, n=10), patients with DILI at onset (DO) and recovery (DR) (n=10 each); acute non-DILI controls at onset (NDO) and recovery (NDR) (n=5 each) and patients with non-alcoholic fatty liver disease (n=10). The performance of top biomarker candidates was assessed in a confirmatory cohort with HV (n=60), DO (n=83), DR (n=85), NDO (n=35) and NDR (n=21) using peptide-based targeted mass spectrometry. Novel biomarkers and patient status were evaluated using univariate and multivariate models.

Results Global proteomic profiling of the discovery cohort revealed 2323 proteins, of which 12 novel biomarkers were chosen based on differential expression, liver specificity, and mechanistic relevance to liver biology/pathogenesis. In the confirmatory analysis, serum concentration of the novel biomarkers was significantly different at DO and returned to levels comparable to HV during recovery (DR). When the diagnostic performance of these 12 biomarkers was assessed

individually, along with the promising biomarker Cytokeratin 18 (CK18, Area Under the Receiver Operator Characteristic (AUROC) Curve = 0.96), the following biomarkers demonstrated the highest sensitivity/specificity (DILI vs HV): Cytoplasmic aconitate hydratase (ACO1, 0.99), Argininosuccinate synthase (ASS1, 0.98), Fumarylacetoacetase (FAH, 0.98), Carbamoyl-phosphate synthase (CPS1, 0.96), Fructose-bisphosphate aldolase B (ALDOB, 0.94), 4-Hydroxyphenylpyruvate dioxygenase (HPD, 0.94), Ornithine carbamoyltransferase (OTC, 0.92).

Conclusion A TMT-based quantitative proteomic profiling approach identified novel putative biomarkers, which are candidates for further evaluation of their role in the diagnosis and prognostication of DILI.

P042 AN AUDIT OF THE KNOWLEDGE OF THE DECOMPENSATED LIVER DISEASE BUNDLE AND ASCITIC TAPS ON PATIENTS PRESENTING ON THE MEDICAL TAKE

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Background The BSG-BASL decompensated cirrhosis care bundle seeks to optimise patient management during the first 24 hours of presentation. The pandemic has impacted on junior doctors' hepatology training, by reducing access to face-to-face teaching. We sought to redress this by assessing how a remote education programme could affect bundle implementation and awareness, shortly after the UK's first COVID-19 wave.

Methods A retrospective snapshot case-note audit was undertaken for 4 weeks (August 2020) at Bristol Royal Infirmary (BRI). Decompensated cirrhosis admissions were identified from coding and bundle usage and compliance with ascitic tap guidance were quantified. An online survey was conducted of BRI junior doctors (medical) to assess knowledge of the bundle and awareness of appropriate ascitic fluid tests. Subsequent quality improvement interventions were developed, with repeat audits in May-June 2021.

Results The baseline audit identified appropriate bundle completion in 50% (n=8/16) decompensated cirrhosis patients, none by foundation doctors, with 2 by hepatology consultants. Ascitic tap was attempted in only 50% of patients with detectable ascites (4/8), with recommended tests requested in 2 of 3 successful taps.

The online survey (40 participants 42% response) revealed good knowledge of when to use the bundle (85%) and how to access it (90%). For patients with new ascites, 46% of participants identified appropriate tests, however 39/40 also selected unnecessary options. Knowledge was poorer for patients with known ascites; 20% selected correct investigations and no participants knew the exact combination to request. Procedural skills varied, 49% of participants had performed an ascitic tap unsupervised, but 33% had never attempted one.

After these audits, remote teaching sessions and posters were used to improve prompting of bundle completion; paper copies were distributed to admission areas. Re-audit (May 2020) identified 15 hepatic decompensation admissions, of

whom 53% (n=8) had a completed bundle. 9 ascitic taps were attempted in 13 patients with ascites (69%); correct investigations were requested in 5 of 7 taps (71%). At a repeat online survey (32% response rate) 10% (3/30) selected only the necessary investigations for new ascites and 13% (4/30) for recurrent ascites. This indicates that knowledge has not significantly improved.

Conclusion There remained low usage of the BSG-BASL decompensated cirrhosis bundle despite an education campaign. Ascitic tap performance improved but test requesting remained suboptimal. Systematic changes such as IT-system alerts and integrated guidance on key ascites tests within bundle documentation may be more sustainable ways of improving compliance (data will be presented).

P043 EXPLORATORY PROTEOMIC ANALYSIS OF SYSTEMIC CHANGES IN ALF PATIENTS UNDERGOING PEX

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Background Acute liver failure (ALF) is defined by hepatic encephalopathy and an International Normalised Ratio greater than 1.5 in a patient with no underlying chronic liver disease. Standard-volume Plasma Exchange (SVPEX) is an extracorporeal procedure that separates plasma constituents from the cellular blood components by centrifugation and replaces it with stored plasma. There is mounting evidence supporting the clinical use of PEX as a therapy in ALF. The primary objective of this prospective pilot-exploratory proteomic study is to investigate the broad systemic changes induced by PEX on circulating proteins in patients with ALF before and after PEX.

Methods Clinical parameters were compared in paracetamol-induced ALF patients receiving PEX (n=3) and ALF patients not receiving PEX (n=4). Circulating plasma protein levels were compared via mass spectrometry in 17 plasma samples from patients receiving PEX (n=2), not receiving PEX (n=2) and healthy controls (n=2).

Results INR and PT medians were 10% higher at baseline in the PEX group compared to ALF controls. Following the first PEX cycle, INR and PT were 20% lower than in ALF controls on day 2. On mass spectrometry, several circulating proteins increased over two-fold immediately or 12 hours following PEX, in particular clotting and complement factors and apolipoproteins. Some proteins decreased to less than 50% following PEX, with the 20S proteasomes being of particular interest.

Discussion This study is the first broad-spectrum proteomic analysis of plasma proteins in patients with ALF during and after SVPEX. PEX may improve patient clinical parameters and prognosis by several mechanisms, including the removal of the 20S proteasomes of the ubiquitin pathway, which may have a role in inducing vascular damages and multi-organ failure. This initial analysis has highlighted the potential of proteomics to profile changes induced in PEX. This will now be extended and validated with additional patients and proteomic approaches by the end of July.

P044

HEALTHCARE RECOURSE USE IN PATIENTS WITH CIRRHOTIC ASCITES: A UK REAL WORLD EVIDENCE STUDY

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Introduction Decompensated cirrhosis is a major cause of morbidity and mortality in the United Kingdom (UK).¹ The development of ascites complicating cirrhosis frequently represents the first manifestation of decompensation, is a hallmark of advanced liver disease and frequently a prelude to other complications. Refractory ascites (RA), characterised by early recurrence after initial paracentesis, is associated with a worse prognosis.² The objective of the present study was to describe healthcare resource utilisation and costs incurred by cirrhotic patients following presentation to the South West Liver Unit with large volume ascites requiring paracentesis.

Methods A retrospective study using the Hospital Episode Statistics (HES) data from University Hospitals Plymouth was performed. Patients with decompensated cirrhosis and ascites based on liver disease ICD-10 codes (K70-K77) requiring paracentesis (T46) between January-2015 and February-2020 were identified and healthcare resource utilisation/costs assessed over the following 12 months or until Transjugular Intrahepatic Portosystemic Shunt (TIPS) insertion, liver transplant, diagnosis of RA or death. RA was defined by the need for 2 or more paracenteses in a month. The subset of patients who developed RA were followed up for 12 additional months. Outpatient visits, elective and non-elective admissions and mortality were quantified and costed for the overall population and the sub-group who developed RA.

Results HES data identified a cohort of 524 cirrhotic patients with ascites. Mean age was 61.8 years and 57.8% were male. 12-month mortality was 22.3%. 3489 outpatient visits, 509 elective day cases, 284 elective admissions and 969 non-elective admissions were required. The mean cost per patient was £12,176 per year. A total of 1061 paracenteses were performed during the 12-month follow-up. RA developed in 129 (24.6%) cases. Patients with RA were more likely to require hospitalisation (421 day cases, 421 non-elective and 206 elective admissions), had more outpatient appointments (1693) and a greater requirement for paracenteses (618 procedures) during the subsequent 12 months. This resulted in a greater mean cost per patient (£23,810 per year).

Conclusions The development of ascites in cirrhotic patients is associated with significant healthcare resource utilisation and high mortality. One in four patients developed refractory ascites within 12 months of first paracentesis and in these patients hospitalisation rates, outpatient appointments and paracentesis more than doubled, with a significant increase in associated cost. Future treatment strategies that can reduce the likelihood of developing RA may help mitigate costs and ease the burden on both health systems and patients.

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