factors for NAFLD were significant predictors of liver pathology. The phenomenon of methotrexate-related hepatotoxicity is likely to have been historically over-estimated. Our results suggest that this cohort had NAFLD as the underlying cause of liver fibrosis. The STrATIFY study continues to recruit participants.

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P1 LONG TERM ABDOMINAL DRAIN FOR PALLIATION IN ADVANCE LIVER CIRRHOSIS: A SURVEY OF RISKS & BARRIERS

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Introduction Ascites is a leading cause of hospital admission in patients with cirrhosis, with up to a third developing refractory ascites (RA.) RA has a median transplant free survival of 6 months,[1] yet palliation remains sub-optimal and practice varies widely. Long term ascitic drains (LTAD) are standard of care in malignant ascites but there is a paucity of data to support use in advanced cirrhosis. Our aim was to establish current views and practices of gastroenterologists and hepatologists towards LTAD as a palliative intervention in advanced cirrhosis.

Methods An electronic survey of 10 questions was designed by a focus group of four hepatologists with a special interest in palliative management of advanced cirrhosis. The survey included seven questions with fixed quantitative options and three exploratory questions with free text space. The survey was logged on survey monkey and distributed electronically via the BASL website and also to relevant departments in Brighton and North East London, with reminder emails in four and eight weeks.

Results The survey was completed by 210 respondents over 16 weeks with 99% completion rates for all questions with quantitative endpoints. Respondents included Hepatologists (36.8%,) specialist nurses (24.4%,) gastroenterologists (16.3%) and trainees (15.3%.) Ninety-six percent of respondents looked after patients with RA and 70% had experience of LTAD. All respondents had access to large volume paracentesis, 86.1% to TIPSS, 67% to LTAD and 6% to the Alpha pump. The commonest deterrent to use of LTAD was infection risk (90%), followed by community management of LTAD in these complex patients (56.5%). Patient/carer dissatisfaction (as reported by clinicians) did not seem to be a major cause of concern.

Fifty-six percent of those with experience reported clinical consequences (bleeding, infection, renal impairment) 41.4% reported technical issues and 35.8% inadequate community support. Additional themes emerged, including: lack of clear guidance on use of LTAD in advanced cirrhosis, the role of human albumin solution, monitoring of renal function and funding.

Conclusions This national survey of clinicians managing RA in the setting of advanced cirrhosis shows that the majority would be willing to consider LTAD, the main deterrent being infection risk. Additional concerns identified were: lack of training, funding concerns and absence of clear guidelines on community management of LTAD. Our survey highlights the need for a robustly designed randomised controlled trial to assess palliative interventions for the management of RA in advanced cirrhosis.

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P2 PDLIM5 IN HEPATIC STELLATE CELLS IS UPSTREAM OF PRO-FIBROTIC YAP1 MECHANO-TRANSDUCTION

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Introduction Liver fibrosis is excessive remodelling of the extracellular matrix (ECM) leading to tissue scarring and eventually impaired liver function. Hepatic stellate cells (HSCs) are the key cellular drivers of liver fibrosis responsible for the formation of stiffened fibrotic ECM in response to liver injury. Activation of HSCs is driven and maintained by increased matrix stiffness. Yes Associated Protein1 (YAP1) appears to be a critical mechano-regulator of HSC activation and fibrotic gene expression. Functional disruption of YAP1 reduces liver fibrosis; we therefore sought to identify how external cues from the ECM are transduced by the HSC cytoskeleton, and regulate YAP1 activity. We identify Enigma family protein PDLIM5 as a potential driver of YAP1 mechano-activation.

Methods Human liver tissue was from the Manchester Biobank (ethical approval NW1260/22). Primary human or mouse HSCs were isolated using standard liver perfusion, digestion and density gradient centrifugation. Total RNA extracted from quiescent and activated mouse (mHSCs) was used for RNA-seq following the HISeq Illumina protocol and identification of differentially expression genes (DEG) by DESeq2. PDLIM5 gene and protein expression was characterized in immortalized human HSCs (LX-2 cells) and primary HSCs by qPCR, western blot (WB) and immunocytochemistry (ICC). siRNA was used to disrupt PDLIM5 expression in LX-2 cells. qPCR, WB and ICC were used to assay LX-2 phenotype.

Results The transcriptome analysis of activated mHSCs revealed 6053 DEGs. Gene ontology analyses showed that the activated HSC transcriptome is characterized biologically by expression of genes related to ECM organization and secretion, and genes implicated in the regulation of the actin cytoskeleton. The transcriptome of activated HSCs had significantly increased expression of Enigma protein coding genes including PDLIM5. Enigma proteins are cytoskeleton associated proteins

involved in mechano-transduction. PDLIM5 mRNA expression was confirmed by qPCR, and PDLIM5 protein expression was demonstrated by WB and ICC in both LX-2 cells and primary HSCs. Stimulation of LX-2 cells with TGFβ (2 ng/ml) for 24 hrs significantly increased expression of enigma proteins. siRNA knock down of PDLIM5 reduced the expression of fibrotic genes including ACTA2, CTGF, and COL1; and was accompanied by increased cytoplasmic localization and phosphorylation (inactivation) of YAP1.

Conclusion In brief, our work defined a new mechanism for activation and nuclear translocation of YAP1 in HSCs via the enigma family protein PDLIM5. Understanding hippo independent mechanisms of YAP1 activation in HSCs may reveal novel targets for urgently needed anti-fibrotics.

P3 PORTO-MESENTERIC THROMBOSIS IN A NON-CIRRHOTIC PATIENT WITH SARS-COV-2 INFECTION

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Introduction During the coronavirus 2019 (COVID-19) pandemic, it is clear this novel coronavirus generates a markedly hypercoagulable state. Thrombotic events are driven by a severe pro-inflammatory response to COVID-19 as well as hypoxia manifested in severe illness. Whilst the commonest thrombotic events associated with COVID-19 remain pulmonary embolism, myocardial infarction and deep vein thrombosis, intra-abdominal thromboses are less well characterised, but are illustrated in this case.

Case Presentation A 42 year-old Eastern European man with chronic hepatitis B (undetectable viral load on Entecavir; eAg negative; sAg positive; alanine transaminase (ALT) 34 IU/l; FibroScan 7.4kPa Nov 2019), and prior trauma-related splenectomy (1998), developed pyrexia and cough on the 23rd March 2020.

His fever resolved on symptom-day 10, following a course of Amoxicillin, then Doxycycline, for presumed bronchitis from his GP. On symptom day 14, he woke with constant non-radiating right hypochondrial pain. The following day he presented to his local hospital and was managed conservatively for suspected biliary colic (no imaging). His bilirubin was 23µmol/l, ALT 55 IU/l, alkaline phosphatase (ALP) 66 IU/l and albumin 31 g/l. Having been discharged with analgesia, he re-presented to his GP with ongoing worsening pain on symptom-day 25. His bilirubin was now 33µmol/l, ALT 31 IU/l, ALP 74 IU/l and albumin 35 g/l. Abdominal ultrasound suggested portal vein thrombosis (PVT) with collateralisation.

He was subsequently admitted by the general surgeons and a CT-abdomen demonstrated loss of enhancement of the entire length of the portal vein and proximal superior mesenteric vein, with expansion and surrounding inflammatory stranding consistent with thrombosis. Concurrent CT-chest demonstrated bilateral patchy ill-defined ground glass opacities with basal predominance, worse on the right, consistent with COVID-19 infection. Whilst his RT-PCR was negative, subsequent SARS-CoV-2 antibody serology was positive. His thrombophilia screen excluded inherited and acquired thrombophilia such as antiphospholipid syndrome. His repeat triple phase CT-abdomen 6 weeks later, confirmed an established PVT with collateralisation extending into the upper abdomen. Having been commenced on Apixaban 5 mg BD in April 2020, he is currently asymptomatic.

Discussion This is one of the first cases of likely COVID-19-related porto-mesenteric thrombosis to be described in the UK. Similar cases have been described in France and Italy in non-cirrhotic patients. With almost a fifth of COVID-19 infections presenting with gastrointestinal symptoms, and a recent meta-analysis suggesting 9.2% developing abdominal pain, our threshold for performing liver ultrasound with doppler assessment must be lower to avoid missing this reversible complication of COVID-19.

P4 A 21 YEAR REVIEW OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT PLACEMENTS IN UNIVERSITY HOSPITAL OF WALES, CARDIFF

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Introduction Decompensated cirrhosis is associated with poor outcomes and the incidence of advanced liver disease has increased in Wales over the last two decades. Transjugular intrahepatic portosystemic shunts (TIPSS) are an effective treatment of recurrent variceal bleeding and refractory ascites.

Methods A retrospective casenote review of all successful and unsuccessful TIPSS procedures at University Hospital of Wales. Clinical scores were calculated from bloods at the time of TIPSS placement. These cases were then compared to the 2020 BSG TIPSS guidelines[1] for concordance.

Results 93 TIPSS procedures were attempted between March 1999 and June 2020, 85 (91%) of which were successful. The average age was 58 (29–84) and 54 (58%) were male. 72 (77.4%) referrals were from Cardiff and Vale, 19 (20.4%) were from the rest of South Wales, and 2 (2.2%) were from England.

The predominant aetiologies of cirrhosis were alcohol (44%), NASH (23%), viral hepatitis (9%) and PBC (6%).

The main indications for TIPSS were oesophageal (53%) and gastric (11%) variceal bleeding, resistant ascites (24%), stomal variceal bleeding (6%). Of note, a caecal varix was the indication in one case and GAVE was the indication in two cases (a failed TIPSS that was then repeated successfully in the same patient). The average MELD-Na was 14 (6–29). The average post-TIPSS gradient was 8.5 mmHg (2–13). 30-day survival was 93%. Poorer survival was associated with increasing MELD-Na. All 4 patients with MELD-Na >24 died by day 32. There has been an increase in TIPSS procedures from an average of 1 per year between 1999–2004 to 8 per year between 2017–2019. 11 TIPSS procedures were performed in 2019, all successful. 6 successful TIPSS performed in 2020 so far.

Discussion TIPSS is an effective therapy in selected cases. The demand for TIPSS is increasing. Formalised referral pathways would improve access across South Wales. In alignment with the 2020 BSG TIPSS guidelines[1] a concordant indication was present in 91/93 (97.8%) of cases.