of this protein lies within its coiled coil region. Two new epitopes, one of which dominant, have being discovered, both in PBC and SS. The fact that the fine epitope specificity of anti-Ro-52 is virtually identical in PBC and SS suggests a common mechanism of tolerance breakdown to this autoantigen in the two conditions.

P06 HEPATIC LUMICAN EXPRESSION IN PAEDIATRIC NON-ALCOHOLIC FATTY LIVER DISEASE

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E Fitzpatrick, R Mitry, A Quaglia, A Dhawan. *Paediatric Liver Centre, King's College Hospital, London, UK*

Introduction Lumican is a glycoprotein involved in collagen cross-linking and modulation of the innate immune system. Over-expression of lumican was recently described in a group of adult patients with histologically progressive non-alcoholic fatty liver disease (NAFLD). It has not yet been evaluated in paediatric NAFLD.
Aim The aim of this study was to determine the degree of lumican expression in the liver of children with varying stages of NAFLD.
Method The study group consisted of 24 children (17 boys), median age 13.1 years, with liver biopsy-proven NAFLD and six children with chronic liver disease other than NAFLD (four with auto-immune hepatitis and two with Wilson disease). Paraffin-embedded biopsy sections were scored according to the NAFLD Activity Score (NAS). Sections were immuno-stained for lumican using HRP-DAB. Quantitative analysis was performed using imageJ (NIH, USA), expressing lumican staining as percentage of the total area. In addition, relative quantification real-time PCR for lumican was undertaken on frozen biopsy specimens.
Results Median BMI z-score of the group with NAFLD was 2.2 and median HOMA-IR; 4.4. 58% had splenomegaly. Thirteen children scored =5 (NASH), 6 scored 3–4 (borderline) and 5 scored=2 (simple steatosis). Fibrosis was minimal in 10 (F<2) and significant in 14 (F=2). Two children had type 1 NASH, the remainder had type 2 or a mixed pattern. Lumican was overexpressed in those with significant fibrosis (F=2) vs those with minimal fibrosis (F<2); (168%, p=0.01). Lumican was also overexpressed in NASH vs simple steatosis (215%, p=0.012). The pattern of lumican staining followed the sinusoidal contour, and marked the portal vascular endothelium and the luminal border of bile ducts. There was no clear staining of hepatocytes. At gene level, lumican was upregulated (compared to normal control liver) in those with F=2 (15.8-fold) and in those with F<2 (10.9-fold). Lumican expression was not related to age, BMI z-score, HOMA-IR, splenomegaly or transaminase levels. There was variable expression of lumican in the biopsies of those with chronic liver disease other than NAFLD. Percentage area stained did not correlate with degree of fibrosis in these patients.
Conclusion Lumican is expressed with increasing severity of paediatric NAFLD. Upregulation at gene level in those with both minimal and histologically more severe disease is also evident. The role of lumican in progression of disease has not yet been elucidated and should be the focus of further investigation.

P07 SPLANCHNIC STEAL IN PATIENTS WITH LIVER DISEASE: A 3T MRI STUDY OF VISCERAL BLOOD FLOW

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N McAvoy, K A Leyland, J M J Richards, S I K Semple, D Patel, D E Newby, P C Hayes. *Liver Unit, Univeristy of Edinburgh, UK*

Introduction Liver cirrhosis and the development of portal hypertension is associated with significant morbidity and mortality. It is widely accepted that patients with liver disease have a hyperdynamic circulation that is associated with an increased cardiac output. We have previously proposed that, rather than a generalised systemic vasodilatation, there is selective splanchnic vasodilatation with concomitant vasoconstriction in other vascular beds: the so-called "splanchnic steal" phenomenon.
Aim To measure regional visceral blood flow using 3T magnetic resonance imaging in patients with liver disease.
Method Single centre pilot study of 19 subjects (10 healthy controls, nine patients with liver disease). Arterial and venous phase magnetic resonance angiograms were obtained using a Siemens 3T Verio MR scanner with gadolinium contrast. From these MRA's, ECG-gated phase contrast flow measurement MR data were then positioned and measured in the hepatic artery, portal vein, superior mesenteric artery, descending thoracic aorta, distal abdominal aorta, and the renal and carotid arteries.
Results Mean MELD score in patient group was 14 (range 7–21) with a range of aetiologies: alcoholic (6), non-alcoholic fatty (1), autoimmune (1), hepatitis C virus (1). In comparison to controls, flow in the descending thoracic aorta was increased by 43% in patients with liver disease (4.74 vs 3.32 L/min; p=0.021) consistent with an increased cardiac output. Hepatic artery flow showed a trend towards increase in patients (0.47 vs 0.27 L/min; p=0.11) whereas portal vein flow decreased dramatically (0.20 vs 1.20 L/min; p=0.006). Overall, in patients with liver disease, there was a 46% reduction in total liver blood flow (0.67 vs 1.47 L/min; p=0.037) and a reversal of hepatic artery/portal vein flow ratio (4.15 vs 0.33 L/min; p=0.009). Although superior mesenteric artery flow was three times greater in patients (0.54 vs 0.15 L/min; p=0.001), renal blood flow showed a trend towards reduction of 32% (0.42 vs 0.62 L/min; p=0.053), no change in carotid blood flow (0.75 vs 0.62 L/min; p=0.129) and no change in inferior aortic flow (1.45 vs 1.12 L/min; p=0.28).
Conclusion There are marked derangements in regional visceral blood flow in patients with liver cirrhosis. Our findings strongly support the splanchnic steal hypothesis that dysregulated splanchnic vasodilatation and porto-systemic shunting induce a high cardiac output state associated with extra-splanchnic vaso-constriction including the renal circulation.

P08 PEOPLE WITH DIABETES HAVE A HIGHER RISK OF DEATH FROM LIVER DISEASE COMPARED TO THE GENERAL POPULATION

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J Parkes. *Public Health Sciences & Medical Statistics, University of Southampton, UK*

Introduction The association between liver disease and diabetes has been described, but less information is available regarding mortality from liver disease among people with diabetes from a population perspective.
Aim To compare mortality from liver disease among people with prevalent diabetes in 2001 and incident diabetes between 2001 and 2007 with that of the general population of Scotland.
Method We used a population-based diabetes register derived from primary and secondary care electronic records linked to death records to compare mortality from liver disease among people with prevalent diabetes in 2001 and incident diabetes between 2001 and 2007 with that among the general population of Scotland for people of 35–84 years for the period 2001–2007. There were just over 1 million person years of data for people with diabetes and almost 20 million person years of data for the general population. Mortality rates were estimated for liver disease as underlying (primary) cause of death on death certificates using conventional ICD-10 codes including those for hepatocellular carcinoma (HCC). Standardised

mortality ratios (SMRs) were estimated adjusting for age, sex and quintile of an area-based measure of socio-economic status, the Scottish Index of Multiple Deprivation 2006 using the population of Scotland in 2004 as the standard.

Results There were 1267 and 10 100 records that mentioned liver disease as the primary underlying cause of death in the diabetes and general populations, giving crude mortality rates of 122.4 and 50.9/100 000 person years, respectively. The major single cause of liver-related death was alcoholic liver disease which accounted for 38% and 63% of liver disease deaths among people with diabetes and the general population respectively, with HCC accounting for 24% and 9% of liver disease deaths in these populations. SMRs (95% CI) for underlying (primary) cause of death for people with diabetes compared to the general population were 169 (160–178) for all liver disease, 116 (106–126) for alcoholic liver disease and 318 (283–356) for HCC. SMRs were similar for any mention of liver disease on death certificate. SMRs for women with diabetes were higher than men. Further analyses will stratify by type of diabetes.

Conclusion Analysis of a very large population based data set has shown that people with diabetes have a raised mortality rate from liver disease compared to the general population. Management of people with diabetes should include strategies to reduce risk of liver disease.

P09 HEPATOCELLULAR CARCINOMA IN PRIMARY BILIARY CIRRHOSIS: DEFINING RISK IN AN ERA OF URSODEOXYCHOLIC ACID USE

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J Maggs, J O'Grady, N Heaton, V Aluvihare, A Quaglia, K Agarwal, M Heneghan, A Suddle. *Institute of Liver Studies, King's College Hosptial, London, UK*

Introduction Hepatocellular carcinoma (HCC) is a rare complication in primary biliary cirrhosis (PBC). Current clinical guidance from the British Society of Gastroenterology advises that only male patients with histologically advanced PBC are at sufficient risk of HCC to justify enrolment in surveillance programs. In this study, we review our experience of HCC in PBC and investigate the utility of serum (s-) bilirubin as a selection criterion in determining enrolment in an HCC surveillance program.

Method Patients with HCC and PBC managed in our centre were identified from the Hepatobiliary Cancer, Liver Transplant and Liver Histopathology Databases. Demographic, clinical, biochemical and outcome data were obtained by retrospective review of the patient's case notes.

Results 32 cases of HCC in PBC patients from 1999 to 2010 were identified, including 1 with concomitant alcohol-related liver disease and one patient with an autoimmune hepatitis–PBC overlap syndrome. No patient had documented hepatitis b surface or hepatitis c antibody positivity. 81% of patients were female. 92% of patients had received ursodeoxycholic acid (UDCA). Liver biopsy result was available in 15 patients, with 7 having stage 3–4 PBC. Median age at diagnosis of HCC was 66 years (range: 42–86) and median time from diagnosis of PBC to development of HCC was 13.5 years (4.3–16). Identification of HCC was made during surveillance in 16 and assessment for liver transplantation in four patients, following hepatic decompensation in four, and incidentally in five, including in the liver explant of three patients. Median α-fetoprotein at diagnosis was 28 kIU/l (IQR: 5–204), and was elevated (>20 kIU/l) in 15 patients (50%). At diagnosis of HCC, median Mayo Risk Score, MELD, MELD-Na, UKELD and Child–Pugh scores were 6.87 (6.08–8.09), 10 (8–14), 14 (10–19), 50 (48–55) and 7, respectively, with no difference between survivors and non-survivors (p=NS) or males and females (p=NS). Median s-bilirubin was 27 μmol/l (14–54), but in 13 (41%) patients the s-bilirubin was normal. 89% (25/28) patients had evidence of portal hypertension defined by the presence of varices, splenomegaly, or ascites; including nine patients with normal s-bilirubin. There was no correlation between the presence of jaundice and outcomes or the presence of portal hypertension (p=NS). However, those patients diagnosed with HCC during surveillance were less likely to be jaundiced (31%), when compared with those with symptomatic presentations (75%).

Conclusion In our patient cohort, s-bilirubin is not an appropriate indicator of HCC risk in PBC, as most PBC patients were not jaundiced when diagnosed with HCC by surveillance. Therefore, a normal s-bilirubin should not be used to exclude patients from HCC surveillance. Further we propose that surveillance should not be limited to male patients. We hypothesise that UDCA is modifying s-bilirubin levels in PBC without altering portal hypertension or HCC risk.

P10 HIGH TROPONIN I IN ACUTE LIVER FAILURE: A MARKER OF MYOCARDIAL INJURY OR METABOLIC STRESS?

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V Audimoolam, J Wendon, W Bernal, C Willars, M Mcphail, G Auzinger. *Institute of Liver studies, King's College Hospital, London, UK*

Introduction ALF is a life-threatening multi-system illness resulting from massive hepatic necrosis. Acute liver failure (ALF), in its more severe forms is invariably complicated by progressive haemodynamic disturbances with a pattern of distributive shock; elevated cardiac output and decreased peripheral vascular resistance being the standard apart from hypoxic hepatitis of cardiac origin. A recent study demonstrated a relatively high incidence of elevated troponin I (TI) in patients presenting with ALF; elevated levels were associated with poorer outcome attributed to myocardial damage. Data pertaining to invasive haemodynamic monitoring or cardiac imaging studies have not been described in conjunction with TI measurement.

Method We prospectively collected invasive haemodynamic data (transpulmonary thermodilution cardiac output measurements PICCO) and echocardiographic studies in a cohort of patients with ALF. These data were analysed along with TI levels, taken routinely on admission to a tertiary liver centre. TI levels were considered positive if >0.05 μg/l or "high" if over the 50th centile.

Results A total of 191 patients who fulfilled criteria for ALF and subacute liver failure (ALF/SALF) were enrolled from 2007 to 2010. 121 patients had an elevated T I > 0.05 μg/l on admission (102/19-ALF/SALF, p=0.128 χ^2 test). 122 patients underwent echocardiogram; 50 of the TI negative group (TI-neg) and 72 in the TI positive group (TI-pos); p<0.001 χ^2 test. Median TI levels was 0.075 μg/L (0–8.52) in those who survived and 0.180 μg/l (0–50) in those who either died or were transplanted; p=0.051, Mann–Whitney U test. There was no statistically significant association identified in regard of regional wall motion abnormalities between TI pos/ neg groups (7/78 vs 1/36, p=0.461 χ^2 test) or TI high (>0.7) or low groups (<0.21) (6/66 vs 2/48; p=0.563 χ^2 test). A borderline association was noted between TI pos and left ventricular dysfunction (LVD) (15/70 vs 1/36, p=0.050, χ^2 test), LVD was seen in (22%) high TI vs (6%) in the low TI group. No difference in haemodynamic parameters were noted between the TI neg and pos groups for MAP (70 (50–124) vs 70 (45–180); p=0.221), Cardiac index (4.45 (3.0–6.9) vs 4.5 (2.0–7.67); p=0.336) Blood volume-ITBVI (720 (488–1186) vs 783 (426–1392); p=0.207) Lung water-EVLWI (9 (6–18) vs 9 (5–34); p=0.998; all Mann–Whitney U test). Subjects with elevated TI had an elevated median creatinine kinase (CK) (329 (6–37840) IU/L vs 81 (14–1417) IU/L (p=<0.001, Mann–Whitney U test). Elevated CK in this cohort may not be representative of cardiac damage as elevated levels secondary to rhabdomyolysis were often seen in patients presenting with recreational drug use.