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PWE-263 LIVER TO ABDOMINAL AREA RATIO: A NOVEL RADIOLOGY TEST FOR PROGNOSTICATION IN LIVER CIRRHOSIS

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Introduction Prognostication in cirrhotic liver disease is difficult. There are several validated indices which are employed including: Child-Pugh score, MELD and UKELD. There is anecdotal data that liver size is important in determining patient survival and likelihood of re-compensation.

Aims To assess a ratio of liver area and abdominal area on cross-sectional imaging using CT to predict the likelihood of death or need for liver transplantation (LT) in patients with liver cirrhosis.

Methods A retrospective analysis of 280 patients referred to the South West Liver Unit. All patients with cirrhosis were included who had liver CT available. Patients with acute liver failure or hepatoma were excluded from the analysis. Using a webpacs system patient imaging were retrieved and the cross sectional image with the largest area of liver was identified. The liver to abdomen area ration (LAAR) was estimated from the hypothesised ellipses represented by the liver and abdomen using the formula $\frac{A}{B}$ (where 'a' being half of the long axis and 'b' being half of the short axis). These values were compared against patient survival vs patient death/LT. Accuracy of LAAR in predicting the outcome was assessed using Mann–Whitney U test.

Results 280 patients were identified. Sex was available in 200 patients (61% male). Aetiology was available in 266 patients: ALD=103, HCV=32, NASH=10, PBC=10, PSC=13, HCC=31, ALF=12, Others=51. HCC and ALF patients were excluded from analysis. The median age 54.2 (46.6–61.1). Ascites was present in 79 of 127 patients (62%). Not all patients had a CT. LAAR was calculated in 108 patients, median 0.37 (0.3–0.43) and was shown to be predictive of death/LT ($p=0.035$). The presence of ascites did not predict survival (χ^2 2.5, $p=0.12$, OR 1.9 (95% CI 0.86 to 4.01)).

Conclusion LAAR is a simple, novel imaging based technique to assess prognosis in patients with cirrhosis. It confirms anecdotal data that liver size is important in assessing survival. It is more accurate in determining survival than the presence of ascites. LAAR could be incorporated into existing algorithms for patient selection for LT and in determining patient survival with cirrhosis. Its accuracy should be compared against Childs-Pugh, MELD and UKELD alone or in combination to evaluate its utility in clinical practice.

Competing interests None declared.

PWE-264 BLOOD LIPIDOMIC PROFILING OF HEPATOCELLULAR CARCINOMA IN HUMAN AND ANIMAL STUDIES IDENTIFIES LYSOPHOSPHATIDYLCHOLINE (24, 0, 0), A DISCRIMINATORY BIOMARKER

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Introduction The liver is a hub of lipid metabolism and previous studies have shown liver disease and hepatocellular carcinoma

(HCC) to be associated with altered blood lipid profiles. The primary aim of this study was to examine the lipid profile of HCC in an animal model and to compare findings to changes observed in human populations in an attempt to identify novel lipid tumour biomarkers.

Methods Plasma samples were obtained from a Fisher rat model of HCC (n=7) and healthy controls (n=8). Serum and plasma samples were obtained from patients with HCC and cirrhosis from UK (n=3 and 4) and Nigerian (n=5 and 5) cohorts. All samples were analysed using ultra performance liquid chromatography mass spectrometry (UPLC-MS), optimised using in-house developed dichloromethane lipid extraction protocols. Data were processed using XCMS software followed by multivariate analysis to identify lipids most discriminatory between disease groups.

Results In the rat model, multivariate statistical modelling was robust in classifying animals with HCC from healthy controls. In the human studies, multivariate analyses of lipid profiles were less robust in distinguishing HCC from cirrhosis. Lysophosphatidylcholine (24, 0, 0) (LPC), a major cellular membrane component, was identified as most contributory to all multivariate models.

Conclusion Altered global lipid profiles were robust in discriminating HCC from healthy controls in a Fisher rat model, but less so in parallel human studies. Differences in LPC (24, 0, 0) were present in all studies, which may indicate heightened altered tumour cell turnover as a result of HCC growth. The increased plasma concentrations of LPC in HCC in both species suggests that this molecule may be a robust marker as a lipid tumour biomarker of HCC and requires further validation in larger studies with respect to disease classification and response to therapeutic intervention.

Competing interests None declared.

PWE-265 PLASMA METABOLITE PROFILING IN A RAT MODEL OF HEPATOCELLULAR CARCINOMA AND THE EFFECTS OF CO-ADMINISTERED ANTIBIOTICS

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Introduction The profiling of metabolites, small molecules representing the end points of cellular processes in biofluids, has allowed the detection of novel biomarkers of disease. There are several rat models of hepatocellular carcinoma (HCC), however, there have been no previous reports of ¹H NMR spectroscopy plasma metabolic profiling in animal models of HCC. Quinolone antibiotics, such as norfloxacin, are known to reduce the inflammatory component of liver fibrosis potentially reducing end-stage complications. The primary aim of this study was to identify blood metabolic profile biomarkers of HCC in a rat model of HCC and the secondary aim was to evaluate the effect of the norfloxacin on metabolic profiles.

Methods HCC was induced in 10 Fisher rats by administration of intra-peritoneal diethylnitrosamine (DEN) and oral N-nitrosomorpholine (NMOR) and plasma was collected upon sacrifice. Five rats were concomitantly administered oral norfloxacin. Six Fisher non-treated rats acted as healthy controls. Proton NMR spectra were acquired for all samples using a Bruker 600 MHz NMR system and results were analysed by visual comparison and multivariate analysis.

Results Proton NMR spectra from diseased rats displayed significant decreases in lipoproteins, unsaturated fatty acids, N-acetyl-glycoproteins, acetoacetate, and glucose ($p \leq 0.001$). Plasma citrate and formate levels were increased ($p=0.02$). Although animals treated with norfloxacin also developed tumours, background fibrosis and tumour nodularity was less marked than non-antibiotic treated

animals. Correspondingly, metabolic profiles from both HCC groups with and without norfloxacin were similar in character with the norfloxacin treated group showing a slightly weaker set of metabolic alterations.

Conclusion The spectral profiles of plasma in rats with HCC display marked changes with relation to lipid metabolism and cellular turnover which may indicate a fundamental repression of fatty acid oxidation and cancer cachexia. Norfloxacin appears to abrogate these effects slightly. This is the first animal model plasma ^1H NMR study to report such findings and may both be translational to human disease and allow the study of the effect metabolic modulation upon HCC progression.

Competing interests None declared.

PWE-266 PROTECTIVE ROLE OF β BLOCKERS IN SBP: MYTH OR REALITY

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Introduction β Blockers may have a protective effect on the development of spontaneous bacterial peritonitis by increasing the intestinal transit time and reducing portal pressure. The aim of this study is to evaluate the significant benefit of β blocker in prevention of spontaneous bacterial peritonitis in patients with chronic liver disease and ascites.

Methods We retrospectively evaluated 332 patients with cirrhosis and ascites admitted over a period of 5 years (males 230, females 102). Diagnosis of spontaneous bacterial peritonitis was based on an ascitic fluid neutrophilic count of $>250/\text{mm}^3$ and/or a positive culture without evidence of secondary peritonitis.

Results Spontaneous bacterial peritonitis was diagnosed in 52 of 332 (15.66%) patients. Of the 92 on β -blockers, 6 (6.5%) had SBP and out of 240 patients who were not on β -blockers, 46 (19.2%) had SBP. The patients who were on β -blockers, had a significantly lower incidence of SBP (χ^2 test with continuity correction; $p=0.008$).

Conclusion Our data indicate that spontaneous bacterial peritonitis significantly increases mortality in patients with cirrhosis. Propranolol therapy was found to be associated with a significantly lower risk for spontaneous bacterial peritonitis, but a Type II statistical error cannot be definitely excluded. The potential protective effect of propranolol on the incidence of spontaneous bacterial peritonitis might deserve evaluation in properly designed prospective studies.

Competing interests None declared.

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PWE-267 URINARY TLR4: A NOVEL BIOMARKER TO IDENTIFY PATIENTS WITH ACUTE KIDNEY INJURY IN PATIENTS WITH ACUTE ON CHRONIC LIVER FAILURE

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Introduction Patients with stable cirrhosis often present with acute deterioration of cirrhosis secondary to precipitating illness which may progress to organ failure, a condition referred to as acute on chronic Liver failure (ACLF). A proportion of these patients develop renal dysfunction which do not fulfil criteria for the diagnosis of hepatorenal

syndrome (HRS). We hypothesised that the kidneys in patients who develop renal dysfunction in ACLF would exhibit histological and biomarker evidence of acute kidney injury (AKI). Since ACLF is associated with systemic inflammatory response (SIRS) we aimed to look for Toll like receptor (TLR) 4 and 2 which recognise pathogens and when activated lead to apoptosis and production of cytokines.

Methods Study 1: 74 subjects [healthy volunteers (6), compensated alcoholic cirrhosis (11), acute deterioration of alcoholic cirrhosis (57)] were included prospectively. Urinary biomarkers, kidney injury molecule-1 (KIM-1, a marker of renal injury), Glutathione S-Transferase (πGST , αGST ; markers of proximal and distal tubular injury) (Commercial ELISA), and urinary TLR4 (Western Blotting) were measured. **Study 2:** Renal biopsies were available from 8 alcoholic cirrhosis patients (3 AKI; 5 HRS) which were stained for TLR4, TLR2 and, Caspase-3.

Results Study 1: Nine patients developed AKI on the background of acute deterioration of cirrhosis and 3 had HRS. KIM-1, πGST and αGST were higher in patients with acute deterioration of cirrhosis compared with controls but did not differ in those with and without AKI. Urinary TLR4 values were significantly higher in patients with acute deterioration of cirrhosis with AKI (4.7 ± 1.1) compared to controls (0.38 ± 0.04) and stable cirrhosis (0.32 ± 0.08) and patients with acute deterioration of cirrhosis without renal dysfunction (1.6 ± 0.32) ($p < 0.01$) respectively.

Conclusion These data provide evidence for severe tubular injury and apoptosis in patients with AKI and identifies urinary TLR4, as a novel biomarker to identify AKI in Acute deterioration of cirrhosis.

Abstract PWE-267 Figure 1

Competing interests None declared.

PWE-268 RECENT TRENDS IN PRIMARY LIVER CANCER IN ENGLAND AND WALES

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Introduction Mortality and incidence rates of Primary Liver Cancer (PLC) have been rising in England and Wales towards the end of the last century. The current trend and ethnic distribution of PLC remain unknown.

Methods We obtained mortality and incidence data for PLC for the whole population of England and Wales for the period 2001–2008.