

western blot for eNOS signalling proteins and NOS activity assay were undertaken in cirrhotic and control kidneys. Markers of oxidative stress and inflammatory cytokines were measured in serum by ELISA. We studied the effects of s.c. infusion of recombinant human RLN (seralaxin; 72 h, 4 µg/h) on these parameters. Doppler USS measured changes in cardiac output (CO) and renal arterial resistive index (RRI) in response to i.v. RLN (4 µg). Kidney endothelial morphology was assessed by electron microscopy, H+E and PAS stained kidney by light microscopy.

Results In renal arteries from control and cirrhotic rats endothelial vasodilatation was eNOS-dependent. In cirrhotic rats endothelium-dependent relaxation (acetylcholine; 10^{-9} – 3×10^{-5} M) was dramatically reduced ($p < 0.0001$) in all renal arteries, with only a modest reduction seen in the mesenteric arteries. Endothelium-independent relaxation (sodium nitropruside; 10^{-9} – 3×10^{-5} M) and vasoconstriction (phenylephrine; 10^{-9} – 3×10^{-5} M) were unaltered. In cirrhotic kidneys, total eNOS expression was up-regulated, as were arginase2 and caveolin1 (negative regulators of eNOS), and NOS activity was reduced ($p < 0.05$). Acute RLN had no effect on CO but decreased RRI ($p < 0.05$). Extended RLN restored endothelium-dependent relaxation, increased kidney NOS activity ($p < 0.05$), increased phosphorylated Akt and eNOS, and reduced serum TNF α levels.

Conclusion Renal vascular endothelial dysfunction characterises experimental cirrhosis, through a reduction in renal eNOS activity. This impairment may contribute to the renal vasoconstriction seen in cirrhosis and is a promising target for therapeutic modulation. RLN treatment restored renal endothelial vasodilatation. The potential for recombinant forms of RLN as a haemodynamic modulator in human cirrhosis and HRS merits investigation in translational studies.

Disclosure of Interest None Declared.

OC-032 SURVEILLANCE LEADS TO IMPROVED OUTCOMES FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC)

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Introduction 6-monthly ultrasound surveillance is recommended in cirrhotic patients at risk of HCC. The benefit of surveillance has never been demonstrated in a western population.

Methods A retrospective, single centre cohort analysis in patients diagnosed with HCC from 2008–2013. From 2008 an automated recall system for 6-monthly ultrasound was instigated by the radiology department, in preference *ad hoc* ultrasound requests. Patients with abnormal lesions proceeded to CT, MRI or liver biopsy according to defined international criteria. The primary end-points evaluated were stage of cancer detection (early i.e. BCLC 0 or A), versus late presentation (BCLC B-D) and patient survival from time of diagnosis to 12 months and 60 months.

Results 160 patients were identified. Surveillance status was known in 132 patients. Median patient age was 68 years (57–75), median number of lesions was one, diameter of largest lesion 30 mm (19–50), and AFP 19.5 (5–250). Patients under surveillance were more likely to have disease at a curative stage 67 vs. 39% ($p = 0.006$, OR 0.59 (0.41–0.84)), and had better survival at 1 year 80 vs. 62% ($p =$

0.04, OR 0.77 (0.62–0.97), and at 5 years 60 vs. 41% ($p = 0.046$, OR 0.69 (0.48–0.98)). On univariate analysis the following variables on survival were evaluated: Age ($p = 0.11$), Number HCC nodules ($p = 0.31$), Total diameter of lesions ($p = 0.001$), Diameter of largest lesion ($p < 0.001$), AFP ($p < 0.001$). The presence on imaging of extra-hepatic metastases ($p = 0.006$), lymph nodes ($p = 0.004$), and portal vein thrombosis ($p < 0.001$), were associated with poorer survival.

Conclusion Surveillance for hepatocellular carcinoma leads to earlier diagnosis and improved survival.

Disclosure of Interest None Declared.

OC-033 THE TWEAK AND FN14 PATHWAY AS POTENTIAL MEDIATOR OF LIVER FIBROSIS

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Introduction The TNF superfamily ligand TWEAK and its cognate receptor Fn14 have been implicated in the pathogenesis of liver disease and have been predominantly associated with liver progenitor cell proliferation and ductular reaction. We hypothesised that TWEAK and Fn14 may also be involved in the establishment and progression of fibrosis via a direct effect on hepatic stellate cell (HSC) function.

Methods TWEAK and Fn14 expression was studied by qPCR, western blot and immunostaining in tissue and stromal cells from explanted human liver specimens and normal donor livers surplus to surgical requirements, or as a byproduct of surgical resection. The responses of HSCs to TWEAK were investigated by western blot, live cell imaging and proliferation assays. TWEAK was measured in HSC supernatant by ELISA.

Results Confocal microscopy revealed localisation of Fn14 to cells expressing stromal markers in normal human livers, with significant upregulation in diseased livers. Fn14 expression was confirmed in both primary human HSCs and myofibroblasts *in vitro*. Stimulation with recombinant TWEAK led to an upregulation of NF- κ B signalling and induced proliferation in cultured HSCs. TWEAK immunostaining localised the protein to the fibrotic areas of ALD and NASH liver sections suggestive of an autocrine regulation of Fn14 signalling. We confirmed that HSCs express TWEAK and release it into their environment by qPCR and ELISA, and demonstrated that function-blocking TWEAK antibodies reduced the proliferative capacity of HSC.

Conclusion Our study suggests that TWEAK/Fn14 promotes liver fibrosis via enhanced proliferation of HSC, possibly through an autocrine mechanism driven by HSC production of TWEAK.

Disclosure of Interest None Declared.

OC-034 OUTCOME OF PATIENTS CONSIDERED UNSUITABLE FOR LIVER TRANSPLANTATION – A MISSED OPPORTUNITY FOR PALLIATIVE CARE?

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Introduction Patients with end stage liver disease (ESLD) and/or hepato-cellular carcinoma (HCC) may be considered unsuitable for liver transplantation (LT) due to disease severity at presentation or de-listed due to disease progression. These patients have complex medical needs and a limited life expectancy and would be expected to benefit from access to palliative care services.

Methods We performed a retrospective audit of patients assessed for LT between 2010–12 at the Royal Free Hospital. We studied patients who were either not listed at the time of assessment, or listed and subsequently de-listed prior to LT. Sources used included transplant meeting records, hospital notes, local death records and palliative care database.

Results 106 patients were identified. Median age was 58 years (IQR 51–72) and 67% were male. The median MELD score at the time of assessment was 13 (IQR 11–18.75) with a UKELD score of 52 (IQR 49–57).

Aetiology of liver disease was divided into Alcohol related Liver Disease (39), Viral (32), Autoimmune (19), Metabolic (8), Cryptogenic cirrhosis (3), other (5).

Reasons for not listing included poor clinical state/co-morbidities (48), tumour outside transplant criteria (25), psychosocial/compliance issues (18) and currently too well for LT (15).

Excluding patients who were 'Too Well' for LT, Kaplan-Meier Survival analysis calculated the median survival following delisting as 219 days (IQR 28–540). Specifically for those delisted for 'poor clinical state' median survival was 29 days.

Overall, 17 (19%) patients were referred to palliative care a median 4 days before death (IQR 2.5–47.5).

Conclusion Those patients who are unfit for LT due to poor clinical state should be referred immediately for palliative care due to limited survival. Patients with HCC outside criteria have a significantly longer survival but still appear to have limited access to palliative care. Liver Transplant programs should have access to dedicated liver palliative care services.

Disclosure of Interest None Declared.

OC-035 LIFETOUGH®: A NOVEL REMOTE MONITORING DEVICE TO IDENTIFY PATIENTS WITH ADVANCED CIRRHOSIS MOST AT RISK OF DECOMPENSATION – A PROOF OF CONCEPT STUDY

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Introduction Hospital readmission from inter-current illness is common in advanced cirrhosis. Community monitoring of these patients with simple information-based technology may facilitate early problem recognition and intervention. Heart rate variability (HRV) has been deemed the 'gold standard' tool to characterise autonomic dysfunction, which is widely reported in cirrhosis, and remains independent of aetiology, and its severity has been shown to correlate with prognosis. However, the methods to study continuous measurement of HRV and studies in advanced cirrhosis are limited.

Aims This study used a wireless-monitoring technology, Lifetouch® system (Isansys), to assess changes of HRV remotely in acute-on-chronic liver failure (ACLF) patients, and evaluated the relationship to the severity of disease and inflammatory indices.

Methods Following ethical and local site approval, nineteen patients (13 male/6 female; mean age 52.5 ± 12.0 years) had HRV

assessment following presentation to The Royal Free hospital, using the Lifetouch® system, with the standard deviation of the R-R interval (SDNN) used to collect changes in HRV. This novel system enabled continuous, wireless evaluation of HRV, which was compared with clinical, biochemical and inflammatory indices (IL-6, IL-8 and IL-10 measured by multiplex cytokine analysis).

Results HRV, as determined by SDNN, was significantly greater in cirrhosis patients with Child-Pugh scores <10 compared to >10 (31.26 ± 14.90 vs. 10.80 ± 5.61 ms). Similarly, UKELD correlated inversely with SDNN ($R^2 = -0.46$; $p < 0.01$). Spearman's rank analysis of SDNN in relation to the inflammatory indices: WCC, CRP, IL-6, IL-8 and IL-10 levels were -0.60 ($p = 0.01$), -0.56 ($p = 0.01$), -0.77 ($p = 0.02$), -0.86 ($p = 0.01$) and -0.79 ($p = 0.04$), respectively. Using a SDNN cut-off of ≤ 20 ms to signify patients with advanced disease (Child C), all inflammatory indices were shown to be significantly increased ($P < 0.01$).

Conclusion This pilot study provides proof of concept that remote monitoring showing reduced HRV, identifies patients with increased inflammation, more advanced liver disease and those most likely to present with acute decompensation of cirrhosis. Further study and refinement of this system may facilitate community monitoring of advanced liver disease patients, to provide 'alarm' signals that highlight acute decompensation and precipitate early intervention care pathways.

Disclosure of Interest None Declared.

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OC-036 NON-INVASIVE VENTILATION DURING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY INSERTION IN MOTOR NEURONE DISEASE PATIENTS – A SAFE AND EFFECTIVE MULTI-DISCIPLINARY APPROACH

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Introduction Percutaneous endoscopic gastrostomy (PEG) is recommended for motor neurone disease patients with dysphagia and accelerated weight loss. However PEG has been suggested as inadvisable in the past in patients with impaired respiratory function. Recent small studies have found satisfactory outcomes using non invasive ventilation (NIV) to assist PEG placement in this setting. We set up a service performing this technique for our region, and analysed our outcomes.

Methods 26 patients with motor neurone disease were included in the study from Nov 2011 – Oct 2013; 11 (42%) were external referrals. Patients had respiratory assessment prior to the procedure including sniff nasal pressures, arterial CO₂ measurement, overnight oximetry and spirometry as directed by our respiratory physician. A modified oro-nasal mask with an endoscopic port was fitted prior to the procedure and NIV initiated and controlled by the respiratory physician. The PEG (Freka PEG, Bad Homburg, Germany) was inserted under continuous NIV which continued until the patient was fully awake in recovery. Prophylactic antibiotics were given routinely. Demographic and technical data, complications and survival were recorded.

Results Median age at time of PEG was 68 yrs (range 43–92), male 42%. Mean BMI was 22 (range 16–33). 3 patients (12%) were receiving NIV prior to referral. Mean dose of midazolam