

# P16 NON-INVASIVE EVALUATION OF FIBROSIS IN PAEDIATRIC CHRONIC LIVER DISEASE

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**Introduction** Outcome of liver disease in children is mainly determined by severity and progression of liver fibrosis. Liver biopsy is the accepted standard for evaluating fibrosis but is limited by the need for sedation in children, sampling error and risks including bleeding.

**Aim** The aim of this study was to compare tools for non-invasive assessment of liver fibrosis in a paediatric cohort.

**Method** Children were recruited at the time of liver biopsy and underwent transient elastography (TE) and blood collection. Liver biopsies were scored by a hepato-histopathologist from F0 (no fibrosis) to F4 (cirrhosis). Serum samples underwent analysis for the Enhanced Liver Fibrosis (ELF) test; comprising hyaluronic acid, P3NP and TIMP1 (iQur, UK). CK18-M30 levels (caspase cleavage fragments) were measured using ELISA. Biomarkers were compared to biopsy score.

**Results** During the study period 101 children (62 boys) were enrolled. Median age: 13.6 (range 6–18) years. Diagnosis was autoimmune liver disease (AILD) in 27; non-alcoholic fatty liver disease (NAFLD) in 37; 13 children were post-transplant; 8 children had Hepatitis B/C; 5 had Wilson disease and the remainder miscellaneous. TE was a good discriminator of fibrosis  $\geq$  F2 ( $p < 0.001$ ),  $\geq$  F3 ( $p < 0.001$ ) and F4 ( $p = 0.003$ ) with areas under the ROC curve of 0.78, 0.8 and 0.96 respectively. Data derived cut-offs for  $\geq$  F1 were 6.1 kPa,  $\geq$  F2; 6.8 kPa,  $\geq$  F3; 8.3 kPa and F4; 14.1 kPa.

Blood biomarkers were not as accurate in distinguishing severity of disease. ELF performed better with increasing stages of fibrosis. Area under the curve for cirrhosis was 0.77. CK18-M30 levels could distinguish significant fibrosis ( $\geq$  F2) ( $p = 0.009$ ) with an area under the ROC curve of 0.77, severe fibrosis ( $\geq$  F3) with an AUROC of 0.69 and cirrhosis (F4) with an AUROC of 0.69. Within the different diagnostic groups, again TE performed better than serum biomarkers with AUROC of 0.75 for  $\geq$  F2 and 0.81 for  $\geq$  F3 in NAFLD; 0.85 for  $\geq$  F2, 0.94 for  $\geq$  F3 and 1.0 for F4 in AILD; and in children post-transplant; 0.9 for  $\geq$  F2 and 0.83 for  $\geq$  F3.

**Conclusion** To our knowledge, this is the largest paediatric study reported to date comparing TE and serum biomarkers for the non-invasive evaluation of fibrosis. TE was a reliable tool in distinguishing different stages of liver fibrosis in paediatric patients. Blood biomarkers may be of use in combination with TE especially in the stratification of more severe disease. Routine use of these techniques may serve as a useful adjunct to liver biopsy for diagnostic purposes and provide a reliable method of non-invasively monitoring liver disease progression in children.

# P17 TIPS OUTCOMES FOR BUDD–CHIARI: A SINGLE TERTIARY CENTRE EXPERIENCE

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**Introduction** TIPS insertion is an important intervention in the management of Budd–Chiari syndrome. We describe the experience of a single tertiary referral centre.

**Aim** The aims of this study were to describe the series of patients undergoing TIPS insertion for Budd–Chiari syndrome at the Royal Free Hospital, survival post-TIPS insertion and re-intervention rates.

**Method** A retrospective analysis of the Royal Free Hospital radiology database was conducted to identify all patients who underwent all

TIPS procedures between January 1991 and January 2011. Patient records were used to subsequently identify those patients in whom Budd–Chiari was the principal indication for TIPS insertion and to characterise this patient cohort.

**Results** 1073 TIPS-related procedures were conducted at the Royal Free Hospital between January 1991 and January 2011. Of these, 51 patients underwent TIPS insertion for Budd–Chiari syndrome between January 1991 and January 2011 of which 61% (31/51) were female and 39% (20/51) were male. The mean age at the time of TIPS insertion was 40 years ( $\pm 1.96$ ). All patients were anticoagulated post procedure. 1-year transplant-free survival post-TIPS insertion was 93%. TIPS insertion could not be achieved in three patients. TIPS stenosis/occlusion was more common than in other TIPS indications. The mean number of TIPS-related interventions was 2.5 (1–10). Local thrombolysis with tissue plasminogen activator was required in three cases and patency/intervention rates were significantly improved with the addition of aspirin to standard warfarin anticoagulation. No patients proceeded to liver transplantation. Regenerative nodules post TIPS were common on surveillance cross sectional imaging.

**Conclusion** Excellent 1-year transplant-free survival can be obtained in Budd–Chiari syndrome with TIPS placement. Patients are complex and may require multiple interventions and therefore probably best managed in experienced centres.

# P18 LIVER FIBROSIS ASSESSED BY TRANSIENT ELASTOGRAPHY PREDICTS RESPONSE IN CHRONIC HEPATITIS C INFECTED PATIENTS TREATED WITH PEG-INTERFERON AND RIBAVIRIN

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**Introduction** Chronic hepatitis C virus infection (HCV) is a common cause of cirrhosis and end stage liver disease. Treatment with Pegylated interferon (PEG-IFN) and ribavirin (RBV) results in sustained virological response (SVR) in approximately 60% of infected individuals. Increasing stage of fibrosis is known to be a key factor associated with non-response to treatment with PEG-IFN + RBV. Traditionally, fibrosis stage has been determined by liver biopsy, but this is invasive. Newer non-invasive methods of assessing fibrosis such as transient elastography (TE) are now available.

**Aim** To assess baseline liver stiffness measurement (LSM) assessed by TE as a predictor of SVR in HCV-infected subjects treated with PEG-IFN + RBV.

**Method** Retrospective review of outcomes of treatment in naïve patients treated with PEG-IFN + RBV for HCV between 7 January and 9 June. Post-transplant and co-infected patients were excluded. Patients who had valid LSM within 6 months of treatment were included in the TE analysis.

**Results** 168 patients (mean age  $39 \pm 10$ , 70% male, 14% cirrhotic, 53% high viral load) received PEG-IFN + RBV for HCV in the study period. The overall SVR rate was 59% (50% for genotype [G] 1/4 and 70% for G2/3,  $p < 0.001$ ). The SVR rate was only 28% in cirrhotics (10% for G1/4 and 43% for G2/3). 87 patients had a pre-treatment TE (median LSM 6.6 KPa [3.3–73]).

LSM was significantly associated with treatment response to PEG-IFN ( $p = 0.01$ ), with the effect more pronounced in HCV G2/3 infection ( $p = 0.001$ ). The optimum cut-off to predict non-response to treatment was 11 KPa. 30 patients (16%) stopped treatment due to side-effects or non-compliance, including 1 death from pneumonitis.

**Conclusion** (1) LSM determined by transient elastography may be used as a non-invasive tool to predict treatment response in subjects infected with HCV.

(2) LSM >11 KPa could be used to identify patients who may have lower response rates and may benefit from longer treatment.

**P19 SYMPTOMATIC EPSTEIN BARR VIRUS (EBV) HEPATITIS IS UNCOMMON, BUT OCCURS IN PATIENTS OF ANY AGE, INCLUDING THE ELDERLY**

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**Introduction** Epstein Barr Virus (EBV) infection typically presents as infectious mononucleosis (IM) in young adults with the classical triad of fever, sore throat and lymphadenopathy. Mildly abnormal liver function tests (LFTs) are common but symptomatic hepatitis is rare. Symptomatic, icteric, EBV hepatitis is rarely reported in those with IM and in the elderly.

**Aim** To review the demographics, presenting features and natural history with EBV hepatitis and to determine what factors might lead a clinician to consider a diagnosis of EBV hepatitis.

**Method** Retrospective study of 2100 patients attending the Jaundice Hotline, a fast track referral system for patients with jaundice at The Cornwall Royal Cornwall Hospital (1998–2011). EBV hepatitis was defined as: symptomatic hepatitis with positive serology for EBV (serology included EBV nuclear antigen, EBV viral capsid antigen (VCA) IgM and VCA IgG). All patients had no evidence of biliary obstruction or parenchymal liver disease on abdominal ultrasound examination (USS), and negative serology for other hepatotropic viruses (HAV, HBV, HCV, HEV, CMV). Other causes of parenchymal liver disease were also excluded by appropriate blood tests.

**Results** Of the total of 2100 consecutive patients with jaundice studied, 17 patients (10 males, 7 females) were diagnosed with EBV hepatitis. All patients were immunocompetent. 47% (8/17) of these patients were aged over 60 years (mean age 44 years, range 18–82). At presentation, mean (range) LFTs were: bilirubin 57 µmol/l (11–161), ALT 428 IU/l (34–1471), ALKP 339 IU/l (132–840). Only 3 patients presented as classical IM. 95% (16/17) had significant lymphocytosis and 82% (14/17) patients had splenomegaly on USS examination at initial assessment. Only 2 patients were unwell enough to be admitted to hospital. All patients fully recovered within 4–6 weeks.

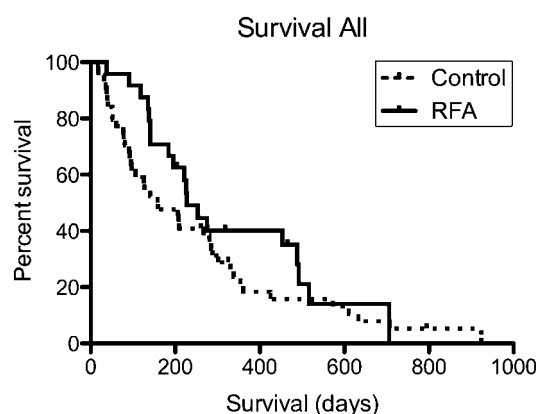
**Conclusion** Symptomatic EBV hepatitis is uncommon and causes a self-limiting illness. EBV hepatitis is not usually associated with classical symptoms of IM and occurred in patients of a wide variety of ages. The diagnosis should be considered in patients of all ages presenting with hepatitis, including those with a cholestatic picture, and especially in those with a lymphocytosis and splenomegaly.

**P20 FIRST REPORT OF THE LONG-TERM EFFICACY OF A NOVEL ENDOSCOPIC RADIOFREQUENCY ABLATION TECHNIQUE FOR MALIGNANT BILIARY OBSTRUCTION**

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**Introduction** Insertion of self-expanding metal stents (SEMS) is standard practice in patients with unresectable malignant biliary strictures. Stent occlusion is a significant clinical problem in patients surviving beyond 3 months. A pioneering phase I/II study in our tertiary referral centre demonstrated good safety and 30-day patency using a novel endoscopic radiofrequency ablation (RFA) technique as



Abstract P20 Figure 1 Kaplan-Meier survival analysis.

an adjunct to SEMS.<sup>1</sup> The longer term impact of combined RFA +SEMS on biliary drainage and overall patient survival is unknown.

**Aim** To investigate long-term safety and efficacy of endobiliary RFA in malignant bile duct obstruction.

**Method** Retrospective cohort analysis of 24 patients undergoing RFA+SEMS (17 pancreatic carcinoma; 7 cholangiocarcinoma) and 44 matched controls undergoing SEMS insertion alone (34 pancreatic carcinoma, 10 cholangiocarcinoma) for malignant biliary obstruction in a single tertiary referral centre. Patients were matched for age, sex, disease, presence of metastases, ASA/co-morbidities, and intention to treat with palliative chemotherapy. Patients with a potential minimum of 6-month follow-up were included and survival, maintenance of stent patency and procedure-related complications were assessed.

**Results** RFA treated and control cohorts were closely matched—mean age 71.8±9.8 yrs vs 68.8±10.3, metastases at treatment 9/24 (38%) vs 17/44 (39%), chemotherapy 16/24 (67%) vs 27/44 (61%). Kaplan-Meier analysis showed a median survival of 227 days in the RFA group vs 159 days in controls (p=0.067). Multivariate analysis showed RFA treatment to be the strongest predictor of survival at 90 days (OR 26.1, p=0.011). Survival benefits may extend beyond 90 days (OR 2.8, p=0.071 at 180 days; OR 2.8, p=0.102 at 360 days), but require further investigation. Within 6 months after treatment, more patients were alive with a patent first SEMS in the RFA cohort than in controls. Complications of RFA were few (1 pancreatitis, 2 cholecystitis) and comparable to those associated with standard ERCP alone. The procedure was well-tolerated with a median post-procedure inpatient stay of 1 day (1–24).

**Conclusion** In the single largest case series studied to date, endobiliary RFA is a safe and efficacious treatment for malignant biliary obstruction, with potential early survival benefit. Large multi-centre prospective trials of this novel treatment modality are warranted.

**REFERENCE**

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**P21 ACTIVELY INJECTING DRUG USERS CAN BE SUCCESSFULLY TREATED WITH ANTIVIRAL THERAPY FOR HCV, ARE UNLIKELY TO BE RE-INFECTED, AND SIGNIFICANTLY REDUCE THEIR ILLICIT DRUG USE**

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**Introduction** Currently the predominant mode of transmission of hepatitis C virus (HCV) in the developed world is injection drug use