

**PTU-056 THE EFFECT OF HEPATITIS C INFECTION ON THE UTILITY OF ALPHA-FETOPROTEIN AS A SURVEILLANCE MARKER FOR TUMOUR RECURRENCE FOLLOWING LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA**

doi:10.1136/gutjnl-2012-302514c.56

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**Introduction** In selected patients, liver transplantation (LT) is considered a curative treatment for hepatocellular carcinoma (HCC). With the application of strict eligibility criteria the risk of tumour recurrence can be minimised but never entirely eliminated. Historically, HCC recurrence is associated with a poor prognosis; however the new and evolving systemic therapies may improve outcomes. Hence, there may be a potential beneficial role for early diagnosis. Although, serum alpha-fetoprotein (AFP) measurement is commonly employed in HCC surveillance in at-risk patients, its role following LT for HCC is not clearly defined. Therefore, we have explored (1) the utility of AFP as a biomarker for tumour recurrence following LT in patients with HCC and (2) the influence of liver disease aetiology on its diagnostic performance.

**Methods** The clinical characteristics, laboratory parameters and outcomes of 302 patients with HCC who underwent LT between January 1999 and July 2011 at our institution were reviewed. Serum AFP levels following LT were analysed and the area under a receiver-operator characteristic curve (AUC) calculated to assess the performance of AFP as a diagnostic test for HCC recurrence.

**Results** Recurrent HCC was observed in 13% of patients during the follow-up period. Recurrence was associated with higher pre-LT AFP (98 ng/ml vs 11.5 ng/ml,  $p > 0.001$ ), vascular invasion in the liver explant, and greater tumour size. Following LT, the median time from initial rise in serum AFP to the diagnosis of recurrence was 16 weeks. In our cohort, AFP was an effective predictor of HCC recurrence (AUC 0.843) and using a cut-off value of  $\geq 10$  ng/ml was an excellent exclusion test (negative predictive value 0.94). Furthermore, its performance was superior in patients with AFP-secreting tumours at LT, in comparison to those with non-secreting tumours (AUC 0.892 vs 0.710). Patients with chronic hepatitis C (CHC), in comparison to non-infected patients, were younger (56 years vs 60 years,  $p = 0.887$ ) and had a lower MELD score (13 vs 10 ng/ml,  $p = 0.002$ ) but higher serum AFP (21 ng/ml vs 10 ng/ml) at LT. However, there was no difference in recurrence rates between groups. In patients with CHC, AFP was an inferior predictor of HCC recurrence, in comparison non-CHC patients (AUC 0.769 vs 0.887).

**Conclusion** We, therefore, conclude that serum AFP measurement is a potentially useful surveillance investigation for tumour recurrence post-LT for HCC particularly in patients without CHC.

**Competing interests** None declared.

**PTU-057 SPLIT LIVER TRANSPLANT RECIPIENTS ARE LESS LIKELY TO REQUIRE PERI-OPERATIVE RENAL REPLACEMENT THERAPY THAN FULL-SIZE LIVER TRANSPLANT CONTROLS**

doi:10.1136/gutjnl-2012-302514c.57

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**Introduction** Several small studies have suggested that split liver transplant (SLT) recipients have an increased frequency of

peri-operative acute kidney injury (AKI). However, given that hepatic ischaemia-reperfusion injury may play a role in the pathogenesis of peri-transplant AKI, the optimal donor selection of split liver transplantation could have a favourable impact on renal outcomes. Our aim was to compare renal outcomes in SLT recipients with matched full-size liver transplant (FSLT) controls.

**Methods** Single-centre study of 72 patients who received a SLT for chronic liver disease 01/2007–06/2011. 72 FSLT (Donation after Brain Death) controls were matched by propensity-risk-score. Definitions: AKI, peak creatinine  $\geq 2$  times baseline; chronic kidney disease (CKD), MDRD4 eGFR  $< 60$  ml/min/1.73 m<sup>2</sup>.

**Results** SLT recipients and FSLT controls were well matched on confounders. Split liver grafts had a younger donor age ( $p < 0.001$ ), longer cold ischaemic time ( $p = 0.026$ ) but similar warm ischaemic time ( $p = 0.213$ ). There was no difference in the intra-operative red cell concentrate requirements between the groups ( $p = 0.460$ ). During the immediate post-operative period, the median peak AST was 1156 U/L for SLT recipients and 1124 U/L for FSLT controls ( $p = 0.960$ ). The frequency of re-laparotomy for bleeding ( $p = 0.310$ ), primary non-function ( $p = 1.000$ ), sepsis ( $p = 0.643$ ) and biliary complications were comparable ( $p = 1.000$ ). Estimated 3-year patient survival was 90.0% and 91.8% for SLT recipients and controls, respectively (log-rank  $p = 0.400$ ). Peri-operative and long-term renal outcomes are outlined in Abstract PTU-057 table 1. There was no difference between the two groups, with the exception of renal replacement therapy; SLT recipients were less likely to require peri-operative renal replacement therapy than FSLT controls ( $p = 0.048$ ).

**Abstract PTU-057 Table 1 Post transplant renal outcomes in SLT recipients and FSLT controls**

	SLT	FSLT	p Value
<b>Peri-operative renal function</b>			
Median peak creatinine ( $\mu\text{mol/l}$ )	113	116	0.585
Median change in creatinine from baseline (%)	+27	+43.6	0.653
AKI (%)	29.2	34.7	0.475
Renal replacement therapy (%)	11.1	23.6	<b>0.048</b>
<b>Long-term renal function</b>			
Mean 1-month eGFR (ml/min/1.73 m <sup>2</sup> )	83	81	0.773
3-year cumulative incidence of CKD (%)	32.5	28.7	0.534

**Conclusion** SLT recipients are less likely to require peri-operative renal replacement therapy than well matched FSLT recipients. Higher graft quality and/or smaller graft volume may have a beneficial renal-sparing effect.

**Competing interests** None declared.

**PTU-058 COMMUNITY BASED RANDOM BLOOD ALCOHOL LEVEL TESTING WITHOUT PRIOR NOTICE DETECTS CONCEALED ALCOHOL INGESTION IN PATIENTS WITH ALCOHOLIC LIVER DISEASE AWAITING LIVER TRANSPLANTATION**

doi:10.1136/gutjnl-2012-302514c.58

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**Introduction** Alcoholic liver disease (ALD) is a common indication for liver transplantation (LT) but recidivism is a significant concern. There is a need for careful assessment and support prior to LT, with monitoring for ongoing alcohol use an important aspect of care for patients on the waiting list (WL).

**Methods** Patients listed for LT in the UK are required to sign a contract committing them to lifelong abstinence from alcohol.

Scheduled appointments for blood alcohol level (BAL) testing may only uncover the most dependent of those who continue to drink. Our transplant unit, with patient consent, conducts community based BAL testing without prior notice as well as breath testing at the time of admission for LT. We evaluated the role of this process in identifying individuals who continue to drink alcohol while claiming abstinence. An update of a retrospective analysis of all patients with a diagnosis of ALD, who were listed for LT from 2006 to 2011, was performed. Patients with a positive BAL and those removed from the WL were identified.

**Results** 206 abstinent patients with ALD were listed for LT after evaluation for risk of recidivism. Four patients on the WL returned a positive BAL at planned appointments and eight upon testing without prior notice. Seven of the latter patients had previously returned negative tests at planned appointments and all were removed from the WL in line with UK national policy. One patient returned a positive test at the time of admission for LT. In addition, two patients admitted to drinking (1 with positive – but below the usual cut-off – BAL tests) and were removed from the WL.

**Conclusion** Random BAL testing is a useful tool in identifying ongoing hidden alcohol use in patients with ALD listed for LT. 6.8% of patients with ALD were removed from the WL due to ongoing alcohol ingestion. These patients may have damaged their grafts through ongoing alcohol ingestion and may recover without LT if they were to become abstinent. Identification of these patients is also important in maintaining public confidence in appropriate allocation of scarce donor livers.

**Competing interests** None declared.

#### PTU-059 HEPATITIS C VIRUS INFECTION ABROGATES THE EFFECT OF LIVER TRANSPLANTATION ON NK CELL ACTIVATION

doi:10.1136/gutjnl-2012-302514c.59

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**Introduction** Hepatitis C virus (HCV) infection is the leading cause for liver transplantation (LT) and recurrence post LT is universal. The role of NK cells in this context is poorly understood, in relation to both alloreactivity and antiviral response. This study investigates whether there are differences in NK cell activation between individuals transplanted for HCV and those transplanted for non-HCV indications.

**Methods** Whole blood was collected from 28 liver transplant patients (18 HCV, 10 non-HCV) and 16 controls. The transplant patients were all on calcineurin inhibitor-based immunosuppression. NK cells from the peripheral blood were analysed for expression of the cell surface inhibitory receptors CD158a/b (killer cell immunoglobulin-like receptors (KIR) specific for HLA-C), and the activating receptors NKp30, NKp46 and NKG2D. Following overnight incubation with IL-15 NK cell function was assessed using a flow cytometry-based killing assay.

**Results** Compared with controls, there was significantly reduced expression of NKp30 and NKp46 in non-HCV LT patients ( $p < 0.001$  for both, Student t test), but no reduction in activating receptor expression in individuals transplanted for HCV. There was no segregation of activating receptor expression with expression of specific KIR. The functional assays correlated with the phenotyping data, with significantly reduced NK cell killing of target cells in non-HCV LT patients compared with controls and with HCV LT patients ( $p = 0.02$  and  $0.01$  respectively, Student t test).

**Conclusion** The recipient NK cell response to liver transplantation is altered in individuals with HCV infection. In the non-HCV setting, we have demonstrated down-regulation of NK activation which may facilitate tolerance. However in the presence of HCV, NK cell function remains intact. We hypothesise that this phenomenon contributes to allograft inflammation and the poorer outcomes observed in LT for HCV.

**Competing interests** None declared.

#### PTU-060 ENTERAL OR PARENTERAL FEEDING IN INTESTINAL GRAFT DYSFUNCTION: ANY CLUES FROM SERUM CITRULLINE?

doi:10.1136/gutjnl-2012-302514c.60

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**Introduction** Citrulline has been successfully used as a marker for intestinal graft dysfunction after intestinal transplantation.<sup>1</sup> We have extended its use to direct enteral vs parenteral feeding in the early post operative period as well as during graft dysfunction presenting as high volume stoma effluent.

**Methods** Weekly serum citrulline concentrations were used in directing nutrition in all recipients of intestinal grafts. A cut off of  $13 \mu\text{mol/l}$  was used. Patients with citrulline levels  $< 13 \text{ mmol/l}$  in the post operative period were kept on low volume enteral feed and maintained on TPN. Once the levels were above  $13 \text{ mmol/l}$ , enteral feeds were advanced to meet target rate and TPN independence was achieved. A similar pattern was followed with patients presenting with high output stomal effluent. These citrulline levels were then matched with histopathological diagnosis.

**Results** From October 2008, nine patients underwent a small bowel transplant at the Oxford transplant centre. Mean citrulline levels week one after transplantation were  $15 \text{ mmol/l}$  (range 12–17). Endoscopic biopsies in the first week showed signs of ischaemia reperfusion with significant oedema in the submucosa of the transplanted ileum. All these patients were maintained on TPN and had enteral feed (Peptisorb) at  $30 \text{ ml/h}$ . As mean citrulline levels increased patients progressed to full feed and TPN discontinued. Four patients presented with intestinal dysfunction after discharge from the hospital. These were all commenced on TPN if the citrulline level fell below  $13 \text{ mmol/l}$ . The first, had a citrulline of  $19 \text{ mmol/l}$  on presentation and. Biopsy demonstrated acute rejection. The second, presented with a high stoma output with a citrulline level of  $9 \text{ mmol/l}$ . Biopsy results revealed increase in mitotic figures as well as apoptosis and loss of tips of villi architecture. The third patient presented with a high stomal output and a citrulline of  $18 \text{ mmol/l}$ . Citrulline fell further to  $9 \text{ mmol/l}$ . The fourth patient presented with a high output and citrulline level of  $13 \text{ mmol/l}$ , dropping further to  $6 \text{ mmol/l}$ . His biopsy revealed dense mitotic activity in the face of increased apoptosis. He recovered in a span of 30 days with subsequent citrulline showing a rise. He was then weaned off TPN and commenced on diet. Mean time to graft dysfunction from transplantation was 240 days (range 46–450).

**Conclusion** Firstly serum citrulline is a good marker to direct nutritional therapy in the early post transplant period as well as during graft dysfunction.

**Competing interests** None declared.

#### REFERENCE

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