P98 PREDICTORS OF EARLY HEPATIC ARTERY THROMBOSIS AFTER PRIMARY LIVER TRANSPLANTATION: A COHORT MULTI-CENTRE STUDY

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Introduction Hepatic artery thrombosis (HAT) is one of the most catastrophic complications of liver transplantation. The risk factors for this complication have rarely been assessed in the setting of a large risk-adjusted analysis.
Method Using the United Kingdom and Ireland Liver Transplant Database, we sought to identify the incidence of and independent risk factors for early (=3 months) HAT among 6297 adult first single-organ liver transplant recipients during the period 1 March 1994–31 March 2006. Univariate and multivariable logistic regression models were fitted to examine the association between early HAT and a wide-range of recipient, donor and graft risk factors.
Results The incidence of early HAT in this cohort was 3.6%. Multivariable analysis identified the following independent risk factors for early HAT: recipient diagnosis of hepatocellular carcinoma (OR 1.64 95% CI 1.08 to 2.47), primary sclerosing cholangitis (OR 1.86 95% CI 1.24 to 2.81), recipient requirement for preoperative renal support (OR 1.81 95% CI 1.26 to 2.60), use of reduced vs whole graft (OR 2.53 95% CI 1.40 to 4.57), use of multiple vs single HA anastomosis (OR 1.55 95% CI 1.11 to 2.18), lower donor weight ($p<0.001$), combination of non-white donor and non-white recipient vs white donor and white recipient (OR 4.67 95%CI 1.41 to 15.47), combination of CMV+ donor and CMV- recipient vs CMV+ donor and CMV+ recipient (OR 1.70 95% CI 1.19 to 2.41), and combination of female donor and female recipient vs male donor and male recipient (OR 1.80 95% CI 1.21 to 2.66). Even after adjustment for the above risk factors, the risk of early HAT was significantly higher in four of the eight liver transplant centres in the UK and Ireland compared to the centre with the lowest incidence, the ORs ranging between 3.5 and 4.6 ($p<0.001$).
Conclusion Our findings suggest that early HAT is predominantly a technical complication that is independent of recipient, donor and graft characteristics. HAT risk-stratification based on the results of this analysis could help identify patients who may benefit from increased surveillance for this complication and/or institution of appropriate prophylactic antithrombotic therapy.

P99 RELATION OF DONOR RISK INDEX AND MODEL FOR END-STAGE LIVER DISEASE SCORE TO OUTCOME OF ELECTIVE LIVER TRANSPLANTATION; A SINGLE CENTRE EXPERIENCE

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Introduction Patients with advanced liver disease, reflected in high model for end-stage liver disease (MELD) scores have the lowest chances of survival without liver transplantation (LT) and yet, may derive greatest survival-benefit from LT. The use of extended criteria (EC) grafts in such patients has been advocated as a means of optimising the chances of successful transplantation.
Aim To determine the effects of graft quality (using Donor Risk Index, DRI) and MELD score at the time of LT on the duration of post-LT intensive care unit (ICU) and hospital length of stay (LOS) and survival.
Method Retrospective analysis of 898 adult patients who underwent elective LT (109 re-do LT) over the period 2000–2008. Pre-LT MELD scores were categorised as low (<15), intermediate (15–25), or High (>25). Graft quality was categorised as low (DRI >1.7) or High (DRI <1.7). Data are presented as median (IQR).
Results Median age was 53 years (44–60) and 64% were male. Median pre-LT MELD was 15 (11–19) and median DRI in the high and low quality groups were 1.5 (1.3–1.6) and 2.0 (1.9–2.1). Increasing MELD score was associated with greater ICU and Hospital LOS ($p<0.0001$, Kruskal–Wallis test). However, within each MELD category there was no significant difference in ICU or hospital LOS between recipients of grafts with DRI < or >1.7. See Abstract P99 table 1.

Abstract P99 Table 1

	DRI <1.7		DRI>1.7	
MELD	**ICU**	**Hospital**	**ICU**	**Hospital**
Low (<15)				
n	245		190	
	3 (2–4)	17 (13–29)	3 (2–4)	18 (13–29)
Intermediate (15–25)				
n	237		139	
	3 (2–5)	22 (14–40)	3 (2–5)	21 (14–41)
High (>25)				
n	64		22	
	7 (3–22)	33 (21–68)	5 (4–18)	29 (18–46)

On multivariate regression analysis MELD was an independent predictor of LOS with no significant effect of DRI identified. Survival at 1-year in the overall cohort was 90%; in MELD <15 92.6%, 15–25 87.4% and >25 82.7%. There were no significant differences in 1 year survival between recipients with DRI < or >1.7 in the group as a whole or in the MELD sub-categories.
Conclusion In this cohort, length of ICU and hospital stay related to pre-LT MELD score and not graft quality as evaluated by DRI. Hospital and ICU stay and consequently resource use was increased particularly in those patients with MELD of 25 and above, but not further prolonged by the use of ECD grafts in the range of DRI used in this cohort.

P100 INTRAHEPATIC AND SYSTEM CYTOKINE PROFILES IN ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE: POSSIBLE MECHANISM OF IMMUNEPARESIS

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Introduction Activation of systemic inflammatory responses in acetaminophen-induced acute liver failure (AALF) is associated with elevated levels of both pro- and anti-inflammatory cytokines. Functional monocyte deactivation has been described and this is thought to contribute to increased susceptibility to sepsis and a higher mortality rate. Anti-inflammatory cytokines play a major part in the resolution of inflammatory responses and promote tissue repair processes but increase the risk of systemic infections. We hypothesise that the levels of anti-inflammatory cytokines mirror the severity of hepatic necrosis and reflect attempts to resolve inflammation during AALF. It is the excessive production of these mediators that "spill-over" and increase the risk of systemic sepsis. We sought to delineate hepatic and systemic cytokine responses in experimental and human AALF, and, determine whether there is production of anti-inflammatory cytokines in the liver which "spill-over" into the systemic circulatory compartment.
Aim We sought to delineate hepatic and systemic inflammatory responses in experimental and human AALF, and, determine

whether there is a "spill-over" of hepatic anti-inflammatory mediators into the systemic, circulatory, compartment.

Method Median levels (pg/ml) of hepatic IL-1ß, IL-4,-6,-10,-12,-17, IFN-Y, MCP-1, TNF-α, TGF-ß1 were measured using proteome arrays in 10 human AALF explants and 8 normal control liver tissue samples.

Hepatic and serum levels of IL-1ß, IL-4,-6,-10,-12,-17, MCP-1, TNF-α, TGF-ß1 were measured in 200mg/kg i.p. APAP treated male C3H/HeH mice (n=5 severe necrosis, n=5 moderate necrosis) and 5 control mice.

Regional levels (portal vein (PV)), hepatic vein (HV), arterial (art)) of TNF-α, IL-10 were determined using ELISA in 3 AALF patients at time of liver transplantation.

Results In human AALF, hepatic levels of IL-6 (115 vs 75; p=0.02), IL-10 (1.8 vs 0.6; p=0.03), TGF-ß1 (3009 vs 1323; p<0.0001) were elevated in AALF compared to controls while IL-1ß, IL-12, IL-17, IFN-Y and TNF-α were unchanged. Higher hepatic levels of IL-4 (37 vs 25; p<0.01), IL-10 (90 vs 66; p<0.01), IL-12 (11 vs 7.8; p<0.01) and TGF-ß1 (2521 vs 540; p<0.01) were detected in mice with severe hepatic necrosis compared to those with moderate necrosis and normal controls. Similar to human AALF, serum pro- (IL-6 (146 vs 13; p<0.01), IL-1ß (104 vs 62 (p=0.07)) and anti-inflammatory cytokines (IL-4 (3 vs 0.8; p<0.01), IL-10 (47 vs 1; p<0.01) were elevated compared to normal controls during murine AALF.

Conclusion We demonstrate a hepatic inflammatory microenvironment favouring resolution of inflammation/tissue repair processes. In vivo hepatic production and systemic "spill-over" of the immunosupressive cytokines is observed and may account for functional monocyte deactivation and the marked predisposition to sepsis in AALF. The marked similarities in anti-inflammatory mediator profiles between human and murine models of AALF provide a rationale on which to base the studies examining evolution of disease and development of immunomodulatory strategies to ameliorate acute liver injury and promote tissue repair.

P101 FK STIMULATION OF HEPATITIS C VIRUS-SPECIFIC AND NONSPECIFIC PERIPHERAL BLOOD MONONUCLEAR CELL OF PATIENTS ON WAITING LIST TO EVALUATE AND TAILOR IMMUNOSUPPRESION BEFORE ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction We previously found that FK did not induce a severe reduction of immune response compared to other clacineurin inhibitor (ILTS 2009 oral presentation).

Aim We aimed to evaluate the in vitro effect of tacrolimus on hepatitis C virus (HCV)-specific immune response by ELISpot to establish early the possible effect of immunosuppression and so tailoring immunosuppressive schedule before OLTx to minimize or delay HCV recurrence.

Method Twenty-five HCV+ve patients (20 male and 5 female) on waiting list were enrolled. Blood samples were taken and at least on $2-2.5\times10^5$ cells per well ELISpot was performed to evaluate IFN-specific response after coculturing with 1 ng/ml or 5 ng/ml of FK for 24 h. CMV and a specific stimulation with PMI-Ionomicin were used as control on HCV patients. Ten healthy donors were used as control.

Results After 24 h of FK stimulation, PMA-Ion IFN-response was reduced in all patients (p<0.05) compared to basal values both with 1 ng/ml that 5 ng/ml while CMV- specific showed reduction only when cocultured with 5 ng/ml. Among patients on waiting list, we had that 8 out 25 had a major reduction of HCV and CMV specific response (p <0.05) while 17 out 25 had no statistical significant changes in their IFN response.

Abstract P101 Table 1 Results

Results				
Patients parameters	**HCV**	**CMV**	**PMI-Ion**	**HD-PMA-Ion**
Age (y, mean SD)	55, 3	55, 3	55, 3	35, 6
Male	20/25	20/25	20/25	7/10
Female	5/25	5/25	5/25	3/10
HCV-RNA (IU/mL mean SD)	310 232×10^3	n.d.	n.d.	n.d.
Genotype				
1a/1b	23/25			
Non-1	2/25			
Immunological parameters				
IFN-ELISpot (SFC) in	17/25	25/25	25/25	10/10
T0 without stimulation	65 25	192 103	225 100*	272 113*
FK stimulation 1 ng/ml	58 19	176 98	176 88*	200 126*
FK stimulation 5 ng/ml	52 50	128 42*	150 45*	133 23*
IFN-ELISpot (SFC) in	8/25 pts			
T0 without stimulation	61 15*			
FK stimulation 1 ng/ml	41 7*			
FK stimulation 5 ng/ml	34 5*			

*p<0.05; p>0.05.

Conclusion Based on these results and our previous data, ELISpot assay before OLTx may useful to establish the impact of immunosuppressive schedule. In those having a major reduction of HCV specific immune response after CNI stimulation (FK) a different drug should be used to minimize or delay the possible HCV recurrence. Further studies are required to establish in vitro effects.

P102 THE UTILITY OF RADIOISOTOPE BONE SCANS IN THE LIVER TRANSPLANT ASSESSMENT FOR HEPATOCELLULAR CARCINOMA

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Introduction The incidence of skeletal metastases from hepatocellular carcinoma (HCC) is estimated to be 2–16%. It is well established that radioisotope bone scans can detect cancer earlier than cross sectional imaging. The role of bone scans in pre-transplant assessment has been discussed in the literature but its place in the assessment algorithm is not clearly established.

Aim The aim of this study is to determine the utility of radioisotope bone scans in patients with a diagnosis of HCC undergoing transplant pre-assessment.

Method Radioisotope bone scan results were reviewed for all patients undergoing liver transplant assessment for HCC at our unit from 1989 to 2009. Patients were initially selected for transplant assessment based on favourable HCC staging on cross sectional imaging. Patients undergoing bone scan had the result reviewed retrospectively as normal or abnormal. All abnormal scans we then reassessed against all available imaging and classified as showing benign or malignant changes. Patient outcomes were considered in relation to bone scan results.

Results During this period 216 patients with a primary or secondary diagnosis of HCC were assessed for liver transplantation. Two hundred and three patients were listed for transplant and 148 were eventually transplanted. The results of their bone scans are as below (Abstract P102 Table 1).