particular they exhibit significantly lower cardiac muscle phosphocreatine-to-ATP ratio (measure of cardiac bioenergetic integrity) compared with control subjects. In other disease settings, such as cardiac failure, changes of this type have been associated with impaired cardiac function and increased risk of cardiac death.

Aim The objective of the present study was to examine whether these changes are reflected in systemic measurements of cardiopulmonary reserve determined by a non-invasive cardiopulmonary exercise test (CPET).

Method Consecutive PBC patients being assessed for liver transplantation underwent CPET. The test was conducted in a consistent environment and reviewed by a trained physician to determine objective measures of cardiorespiratory reserve. A control group of consecutive patients with primary sclerosing cholangitis (PSC), also being assessed for liver transplantation was also tested. We compared the results of CPET of all patients with a diagnosis of PBC with those with PSC. Patient demographics and MELD scores at assessment were also collected. A non-paired t test was used to determine group differences.

Results In total, 38 patients had a diagnosis of either PBC or PSC. Three patients (2 PBC and 1 PSC) did not exercise sufficiently to gather meaningful results and were excluded from the analysis. The PSC patients assessed for transplantation had significantly worse liver disease as assessed by the MELD score. However, all measures of cardiorespiratory reserve derived from CPX testing were significantly lower in the PBC group. There was no statistical difference between the two groups with respect to age, thus excluding age as the underlying factor in decreasing their fitness.

Conclusion In this cohort, patients with PBC, despite having lower MELD scores and equivalent age at transplantation assessment, had significantly impaired cardiorespiratory reserve, when compared to patients with PSC. The results add to the evidence that there is a specific PBC-related bioenergetic effect due to the immunology of PBC that is absent in PSC. This finding could have significant relevance on both future studies and treatment regimes to improve cardiovascular fitness.

Abstract P75 Table 1

	PBC	PSC	p Value
Number	24	11	
Age yrs mean (SD)	56.1 (8.9)	56.1 (12.9)	0.999
MELD mean (SD)	13.0 (6.60)	18.8 (4.15)	0.004
AT mean (SD)	10.7 (2.8)	13.3 (3.0)	0.017
Peak VO_2 mean (SD)	13.6 (3.4)	17.9 (4.7)	0.004
OEUS/kg mean (SD)	18.7 (4.5)	22.8 (4.5)	0.018
VO2/HR mean (SD)	7.6 (2.7)	9.7 (1.5)	0.022

P76 META-ANALYSIS OF PUBLISHED EVIDENCE SUPPORTS USE OF KING'S COLLEGE CRITERIA OVER MODEL FOR END STAGE LIVER DISEASE IN OUTCOME PREDICTION IN ACUTE LIVER FAILURE

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[1 2]M J W McPhail, [2]N Senvar, [3]J A Wendon, [3]W Bernal. *[1]Institute of Liver Studies, King's College Hospital, Denmark Hill, London, UK; [2]Liver & Anti-viral Centre, St Mary's Hospital, South Wharf Street, Imperial College London, UK; [3]Institute of Liver Studies, King's College Hospital, Denmark Hill, London, UK*

Introduction Outcome prediction is a cornerstone of the management of Acute Liver Failure (ALF) where Emergency Liver Transplantation (ELT) is indicated for predicted death. The King's College Criteria (KCC) for paracetamol overdose (POD) and non-POD ALF are the benchmark prognostic scores but recent reports have suggested the Modified End Stage Liver Disease (MELD) score could replace KCC.

Aim To meta-analyse and compare diagnostic performance for outcome prediction of KCC and MELD in ALF.

Method A systematic database search was performed and retrieved articles graded according to a pre-agreed proforma of methodological quality. Collated data were meta-analysed for summary sensitivity, specificity, Diagnostic OR, DOR meta-regression and ROC curve analysis. Pre-specified subgroup analysis was performed on the basis of methodological quality, the severity of hepatic encephalopathy (HE) of reported patients, and exclusion of those who underwent ELT.

Results 32 studies published between 1992 and 2009 with data on 3008 patients (2464 from KCC and 544 MELD) were available for production of 2×2 tables. Taking data where transplanted patients were excluded summary sensitivity for KCC was 63 (95% CI 60 to 66) %, specificity 91 (90 to 93) % and DOR 18 (8.9 to 37). Summary sensitivity for MELD was 82 (95% CI 77 to 86) %, specificity 65 (59to71) % and DOR 11 (5.3 to 23; RDOR 0.75 (0.18 to 3.13))). Despite different MELD cut-offs between studies no statistical evidence of threshold was found and the AUROC for MELD was 0.83 (SE 0.05) and 0.88 (0.03) for KCC. A lack of patient level data prevented statistical comparison between these areas. The DOR for KCC in POD ALF was 27 (9–83) and 13 (5–31) in non-POD ALF. Heterogeneity (using the I^2 statistic) in the DOR for MELD was 49% and 80% for KCC although this was not dependent on aetiology. The lower sensitivity for KCC could be overcome by dynamic application of the criteria.

Conclusion MELD is not superior to KCC on the basis of quantitative analysis of published evidence. While both scores may give complementary sensitivity and specificity (particularly in cases where bilirubin may have more prognostic value) the DOR and AUROC superiority of KCC suggest they should remain the preferred method of outcome prediction and listing decision for ELT in ALF, particularly in cases of POD-ALF.

P77 A PHARMACIST DELIVERED STRATIFIED CONVERSION PROTOCOL FROM HEPATITIS B IMMUNOGLOBULIN (HBIG) TO TENOFOVIR OR ENTECAVIR IS EFFICACIOUS, SAFE AND COST-EFFECTIVE FOR PREVENTION OF RECURRENCE OF HEPATITIS B VIRUS (HBV) IN LIVER TRANSPLANT (LT) RECIPIENTS

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[1]S Knighton, [2]K Agarwal, [2]M Heneghan, [2]J O'Grady, [2]M Bruce, [2]I Carey, [2]N Heaton, [2]A Suddle. *[1]Pharmacy Department and Institute of Liver Studies and Transplantation, King's College Hospital NHS Foundation Trust, London, UK; [2]Institute of Liver Studies and Transplantation, King's College London School of Medicine at King's College Hospital NHS Foundation Trust, London, UK*

Introduction The use of HBIG based prophylactic regimensto prevent recurrence of HBV in patients who have undergone LT is highly efficacious and well documented. However the long-term administration of HBIG can be time consuming, costly and inconvenient for the patient. With the advent of more potent oral anti-HBV agents the optimal long-term prophylactic strategy remains debatable.

Aim A prospective single centre experience of switching from an intra-muscular (IM) HBIG based regimen to monotherapy tenofovir (TDF) or entecavir (ETV) to prevent HBV recurrence post LT.

Method Patients receiving HBIG based prophylactic regimens were referred to a Pharmacist led clinic. Those with no serological evidence of HBV recurrence were considered for switch to monotherapy TDF or ETV. Decisions were based on clinical assessment and renal function, following an agreed stratified protocol. Data reported is an interim analysis 6 months post-switch. All results are presented as median.

Results Patients: To date 29 patients have been switched. The median time since switch is 9 months. 25 patients are >6 months post switch and included in the analysis. The median age was 61 (range: 28–81) years, 84% male, 60% Caucasian, 28% Black African and 12% Asian. At LT 6 were acute HBV with Liver failure, 7 had HCC and 4 had delta co-infection. At LT 22 had detectable HBV DNA, 11 were on lamivudine (LAM) and 1 was on LAM and adefovir (ADV). 52% patients had archived samples suitable for drug resistance testing. None had evidence of any drug resistant mutations.

Results: Since LT all had received HBIG IM with HBsAb levels of 170 (range 101–454) mIU/ml. 80% were receiving concurrent LAM, 4% LAM and ADV and 16% no oral anti-HBV agent. The median time from LT to switch was 10 (range 2.6–20.3) years. At switch HBsAg and HBV DNA was undetectable in all subjects. 92% were on calcineurin inhibitor based immunosuppressive regimens. Serum creatinine was 104 (range 62–170) μmol/l, estimated glomerular filtration rate (eGFR) was 65 ml/min, 24 h urine creatinine clearance was 76 (range 41–150) ml/min and total protein excretion was 81 (range 31–441) mg/day. Serum ALT was 26 IU/l, phosphate was 0.98 mmol/l and vitamin D was 14 μg/l. 12 had hypertension and/or diabetes. 16 patients were switched to TDF, 9 patients with eGFR <60 ml/min or renal risk factors were switched to ETV. Six months after switch all patients remained HBsAg and HBV DNA undetectable and there was no difference in serum creatinine [103 (TDF 93, ETV 115) μmol/l], eGFR [65 (TDF 70, ETV 57) ml/min], ALT (23 IU/l), phosphate [1.03 (TDF 1.00, ETV 1.05) mmol/l] and vitamin D [17 (TDF 16.3, ETV 18.5) μg/l]. No therapy withdrawal/change was required due to adverse effects. The approximate drug cost saving made per patient/year from switching from HBIG to TDF or ETV is £11 000 and £10 000 respectively.

Conclusion A stratified conversion protocol, based on the assessment of virological parameters and renal co-morbidities, ensures patients can safely and effectively be switched from HBIG to TDF or ETV to prevent HBV recurrence post LT. HBsAg and HBV DNA remains undetectable and no deterioration in renal function has been observed to date. Significant drug cost savings can be achieved utilising this protocol.

P78 LONG-TERM ANTIBIOTIC PRESCRIPTION IN PATIENTS RELISTED FOR LATE HEPATIC ARTERY THROMBOSIS IS ASSOCIATED WITH GREATER WAITING LIST MORTALITY INDEPENDENT OF MELD

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M Smith, J Leithead, L Materacki, V Sagar, B Gunson, S Bramhall, D Mutimer, T Shah. *Liver Unit, Queen Elizabeth Hospital, Birmingham*

Introduction Optimal prioritisation and medical management of patients with late hepatic artery thrombosis (HAT) awaiting liver transplantation remains unclear.

Aim To examine the association of complications of late HAT and their interventions with liver transplant waiting list mortality.

Method Single centre study of 49 patients listed for late HAT 01/1995–06/2010. Late HAT was defined as occurrence >4 weeks following liver transplantation. Cox regression was adjusted for listing MELD score at all times. Despite increasing waiting time statistical analyses did not demonstrate any influence of listing time period.

Results Mean listing MELD score was 16 (SD 7). 29% of patients demonstrated biliary stricture/s, 20% cholangitis and 63% biloma/abscess/s. The estimated 3- and 12-month transplant-free survival following listing was 85% and 53%, respectively. 36 patients were regrafted, with a median time from listing to transplantation of 45 (IQR 13–167) days.

No relationship was demonstrated between the presence of biliary stricture/s (p=0.984), cholangitis (p=0.770) or biloma/abscess/s (p=0.143), and wait-list mortality. Instead, an increasing number of biloma/abscess drain insertions (p=0.038) and long-term (LT) prescription of antibiotics (p=0.029) were linked with an increased risk of death. Multi-drug resistant bacteria (MDRB) were cultured in bile/blood more frequently in those receiving LT antibiotics (44% vs 8%, p=0.004), and MDRB positivity was also a risk factor for waiting list mortality (p=0.033). On multivariate analysis the only predictor of death was LT antibiotics (MELD, HR 1.23; 95% CI 1.04 to 1.44, p=0.013: antibiotics, HR 24.20; 95% CI 1.28 to 455.88, p=0.033).

Following regraft, LT antibiotics (p=0.025) and MDRB positivity while listed (p=0.002) remained predictors of patient mortality independent of the preoperative MELD score. The estimated 3- and 12-month post transplant survival of patients with MDRB positivity was 63% and 25%, respectively, and for those without 89% and 86% (log-rank p=0.001).

Conclusion Patients listed for late HAT receiving LT antibiotics are a high risk group who require greater priority for liver transplantation. Our results raise the possibility that by increasing bacterial resistance LT antibiotics may have a detrimental effect on patient survival.

P79 PLASMA SUCCINYLACETONE IS RAISED AFTER LIVER TRANSPLANTATION FOR TYROSINAEMIA TYPE 1 AND IS ASSOCIATED WITH REDUCED PORPHOBILINOGEN SYNTHASE ACTIVITY SUGGESTING IT IS FUNCTIONAL

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[1]D C Bartlett, [2]M A Preece, [3]E Holme, [4]C Lloyd, [1]P N Newsome, [4]P J McKiernan. *[1]Centre for Liver Research, University of Birmingham and Liver Unit, Queen Elizabeth Hospital Birmingham, UK; [2]IMD Laboratory, Birmingham Children's Hospital, Birmingham, UK; [3]Department of Clinical Chemistry, Sahlgrenska University Hospital, Gothenburg, Sweden; [4]Liver Unit, Birmingham Children's Hospital, Birmingham, UK*

Introduction Tyrosinaemia type 1 (TT1) is a rare disorder of tyrosine metabolism leading to accumulation of toxic metabolites such as succinylacetone (SA) and a high risk of hepatocellular carcinoma. Children with TT1 traditionally required liver transplantation (OLT) and while the need for this has reduced since the introduction of nitisinone some still go on to require OLT. Circulating SA inhibits the enzyme porphobilinogen (PBG) synthase and its activity can be used as a marker of functional circulating SA. Elevated urinary SA post OLT thought to be due to local production has been reported.

Aim This study describes a novel finding of elevated plasma SA following OLT for TT1.

Method A retrospective analysis was performed of patients treated for TT1 at our institution from 1989 to 2010.

Results In patients who received nitisinone prior to OLT mean urinary SA was elevated at presentation (159.6 mmol/mol creatinine, ref. range <1) as was plasma SA (17.58 mol/l, ref. range <0.01) but both became undetectable on nitisinone prior to OLT (p<0.05). This was associated with increased mean PBG synthase activity from 0.032 to 0.99 nkat/g Hb (ref. range 0.58 1.25). In patients who did not receive nitisinone, mean urinary SA was 274.6 mmol/mol creatinine immediately prior to transplant. Plasma SA levels/PBG synthase activity prior to OLT were not available in this group. Following OLT in patients treated with nitisinone, mean urinary SA levels quickly rose and remained elevated for the duration of follow-up. Plasma SA levels also rose with a progressive decrease in mean PBG synthase activity to low-normal levels. In patients who had not received nitisinone, mean urinary SA fell quickly by 1 year post OLT but remained above normal at levels similar to those seen in the nitisinone treated group. No data were available for plasma SA/PBG synthase activity in this group until