P94 PREVALENCE AND CLINICAL SIGNIFICANCE OF HEPARIN INDUCED THROMBOCYTOPAENIA IN PATIENTS TRANSPLANTED FOR BUDD CHIARI SYNDROME

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Introduction Budd Chiari Syndrome (BCS) is associated with an underlying pro-coagulant haematological disorder in up to 87% of cases. Following liver transplantation (LT), anticoagulation with heparin is commonplace in order to prevent thrombotic complications. Heparin induced thrombocytopaenia (HIT) is a rare but life threatening complication of heparin therapy, where the thrombotic risk is 30 times that of control populations. HIT associated thrombosis has a reported incidence of between 0.5 and 3% in patients on un-fractionated heparin. We reviewed all our patients with BCS who underwent LT to assess the incidence and clinical significance of HIT.

Results In total, 36 patients underwent LT for BCS between 1995 and 2008. An underlying pro-coagulant disorder was identified in 22 patients (myeloproliferative disorder (MPD) n=17, Protein C Deficiency n=2, Behcet's n=2 and lupus anti-coagulant n=1). One third of patients were thrombocytopenic (platelets <150 cells/μl) prior to LT. All patients had received un-fractionated heparin prior to and following LT. Thrombocytopaenia occurred in 85% of patients within the first 10 post operative days (median 49 cells/μl, range 7–292 cells/μl). A diagnosis of HIT was made when patients had a platelet count of <150 cells/μl and circulating PF4-heparin antibodies were identified. The overall incidence of HIT was 22% (8/36 patients), however in patients with a MPD the incidence was 41% (7/17). Furthermore a MPD was present in 7/8 (88%) patients who developed HIT vs 10/28 (36%) patients who did not develop HIT (p=0.016). An acute post operative thrombotic complication occurred in 50% (4/8) of patients who developed HIT compared to 4% (1/28) of patients that didn't (p=0.005). Bleeding complications occurred in 38% (3/8) of patients that developed HIT compared to 14% (4/28) who didn't (p=0.16). In hospital mortality was 38% in those patients that developed HIT compared to 7% in those who did not develop HIT (p=0.06). The fall in platelet count was not statistically different between those patients who did and did not develop HIT. In a cohort of patients (n=30) transplanted for hepatic artery thrombosis, who had also received un-fractionated heparin pre and post LT, HIT occurred in 1/30 (3%).

Conclusion We have demonstrated that HIT is a common complication of patients treated with un-fractionated heparin following LT for BCS. Moreover, the presence of an underlying MPD is a strong predisposing factor for its development. In patients that develop HIT the thrombosis rate, bleeding complication rate and pre-hospital discharge mortality are all increased. The diagnosis requires a high index of suspicion due to the frequency of thrombocytopaenia following LT. Due to the exceptionally high incidence of HIT in patients with MPD, these patients may benefit from standardised treatment with lepirudin following LT.

P95 OUTCOMES OF PREGNANCY FOLLOWING LIVER TRANSPLANTATION

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Introduction Pregnancy in liver transplant (LT) patients has been reported to have largely favourable outcomes for the mother, foetus and allograft. Concerns remain with regards to graft rejection, the type and optimal level of immunosuppression and the ideal timing for conception following LT. We report a review of all pregnancies in LT recipients at our centre from 1988 to 2010 concentrating on maternal, foetal and graft outcomes.

Results 115 pregnancies occurred in 84 LT recipients. The median age at conception was 26 years and the median interval between LT and conception was 53 months (range 1–239 months). There were 82 (71%) live births, 13 terminations, 18 spontaneous abortions, 1 molar pregnancy and 1 intrauterine death. The mean gestation was 38 weeks (range 24–42 weeks). Regarding foetal outcomes, no congenital abnormalities occurred. A very low birth weight (<1500 g) occurred in 6% (7 babies), and all required neonatal intensive care support following delivery. On follow-up one has delayed developmental milestones. Prematurity (gestation <37 weeks) occurred in 34% 28/82. Neither choice of maternal immunosuppression nor an episode of rejection during pregnancy impacted on the birth weight or gestational period. Maternal complications encountered during pregnancy included renal failure (n=9, 8%), hypertension (n=27, 23%) and pre eclampsia (n=16, 14%). 18 (16%) cases of graft rejection occurred in association with pregnancy. Sixteen were consistent with acute cellular rejection on biopsy; with 5/16 occurring post partum. Overall 15 responded to immunosuppression augmentation and three required methyl prednisolone. The risk of graft rejection was significantly higher in patients conceiving within 12 months of LT (p<0.006). No maternal deaths occurred as a direct result of pregnancy, however two mothers required ITU support and 1 developed decompensated liver disease post partum. Seventy eight patients were on tacrolimus, 35 on cyclosporine, 1 on mycophenolate and 1 on sirolimus. Patients on cyclosporine had a higher incidence of acute rejection (p=0.04) and were more likely to be on a second immunosuppressive agent (p<0.001) or prednisolone (p<0.001) when compared to those patients on tacrolimus. Immunosuppression choice had no significant effect on pregnancy induced hypertension, pre eclampsia or gestational diabetes. The conception on mycophenolate was terminated, however the patient on sirolimus delivered at 37 weeks.

Conclusion Overall pregnancy following LT has a favourable outcome, with the majority of wanted conceptions resulting in a live birth. Immunosupression appears safe with no congenital abnormalities in this cohort. Risks however do remain with regards to acute cellular rejection and very low foetal birth weights. Patients should be educated with regards to the above information so an informed decision regarding pregnancy can be made.

P96 LONGITUDINAL CHANGES IN RENAL FUNCTION IN LIVER TRANSPLANT RECIPIENTS: IMPACT OF ACUTE KIDNEY INJURY AND THE ASSESSMENT OF THE DECLINE IN ESTIMATED GLOMERULAR FILTRATION RATE OVER 5 YEARS POST LIVER TRANSPLANTATION

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Introduction Orthotopic liver transplantation (OLT) can valuably increase long term survival in patients with cirrhosis. After the immediate transplant period cardiovascular morbidity and mortality become increasingly important and chronic kidney disease (CKD) stage 3 or more has been described as an independent risk factor for cardiovascular adverse events. The effect of acute kidney injury (AKI) on long term mortality and the pattern of renal morbidity post OLT have not been well described.

Method 211 OLT recipients (median age 53 (20–70) years: 140 male; 71 female) for chronic liver disease were studied to assess longitudinal long term changes in renal function. The MDRD (version 4) equation was used to estimate glomerular filtration rate (eGFR) pre-OLT and at 1 week, 1 month, 6 months 1 year, 2 years and 5 years post-OLT. Acute Kidney Injury was defined according to Acute Kidney Injury Network criteria and CKD staging according to Kidney Dialysis Outcomes Quality Initiative criteria.

Results Median follow-up was 2023 (3–3188) days and median survival was not reached in this study (76% 5 year survival). Median eGFR at time of transplant was 67 (29–149) ml/min/1.73 m^2 falling to 59 (24–165) ml/min/1.73 m^2 at 6 months post-OLT ($p<0.001$, Wilcoxon signed test) and 57 (11–203) ml/min/1.73 m^2 at 5 years post-OLT ($p<0.001$; Friedman test for eGFR over study period $p<0.001$). A reduction in eGFR was noted at 6 months post-OLT in patients with post-OLT AKI ($p=0.010$, Kruskal–Wallis test) but this difference was not detectable at 5 years (p-0.557). 40% of patients had CKD 3 or more pre-OLT with 60% with CKD 3 at 5 years ($p<0.001$, ?2 test). AKI stage >1 during the first week post OLT did not influence long term survival (HR 1.43 (95% CI 0.65 to 3.1, $p=0.315$, Kaplan–Meier method) neither did the use of renal replacement therapy post OLT (HR 1.56 (95% CI 0.60 to 4.1, $p=0.268$, KM method).

Conclusion In this cohort a decline in eGFR of 10 ml/min/1.73 m^2 was noted over the 5 year follow-up; twice the rate of decline expected in the general population. The higher proportion of patients at CKD stage 3 or more at 5 years compared to pre-OLT suggest greater awareness of this potentially important risk factor for cardiovascular disease is required. AKI post-OLT was not associated with a higher risk of long term reduction in eGFR beyond 6 months post-OLT; nor did the use of RRT post-OLT impact on 5-year mortality.

P97 POST-LIVER REPERFUSION HEPATIC VEIN PORTAL GRADIENT PRESSURE MEASUREMENT AND THE RISK OF GRAFT DYSFUNCTION IN WHOLE LIVER TRANSPLANTATION

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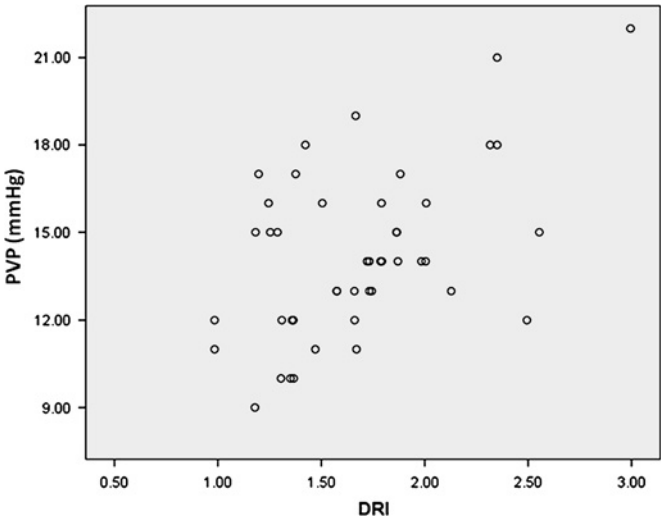
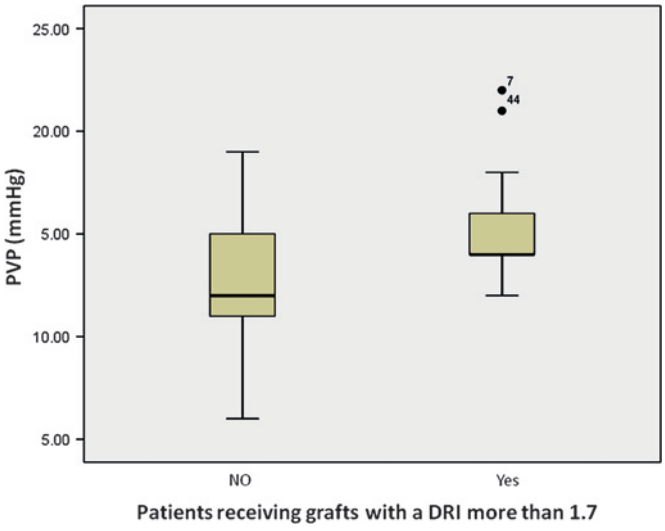
Introduction "Small for size liver syndrome" is relatively uncommon after whole liver transplantation. Portal hyperperfusion is thought to damage the hepatic microvasculature, and drive Small for size liver syndrome. Post-perfusion portal venous pressure (PVP) may be an indirect reflection of sinusoidal injury. Donor Risk Index (DRI) can be utilised to assess the quality of the graft, with those having a DRI>1.7 considered as marginal[1]. This study looked at the association of portal pressure and graft quality in a whole liver transplant setting.

Method 50 adult patients who underwent liver transplantation underwent portal venous pressure measurements by direct pressure transduction during surgery. Central venous pressure was recorded at the same time points to be used to derive the Hepatic Venous Portal Gradient (HVPG) (HVPG=PVP-CVP). DRI was calculated for all the grafts used. The degree of fatty infiltration (%) was assessed on post-perfusion biopsies. Graft function was monitored post-operatively by recording INR (peak and days 1, 2, 3, 5 and 7), lactate (peak level and day 1 and 2) serum AST (peak and days 1, 2, 3 and 7) and serum bilirubin (days 1, 5 and 7). The presence of ascites, jaundice and coagulopathy were documented. Ascitic drain loss (ml/day) was recorded up to the time of drain removal.

Results A statistically significant correlation was found between PVP and DRI ($p<0.05$) (Abstract P97 Figure 1).



Abstract P97 Figure 1 Scatter plot graph showing a statistically significant correlation PVP with DRI. (p=0.022)



Abstract P97 Figure 2 Box plot graph showing the difference of PVP in liver grafts with a DRI >1.7 and those with DRI <1.7. (p=0.069)

This was supported by higher mean and median values of PVP in the group receiving grafts with a DRI>1.7 n=22) (Abstract P97 Figure 2).

Patients in this group had a mean PVP of 15 (±2.976) mm Hg and a median of 14 mm Hg (range: 8–22), in contrast to those receiving grafts of DRI<1.7 (n=28) who had a PVP mean of 13.89 (±5.513) mm Hg and a median of 12.5 mm Hg (range: 6–34). No statistically significant correlation could be found between PVP and the degree of fatty infiltration. Post-perfusion HVPG had a significant correlation ($p<0.1$) with increased ascitic drainage on day 7.

Conclusion The HVPG should be evaluated as a tool for assessment of portal pressure post-reperfusion, particularly in patients transplanted with a high DRI, to predict morbidity post-transplant.

REFERENCE

1. **Maluf DG,** Edwards EB, Kauffman HM. Utilization of extended donor criteria liver allograft: is the elevated risk of failure independent of the model for end-stage liver disease score of the recipient? *Transplantation* 2006;**82**:1653–7.